Perioperative Anticoagulation Management in NVAF Patient Population

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Case Studies

- A 65 y/o male with a history of Paroxysmal Atrial Fibrillation, HTN, DM II, and Obstructive Sleep apnea. He is scheduled for a screening Colonoscopy. You have been asked to address his DOAC dose for his peri procedural management?

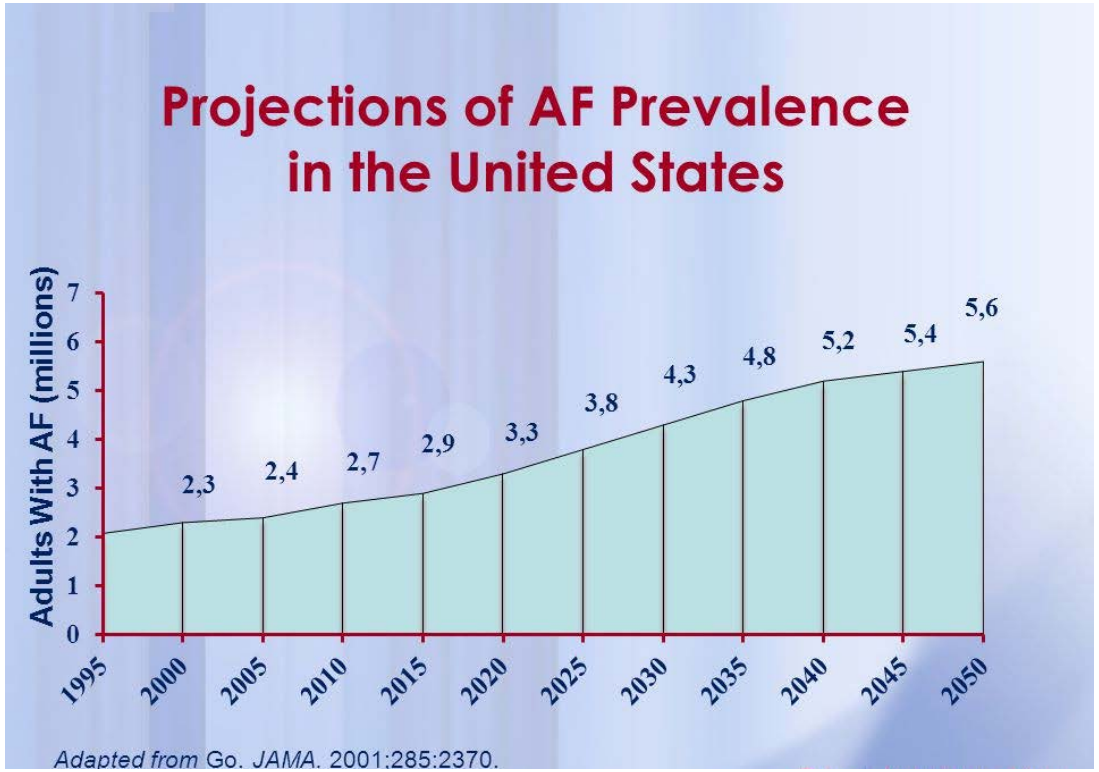
- A 78 y/o female with a history of permanent Atrial fibrillation, HTN, DMII, CVA 6 months ago and is scheduled for laparoscopic cholecystectomy. You have been asked to addressed her Coumadin for her the perioperative period?

Objectives

- Whether and when anticoagulant therapy should be interrupted?
- Whether and how anticoagulant bridging with a parenteral agent should be performed?
- When and how anticoagulant therapy should be restarted for those who require Temporary Interruption (TI)?

Introduction

- Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide.
- Increasing in prevalence with age
- Occurring in 1 in 4 individuals over their lifetime
- This risk begins at age 40 years and increases thereafter, such that at age 85 years, the prevalence of AF in an otherwise healthy population approaches 18%.

