Management of Bleeding in Patients on Oral Anticoagulation

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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. ■, NO. ■, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
https://doi.org/10.1016/j.jacc.2017.09.1085

EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Definitions

- OAC = DOAC + VKA
- OAC: Oral Anticoagulant
- DOAC: Direct oral anticoagulant
- VKA: Vitamin K antagonist
- Reversal agents: Prothrombin complex concentrates (PCCs), Plasma (PFC), vitamin K, specific reversal agents for DOACs (e.g idarucizumab for dabigatran)

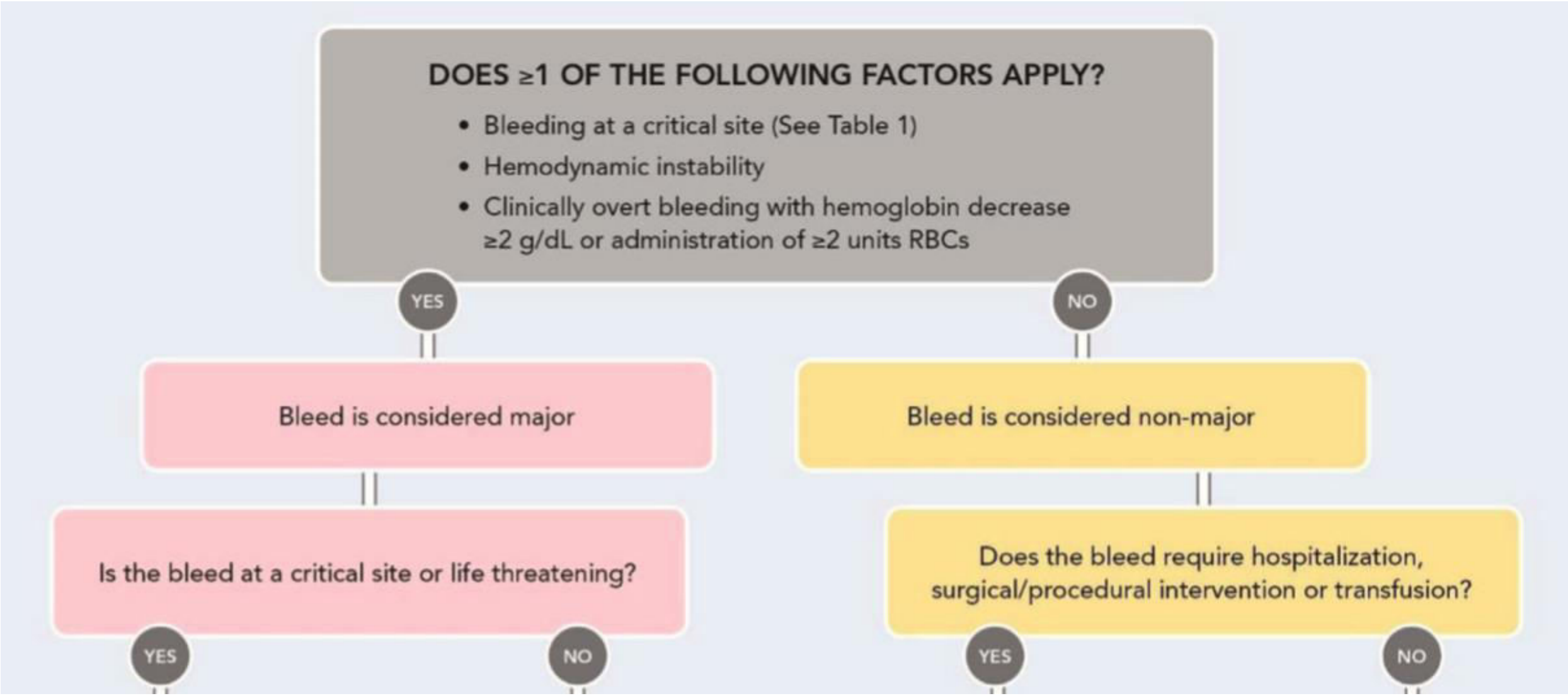
Definition of Bleed Severity

- **If ≥ 1 of the following factors → major bleeding**
  - Bleeding in a Critical site: intracranial hemorrhage and other CNS bleeds, thoracic, intra-abdominal, retroperitoneal, intra-articular, and intramuscular bleeds (cause severe disability , require surgical procedures)
  - Hemodynamic instability: BP < 90 mmHg, ↓BP > 40 mmHg, orthostatic BP changes, mean arterial pressure < 65 mmHg (invasive BP), ↓ organ perfusion (urine output < 0.5 mL/kg/h)
  - Hemoglobin drop ≥ 2 g/dL or administration of ≥ 2U of packed RBCs

Pathway summary

- Initially assess and identify severity of bleed:
  - Time of onset
  - Location
  - Severity
  - Ongoing
- Manage and control bleed
- Determine whether and when to restart anticoagulation

ASSESSING BLEED SEVERITY AND MANAGING MAJOR AND NONMAJOR BLEEDS



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Is the bleed at a critical site or life threatening?

YES

- Stop OAC
- If patient is on a VKA, give 5-10 mg IV VitK
- Provide local therapy/ manual compression
- Provide supportive care
- If applicable, stop antiplatelet agent(s)
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Consider surgical/ procedural management of bleeding site

NO

- Stop OAC
- If patient is on a VKA, give 5-10 mg IV VitK
- Provide local therapy/ manual compression
- Provide supportive care
- If applicable, stop antiplatelet agent(s)
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Consider surgical/ procedural management of bleeding site

Does the bleed require hospitalization, surgical/procedural intervention or transfusion?

YES

- Stop OAC
- If patient is on a VKA, consider 2-5 mg PO/IV VitK
- If patient not on VKA, do not administer reversal agent
- Provide local therapy/ manual compression
- Provide supportive care
- If applicable, stop antiplatelet agent(s)
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Consider surgical/ procedural management of bleeding site

NO

- Consider continuing OAC (provided there is an appropriate indication)
- Provide local therapy/ manual compression
- If patient is on concomitant antiplatelet therapy, assess risks and benefits of stopping
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Determine if dosing of OAC is appropriate

give 5-10 mg IV VitK

- Provide local therapy/ manual compression
- Provide supportive care
- If applicable, stop antiplatelet agent(s)
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Consider surgical/ procedural management of bleeding site

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consider 2-5 mg PO/IV VitK

- If patient not on VKA, do not administer reversal agent
- Provide local therapy/ manual compression
- Provide supportive care
- If applicable, stop antiplatelet agent(s)
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Consider surgical/ procedural management of bleeding site

appropriate indication)

- Provide local therapy/ manual compression
- If patient is on concomitant antiplatelet therapy, assess risks and benefits of stopping
- Assess for and manage comorbidities that could contribute to bleeding (e.g., thrombocytopenia, uremia, liver disease)
- Determine if dosing of OAC is appropriate

Suggest administering reversal agent* (See Figure 3)

NO

Did the above measures control the bleed?

YES

Once patient is stable, consider

TABLE 1 Critical Site Bleeds

Type of Bleed	Initial Signs and Symptoms	Potential Consequences of Bleed
Intracranial hemorrhage: Includes intraparenchymal, subdural, epidural, and subarachnoid hemorrhages	**Unusually intense headache, emesis** **Neurological signs:** e.g., reduced LOC, vision changes, numbness, weakness, aphasia, ataxia, vertigo, seizures	Stupor or coma Permanent neurological deficit Death
Other central nervous system hemorrhage: Includes Intraocular, intra- or extra-axial spinal hemorrhages	**Intraocular:** monocular eye pain, vision changes, blindness **Spinal:** back pain, bilateral extremity weakness or numbness, bowel or bladder dysfunction, respiratory failure	**Intraocular:** permanent vision loss **Spinal:** permanent disability, paraplegia, quadriplegia, death
Pericardial tamponade	Shortness of breath, tachypnea Hypotension, jugular venous distension Tachycardia, muffled heart sounds, rub	Cardiogenic shock Death
Airway, including posterior epistaxis	**Airway:** hemoptysis, shortness of breath, hypoxia **Posterior epistaxis:** profuse epistaxis, hemoptysis, hypoxia, shortness of breath	Hypoxemic respiratory failure, Death
Hemothorax, intra-abdominal bleeding, and RPH	**Hemothorax:** tachypnea, tachycardia, hypotension **Intra-abdominal (nongastrointestinal):** abdominal pain, distension, hypotension, tachycardia **RPH:** Back/flank/hip pain, tachycardia, hypotension	**Hemothorax:** respiratory failure **RPH:** femoral neuropathy **All:** hypovolemic shock, death
Extremity bleeds: includes intramuscular and intra-articular bleeding	**Intramuscular:** pain, swelling, pallor, paresthesia, weakness, diminished pulse **Intra-articular:** joint pain, swelling, decreased range of motion	**Intramuscular:** compartment syndrome, paralysis, limb loss **Intra-articular:** irreversible joint damage

LOC = loss of consciousness; RPH = retroperitoneal hematoma.

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TABLE 3 Suggestions for Laboratory Measurement of DOACs When Specialized Assays are not Available

	Clinical Objective			
	Exclude Clinically Relevant* Drug Levels		Determine Whether On-Therapy or Above On-Therapy Levels Are Present	
Drug	**Suggested Test**	**Interpretation**	**Suggested Test**	**Interpretation**
Dabigatran	TT, aPTT	**Normal TT** excludes clinically relevant* levels **Prolonged TT** does not discriminate between clinically important and insignificant levels **Normal aPTT** usually excludes clinically relevant* levels, if a sensitive reagent is used.	aPTT	**Prolonged aPTT** suggests that on-therapy or above on-therapy levels are present **Normal aPTT** may not exclude on-therapy levels, particularly if a relatively insensitive aPTT reagent is used
Apixaban	None	**Normal PT and aPTT** do not exclude clinically relevant* levels	PT	**Prolonged PT** suggests that on-therapy or above on-therapy levels are present **Normal PT** may not exclude on-therapy *or above on-therapy levels*, particularly if a relatively insensitive PT reagent is used
Edoxaban or rivaroxaban	None	**Normal PT and aPTT** do not exclude clinically relevant* levels	PT	**Prolonged PT** suggests that on-therapy or above on-therapy levels are present **Normal PT** may not exclude on-therapy levels, particularly if a relatively insensitive PT reagent is used

*The term "clinically relevant" refers to DOAC levels that may contribute to bleeding or surgical bleeding risk. The minimum DOAC level that may contribute to bleeding or surgical bleeding risk is unknown. The International Society on Thrombosis and Hemostasis recommends consideration of anticoagulant reversal for patients with serious bleeding and a DOAC level >50 ng/mL, and for patients requiring an invasive procedure with high bleeding risk and a DOAC level >30 ng/mL (17).