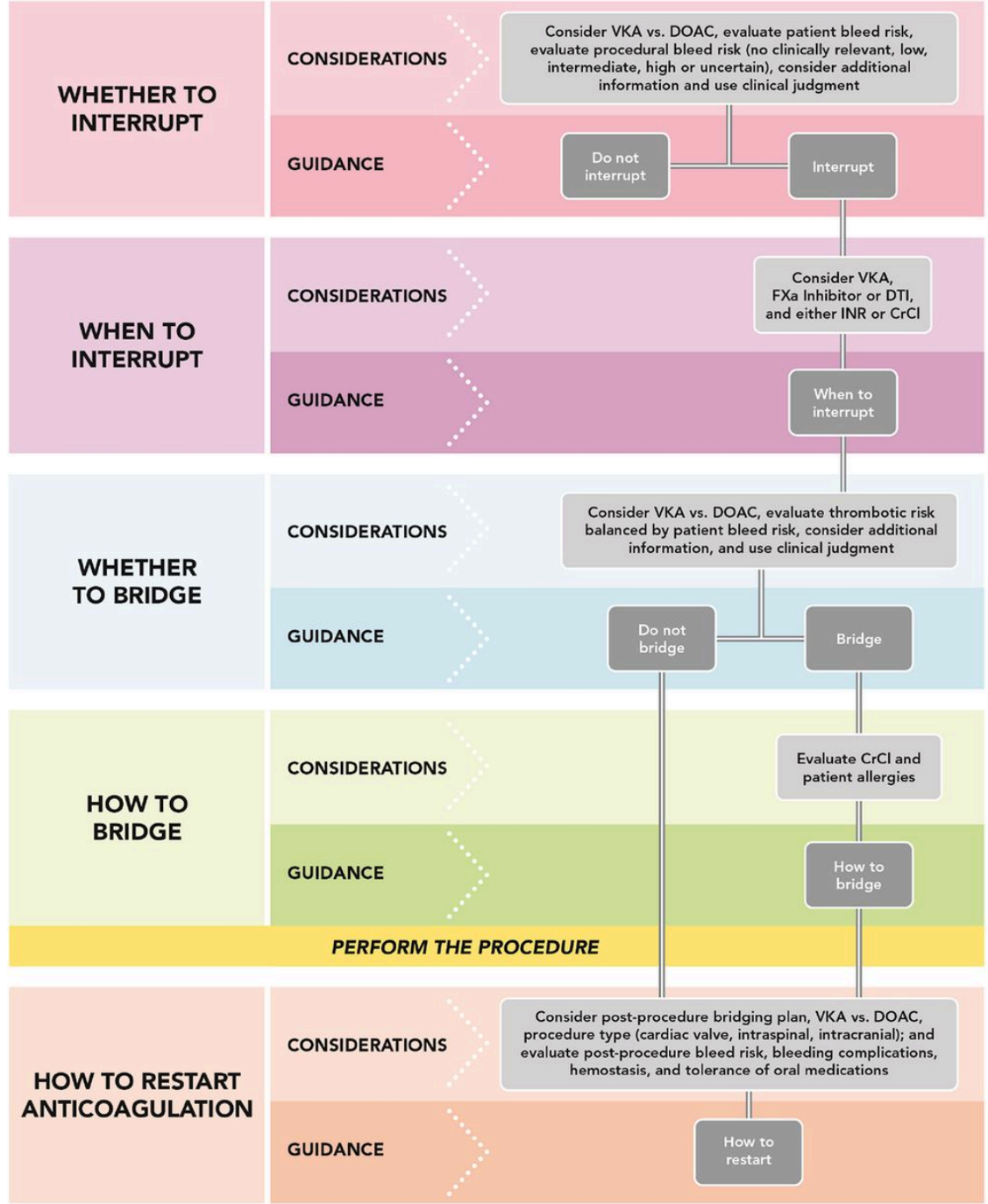


Definitions

- ***Bridging:*** The process whereby an OAC is discontinued and replaced by a subcutaneous or intravenous anticoagulant before and/or following an invasive procedure.
- ***Temporary interruption:*** The process whereby an anticoagulant is stopped for ≥1 doses, resulting in full or partial dissipation of anticoagulant effect prior to the invasive procedure.
- ***Nonvalvular AF:*** AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.
- ***Periprocedural:*** The period of time prior to, during, and shortly after an invasive procedure.