Anti-Xa = anti-factor Xa; aPTT = activated partial thromboplastin time; DOAC = direct-acting oral anticoagulant; PT = prothrombin time; TT = thrombin time.

Managing major bleeds

- Stop OAC
- Resuscitation and local hemostatic measures.
- Reversal agents
- Supportive measures (blood products): Hb ≥ 7g/dL (≥ 8g/dL if ACS), Platelets ≥ 50. 10^9/L, Fibrinogen > 100 mg/dL.
- Comorbidities: renal dysfunction (↑T1/2 of DOAC, uremia-associated platelet dysfunction), hepatic dysfunction, and underlying hemostatic defects.
- Consider surgical/procedural managements

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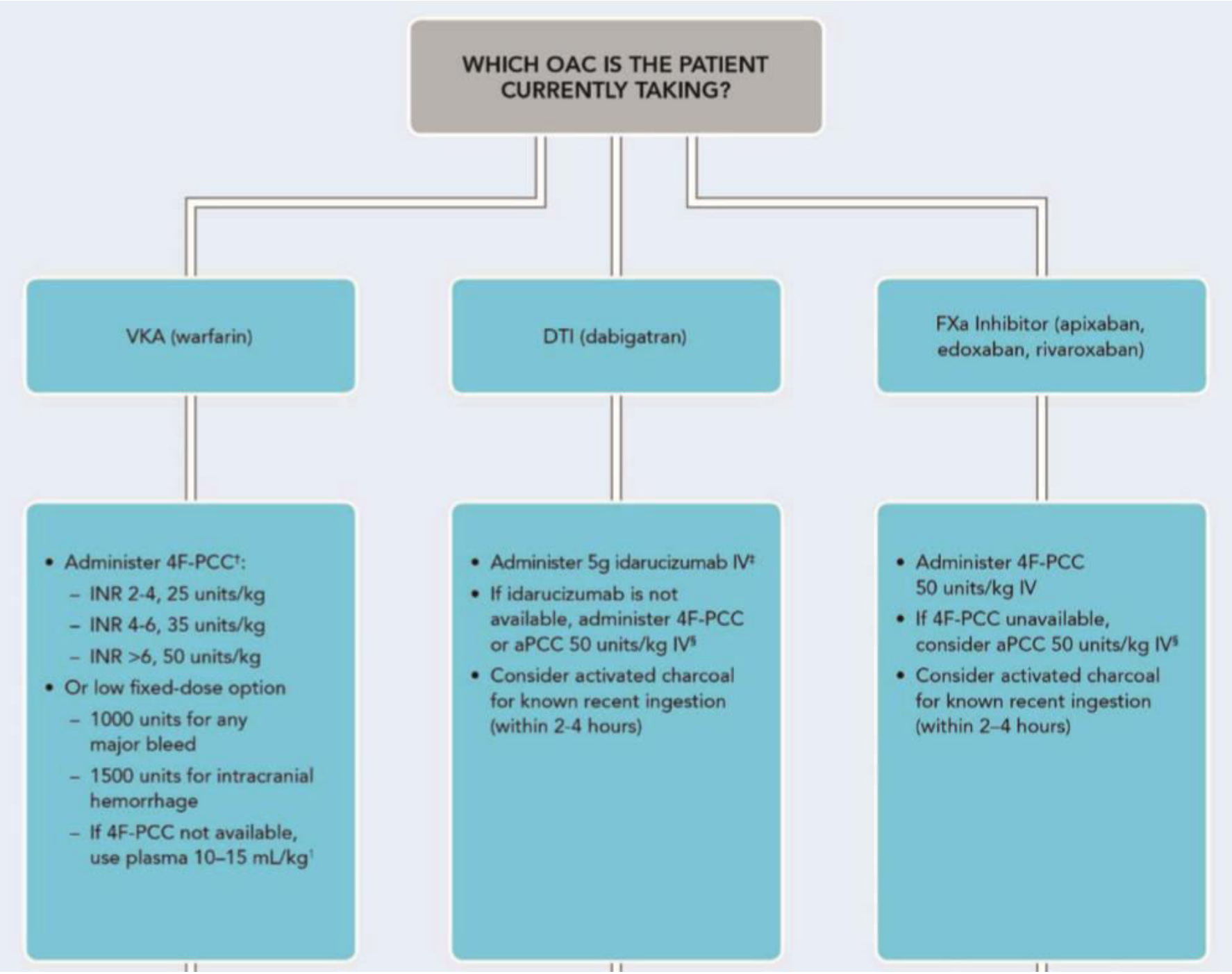
Managing nonmajor bleeds

- Stop OAC (hospitalization, a procedure, or a transfusion)/Continuing OAC
- Volume resuscitation and local hemostatic measures.
- Reversal agents
- Supportive measures (blood products)
- Comorbidities: renal dysfunction, hepatic dysfunction, and underlying hemostatic defects.
- Consider surgical/procedural managements

OAC Reversal Strategies



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Vitamin K antagonist (VKA)

- Vitamin K: 1-10 mg (Oral, IV 20-30 mins)
- Prothrombin Complex Concentrates (PCCs): 4F-PCCs (II, VII, IX, X)
- Plasma: 10-15 mL/kg

Factors II inhibitors (Dabigatran)

1. The RE-VERSE AD (Reversal of Dabigatran Anticoagulant Effect with Idarucizumab) study: Idarucizumab, a 2.5 – 5 mg fixed-dose intravenous infusion
   - Dabigatran-treated patients with severe or life-threatening hemorrhage
   - 100% reversal of anticoagulant effect in 4 hours.
   - 6% rate of thrombotic complications
2. PCC 50U/kg
3. Hemodialysis
4. Charcoal (50gr)

Factor Xa inhibitors (Rivaroxaban, Apixaban, Edoxaban)

- No specific antidotes
- PCCs: 4F-PCC 50 U/kg
- Agent in development: andexanet (ANNEXA-4 trial), ciraparantag (PER977 study)

TABLE 5 Available Reversal Agents and Suggested Use

Reversal Agent	Vitamin K Antagonists (Warfarin)	Factor IIa Inhibitor (Dabigatran)	Factor Xa Inhibitor (Apixaban, Edoxaban and Rivaroxaban)
4F-PCC (56)	First line	Second line	First line
aPCC	Not indicated	Second line	Second line
Idarucizumab	Not indicated	First line	Not indicated
Plasma	If 4-PCC is unavailable	Not indicated	Not indicated

4F-PCC = 4-factor prothrombin complex concentrate; aPCC = activated prothrombin complex concentrate.

TABLE 4 Recommended Durations for Withholding DOACs Based on Procedural Bleed Risk and Estimated CrCl When There Are No Increased Patient Bleed Risk Factors

	Dabigatran					Apixaban, Edoxaban, or Rivaroxaban		
CrCl, mL/min	≥80	50-79	30-49	15-29	<15	≥30	15-29	<15
Estimated drug half-life, h	13	15	18	27	30 (off dialysis)	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	≥48 h	≥72 h	No data. Consider measuring dTT and/or withholding ≥96 h	≥24 h	≥36 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥48 h
Uncertain, intermediate, or high	≥48 h	≥72 h	≥96 h	≥120 h	No data. Consider measuring dTT	≥48 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥72 h	

NOTE: The duration for withholding is based upon the estimated DOAC half-life withholding times of 2 to 3 half-lives for low procedural bleeding risk and 4 to 5 drug half-lives for uncertain, intermediate, or high procedural bleeding risk (47-55).

CrCl = creatinine clearance; DOAC = direct-acting oral anticoagulant; dTT = dilute thrombin time.

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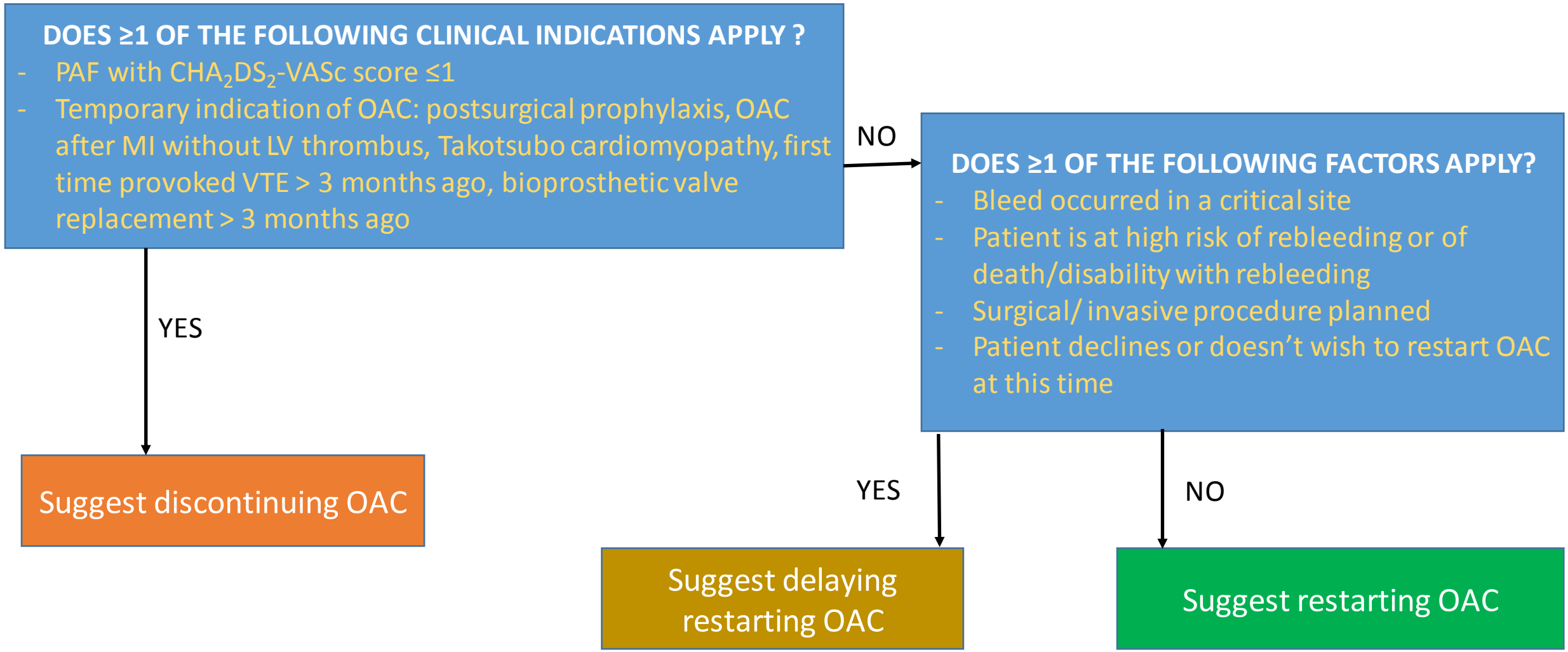
Considerations for restarting Anticoagulation



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PATIENTS WITH HIGH RISK OF THROMBOTIC EVENTS

TABLE 6 Indications for Anticoagulation With High Thrombotic Risk

Indication	Patient Characteristics
Mechanical valve prosthesis	■ Mechanical valve + additional thrombotic considerations: AF, CHF, prior stroke/TIA ■ Caged-ball or tilting disc aortic valve prosthesis ■ Stroke/TIA within 6 months
AF	■ AF with $CHADS_2$ score ≥4 (or CHA_2DS_2-VASc score ≥6) (84) ■ Stroke/TIA within 3 months ■ Stroke risk ≥10% per year ■ Rheumatic valve disease or mitral stenosis
VTE	■ VTE within 3 months ■ History of unprovoked or recurrent VTE ■ Active cancer and history of cancer-associated VTE
Prior thromboembolism with interruption of anticoagulation	
Left ventricular or left atrial thrombus	
Left ventricular assist device (LVAD)	

AF = atrial fibrillation; CHF = congestive heart failure; TIA = transient ischemic attack; VTE = venous thromboembolism.

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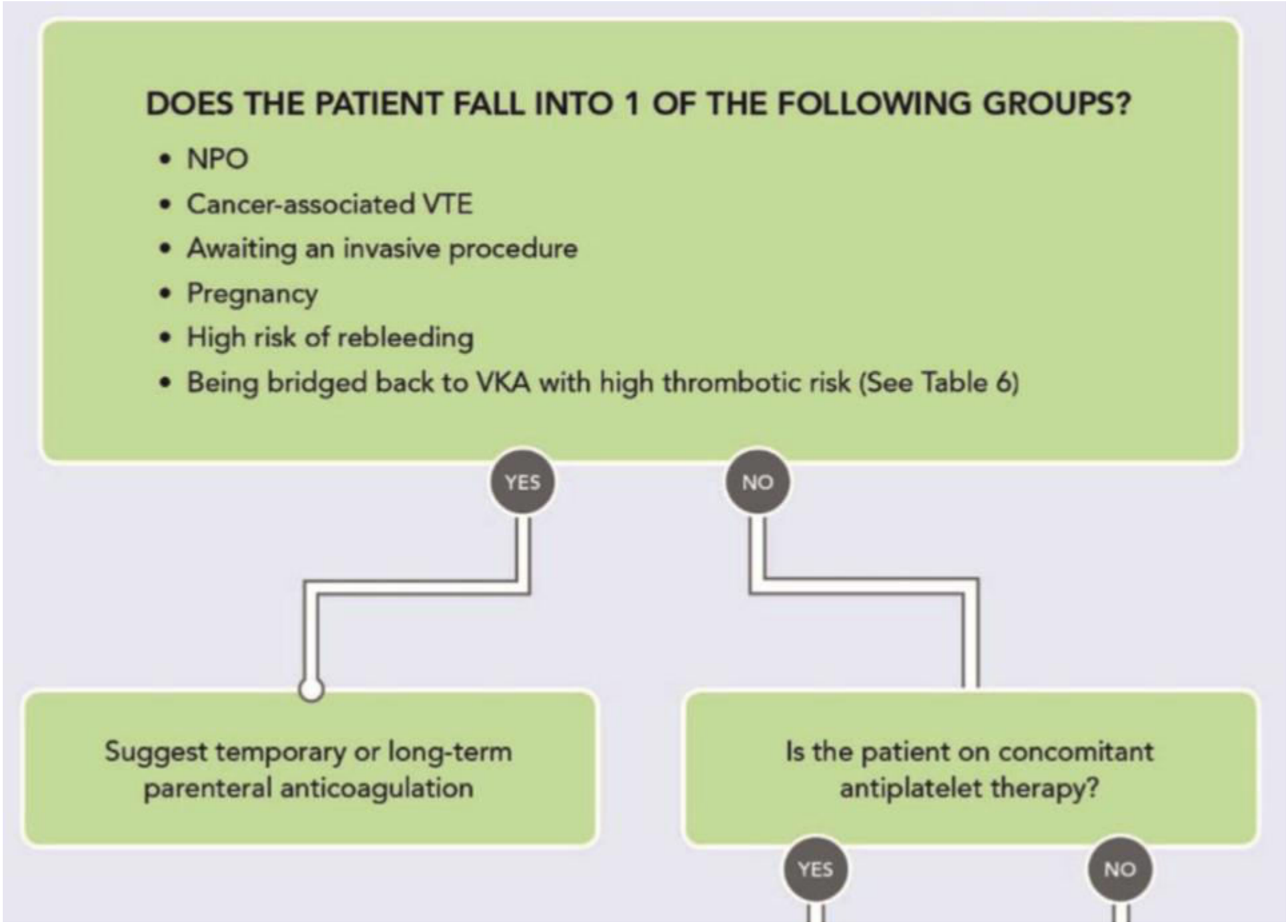
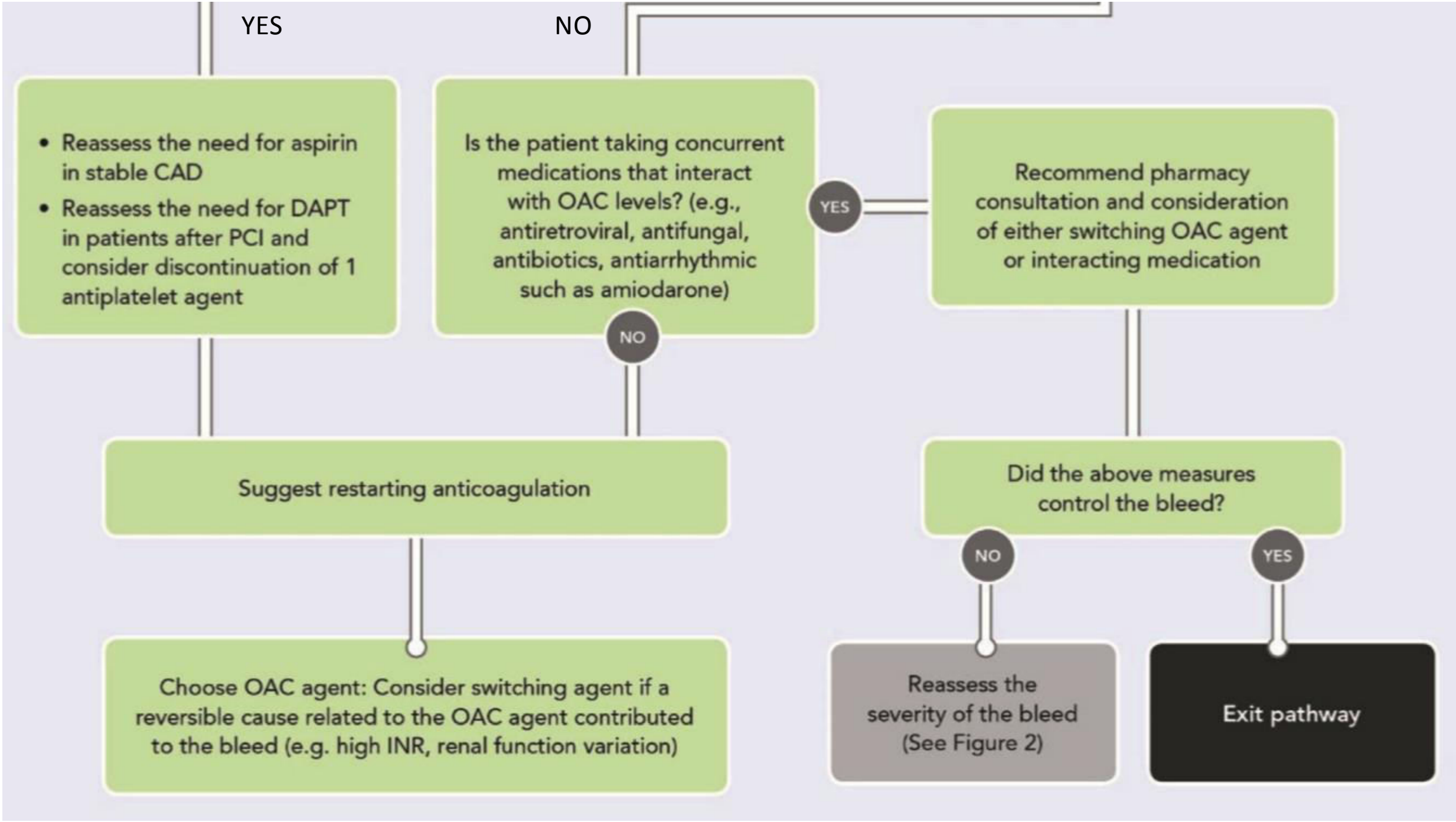
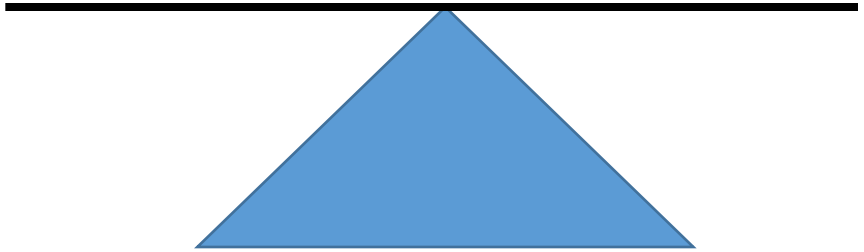

DOES THE PATIENT FALL INTO 1 OF THE FOLLOWING GROUPS?
• NPO
• Cancer-associated VTE
• Awaiting an invasive procedure
• Pregnancy
• High risk of rebleeding
• Being bridged back to VKA with high thrombotic risk (See Table 6)
YES
NO
Suggest temporary or long-term parenteral anticoagulation
Is the patient on concomitant antiplatelet therapy?
YES
NO


YES
NO
• Reassess the need for aspirin in stable CAD
• Reassess the need for DAPT in patients after PCI and consider discontinuation of 1 antiplatelet agent
Is the patient taking concurrent medications that interact with OAC levels? (e.g., antiretroviral, antifungal, antibiotics, antiarrhythmic such as amiodarone)
YES
Recommend pharmacy consultation and consideration of either switching OAC agent or interacting medication
NO
Suggest restarting anticoagulation
Did the above measures control the bleed?
NO
YES
Choose OAC agent: Consider switching agent if a reversible cause related to the OAC agent contributed to the bleed (e.g. high INR, renal function variation)
Reassess the severity of the bleed (See Figure 2)
Exit pathway

TIMING OF ANTICOAGULATION REINITIATION

Thrombotic risk **Rebleeding risk**



Gastrointestinal Bleeding

- A systemic review: restart OAC after GI bleeding had a lower risk of thromboembolism and death, nonsignificant increase in recurrent bleeding (*).
- The timing of reinitiation: once bleeding has been controlled.
  - Time of discharge (mean: 5 days)(**)
  - > 7 days (***)

(*): Chai-Adisaksopha C. Thromb Haemost. 2015;114:819-25
(**): Sengupta N. Am J Gastroenterol. 2015;110:328-35.
(***): Qureshi W. Am J Cardiol. 2014;113:662-8.

Overall Outcomes Among Warfarin-Treated Patients With GIB

Outcome	Overall Cohort (n = 442)	Resumed Warfarin Therapy (n = 260)	Did Not Resume Warfarin Therapy (n = 182)	*P* Value[b]
Index GIB management				
Warfarin therapy stopped	400 (90.7)	219 (84.2)	182 (100)	<.001
Phytonadione administered	282 (63.8)	157 (60.4)	125 (68.7)	.07
Fresh-frozen plasma provided	211 (47.7)	106 (40.8)	105 (57.7)	<.001
Blood transfusion	252 (57.0)	119 (45.8)	133 (73.1)	<.001
Treated in ED only	107 (24.2)	83 (31.9)	24 (13.2)	<.001
Treated in ICU	135 (30.5)	55 (21.2)	80 (44.0)	<.001
Length of stay, median (IQR), d	3 (1-4)	2 (1-4)	3 (2-5)	<.001
Days to warfarin therapy resumption, median (IQR)[c,d]	4 (2-9)	4 (2-9)	NA	NA
Low-molecular-weight heparin use	44 (10.0)	39 (15.0)	5 (2.8)	<.001
Primary outcomes[e]				
Thrombosis	11 (2.5)	1 (0.4)	10 (5.5)	<.001
Recurrent GIB	36 (8.4)	26 (10.0)	10 (5.5)	.09
Deceased	52 (11.8)	15 (5.8)	37 (20.3)	<.001

Arch Intern Med. 2012;172(19):1484-1491.

Restarting Anticoagulation and Outcomes After Major Gastrointestinal Bleeding in Atrial Fibrillation

Waqas Qureshi, MD[a,*], Chetan Mittal, MD[b], Iani Patsias, MD[b], Kiran Garikapati, MD[b], Aishwarya Kuchipudi, MD[b], Gagandeep Cheema, MD[b], Mohammad Elbatta, MD[b], Zaid Alirhayim, MD[b], and Fatima Khalid, MD[c]

Data regarding the outcomes of restarting anticoagulation in patients who develop gastrointestinal bleeding (GIB) while anticoagulated are sparse. We hypothesized that restarting anticoagulation in these patients is associated with better outcomes. This is a retrospective cohort study that enrolled subjects who developed GIB while on anticoagulation from 2005 to 2010. Atrial fibrillation was defined by history and electrocardiography on presentation. GIB was defined as a decrease in hemoglobin by 2 g, visible bleeding, or positive endoscopic evaluation. Time-to-event adjusted analyses were performed to find an association of restarting warfarin and recurrent GIB, arterial thromboembolism, and mortality. Stratified analysis by duration of interruption of warfarin was also performed. Overall, 1,329 patients (mean age 76 years, women 45%) developed major GIB. Warfarin was restarted in 653 cases (49.1%). Restarting warfarin was associated with decreased thromboembolism (hazard ratio [HR] 0.71, 95% confidence interval [CI] 0.54 to 0.93, $p = 0.01$) and reduced mortality (HR 0.67, 95% CI 0.56 to 0.81, $p < 0.0001$) but not recurrent GIB (HR 1.18, 95% CI 0.94 to 1.10, $p = 0.47$). When the outcomes were stratified by duration of warfarin interruption, restarting warfarin after 7 days was not associated with increased risk of GIB but was associated with decreased risk of mortality and thromboembolism compared with resuming after 30 days of interruption. Decision to restart warfarin after an episode of major GIB is associated with improved survival and decreased thromboembolism without increased risk of GIB after 7 days of interruption. (Am J Cardiol 2014;113:662–668)

Sử dụng lại thuốc AVK ở bệnh nhân XHTH

- ESGE 2015 : Có thể sử dụng AVK trong vòng 7 ngày sau khi kiểm soát chảy máu ở những BN có nguy cơ cao, tuy nhiên thời điểm an toàn là 7-14 ngày sau biến cố XH (*Strong Recommendation, Moderate quality evidence).*
- ASGE 2016: Cùng ngày nội soi nếu không có bằng chứng chảy máu tiến triển (*Low quality)*
- Tiếp tục sử dụng PPI , kiểm soát các YTNC khác của XHTH

American Society for Gastrointestinal Endoscopy guide 2016
ESGE Guideline Endoscopy 2015; 47: a1–a46

Intracranial hemorrhage

- 30-day mortality rate was 50%.
- Observational studies of patients with warfarin-associated ICH, resumption OAC reduced 50-70% risk of thrombosis, risk of death without a significant increased risk of rebleeding compared with discontinuation (*).
- Optimal modification cardiovascular risk factors.
- Consultation with neurology or neurosurgical expertise.
- Reinitiation of OAC for at least 4 weeks in patients without high thrombotic risk (**).

(*): Kuramatsu JB. JAMA, 2015;313:824-36.
(**): Hemphil JC. Stroke.2015;46:2032-60

Restarting Anticoagulant Therapy After Intracranial Hemorrhage

A Systematic Review and Meta-Analysis

Santosh B. Murthy, MD, MPH; Ajay Gupta, MD; Alexander E. Merkler, MD;
Babak B. Navi, MD, MS; Pitchaiah Mandava, MD, PhD, MSEE; Costantino Iadecola, MD;
Kevin N. Sheth, MD; Daniel F. Hanley, MD; Wendy C. Ziai, MD, MPH; Hooman Kamel, MD

8 studies , 5036 patients, AVK

Follow up : 12-42 months

Results Reinitiation of anticoagulation was associated with a signifcantly lower risk of thromboembolic complications (pooled relative risk, 0.34; 95% confdence interval, 0.25–0.45; *Q*=5.12, *P* for heterogeneity=0.28).

There was no evidence of increased risk of recurrent ICH after reinstatement of anticoagulation therapy, although there was signifcant heterogeneity among included studies (pooled relative risk, 1.01; 95% confidence interval, 0.58–1.77; *Q*=24.68, *P* for heterogeneity <0.001).

No signifcant publication bias was detected in our analyses

Stroke. published online April 17, 2017

Rates of Thromboembolic Complications and ICH Recurrence

Study	Anticoagulant Medications			No Anticoagulant Medications		
	Stroke+MI (%)	ICH Recurrence (%)	Total Population	Stroke+MI (%)	ICH Recurrence (%)	Total Population
De Vleeschouwer et al[17]	0 (0)	1 (4.0)	25	3 (3.7)	7 (8.6)	81
Claassen et al[18]	6 (26.1)	1 (4.3)	23	8 (32.0)	0 (0)	25
Majeed et al[20]	1 (2.2)	8 (17.8)	45	18 (20.7)	10 (11.5)	87
Yung et al[19]	N/A	14 (15.4)	91	N/A	29 (15.0)	193
Gathier et al[12]	2 (16.7)	1 (8.3)	12	2 (15.4)	0 (0)	13
Nielsen et al[16]	35 (6.9)	36 (7.1)	509	108 (21.4)	72 (14.3)	505
Kuramatsu et al[11]	9 (5.2)	14 (8.1)	172	82 (14.9)	36 (6.6)	547
Ottosen et al[15]	N/A	91 (8.9)	1022	N/A	113 (5.8)	1956
Total events	53 (6.7)*	166 (8.7)	1,899	221 (17.6)*	267 (7.8)	3407

ICH indicates intracranial hemorrhage; MI, myocardial infarction; and N/A, not available.
*Studies by Yung et al[19] and Ottosen et al[15] were excluded because stroke and MI were not reported.

Stroke. published online April 17, 2017

Restarting Anticoagulant Therapy After Intracranial Hemorrhage

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8 studies , 5036 patients, AVK

Follow up : 12-42 months

Conclusions—In observational studies, reinstitution of anticoagulation after ICH was associated with a lower risk of thromboembolic complications and a similar risk of ICH recurrence.

Randomized clinical trials are needed to determine the true risk–benefit profile of anticoagulation resumption after ICH.

Stroke. published online April 17, 2017

Khuyến cáo	Thời gian dùng lại VKA	Đô tin cậy - mức chứng cứ
AHA/ASA 2010	7-10 ngày	Class IIb - C
AHA/ASA 2015	Không chắc chắn, sớm nhất có thể	
ESO 2014	14 ngày	Qo E : very low Streng of Recommendation Non

Không có khuyến cáo nào mạnh cho thời điểm tốt nhất dùng lại thuốc kháng đông AVK cho BN mang van cơ học do không có NC Randomized

In summary

- OAC-associated bleed was increasing and management is challenging.
- Assessment (Major bleed) – Control Bleed – Restarting OACs.
- Reversal agents: vitamin K, PCCs, plasma, specific reversal agents.
- Evaluate comorbidities and drug interactions that cause bleeding.
- Timing to restard OACs: controversial, balance between risks and benefits (thrombotic/rebleeding).

Case 1:

- A 75-year old female patient (B.T.L)
- Admitted: Nov 20, 2017
- Chief complain: dyspnea and chest compression for 2 weeks.
- Past medical history: 1 DES/LAD1 (Dec 16, 2016) – Hypertension – AF– Dyslipidemia – CKD (eGFR: 35 ml/p/1.73)
- Medication: Duoplavin, Pradaxa 110 mg bid, Diovan 80, Atorvastatin 20 mg.
- Diagnosed: Hemothorax
- On admission day: INR: 1.49 TCK: 49” (32”)

Case 1 (cont)

- Management: pleuracentesis (850 mL of bloody fluid) + PFC (2 unit)
- Fluid test: infection (-), PCR of TB (-), antibody of Lupus (-), cellblock (-)
- MSCT of lung: undiagnosed.
- Pneumologist consultation: pleural biopsy and broncheal endoscopy

➔ **Hemothorax due to overdose of anticoagulant?**

Case 2:

- A 82-year old female patient (D.T.M)
- Admitted: Dec 15, 2017
- Chief complain: edema
- Past medical history: Severe MR – ASD – AF – PAH – Hypertension - CKD (eGFR: 25 ml/p/1.73) – Left knee arthritis
- Medication: Pradaxa 75 mg bid, Digoxin, Concor.cor, Furosemide, Spiromide, Diovan 80, Atorvastatin 20 mg, Imdur.
- For 2 weeks, she took Medrol 8 mg qd, Co-padein 1tab x 3 and Augmentin for left knee swollen.
- On admission day: INR: 1.9 TCK: 75” (32”) Hb: 12.3 g/dL
- No bleeding.

→What causes high INR and TCK?