Methods and Assumptions

- This lecture is only for patients with NVAF.
- Patient is not taking concomitant antiplatelet agents or, if they are, that bleed risk estimates may vary.
- Elective planned procedures only.
- The recommendations about withholding and resuming vitamin K antagonist (VKA) therapy refer specifically to warfarin.
- Assumes that the clinician will seek additional input from the prescribing physician, cardiologist, and proceduralist to guide clinical judgment, in tandem with patient preference.



CrCl = creatinine clearance; DOAC = direct oral anticoagulent; DTI = direct thrombin inhibitor
FXa = factor Xa; INR = international normalized ratio; VKA = vitamin K antagonist

Introduction

- Temporary interruption (TI), the omission of ≥1 dose of an OAC in preparation for a procedure, is frequently necessary, most often to mitigate bleed risk with surgical or invasive procedures.
- Several factors are taken into consideration when making the decision to interrupt anticoagulation
  - bleeding risk of the procedure
  - thrombotic risk associated with anticoagulant interruption,
  - bleeding risk specific to the patient
- The practice of perioperative anticoagulation management varies widely.

Periprocedural Interruption of Oral Anticoagulant(OAC)

- Whether TI is required for a given procedure, it is important to first understand:
  - The propensity for bleeding with the procedure.
  - The clinical effect of bleeding should it occur.
  - Whether patient factors that impart increased bleed risk are present.

Assessing Procedural Bleeding Risk

- Most recommendations guiding periprocedural anticoagulation are based on expert consensus.
- The prevalence of bleeding with consequences.
  - Small amounts of bleeding in association with neuraxial anesthesia or after cardiac, intraocular, intracranial, or spinal surgery may result in significant morbidity or mortality. Therefore, procedures with **low rates of bleeding** but **significant associated sequelae** should be categorized as **high risk**.
- Many Specialty Colleges disagree on bleeding risk or use different Bleeding risk levels definitions.
- Opinions vary from different proceduralist.

http://jaccjacc.acc.org/Clinical_Document/PMAC_Online_Appendix.pdf

Assessing Procedural Bleeding Risk

- Most commonly performed procedures into 4 bleeding risk levels:
  - No clinically important bleed risk
  - Low procedural bleed risk
  - Uncertain procedural bleed risk
  - Intermediate/high procedural bleed risk

- Low risk
  - Minor soft tissue surgery, Ophthalmology procedures, Dental extractions < 3 teeth
- Intermediate risk
  - EGD with EPEG tube placement, Dental extraction > 3 teeth, prostate outlet procedures, Insertion of Temp HD catheter
- High Risk
  - Neural Axial Procedures, Percutaneous Kidney Biopsy, Esophageal biopsy

Patient's Bleeding Risk

HAS-BLED score

Condition	Points
H - Hypertension	1
A - Abnormal renal or liver function (1 point each)	1 or 2
S - Stroke	1
B - Bleeding	1
L - Labile INRs	1
E - Elderly (> 65 years)	1
D - Drugs or alcohol (1 point each)	1 or 2

HAS-BLED score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.

Pisters R et al. Chest 2010;138(5):1093-1100.

Considerations

- HAS-BLED does have some predictive value. The score is limited by its modest discriminatory performance and is not specifically endorsed by current guidelines for this purpose.
- In 1 review, procedures were considered to be high risk if the major bleed rate within 48 hours was 2% to 4% and low risk if the rate was 0% to 2%. In another, high versus low risk levels were defined by procedural rates of major bleeding >1.5% versus ≤1.5%, respectively. This latter cut point was based on criteria previously set by the American Society for Gastrointestinal Endoscopy for individuals on no antithrombotic therapy

Patients at increased Bleeding risk

- Any one of the following risk factors
  - Major Bleed
  - Intra Cranial Hemorrhage < 3 months
  - Quantitative or qualitative platelet abnormality (ex. ASA use)
  - INR above therapeutic range
  - Prior bleeding during previous bridging or similar procedure

TI in VKA patients

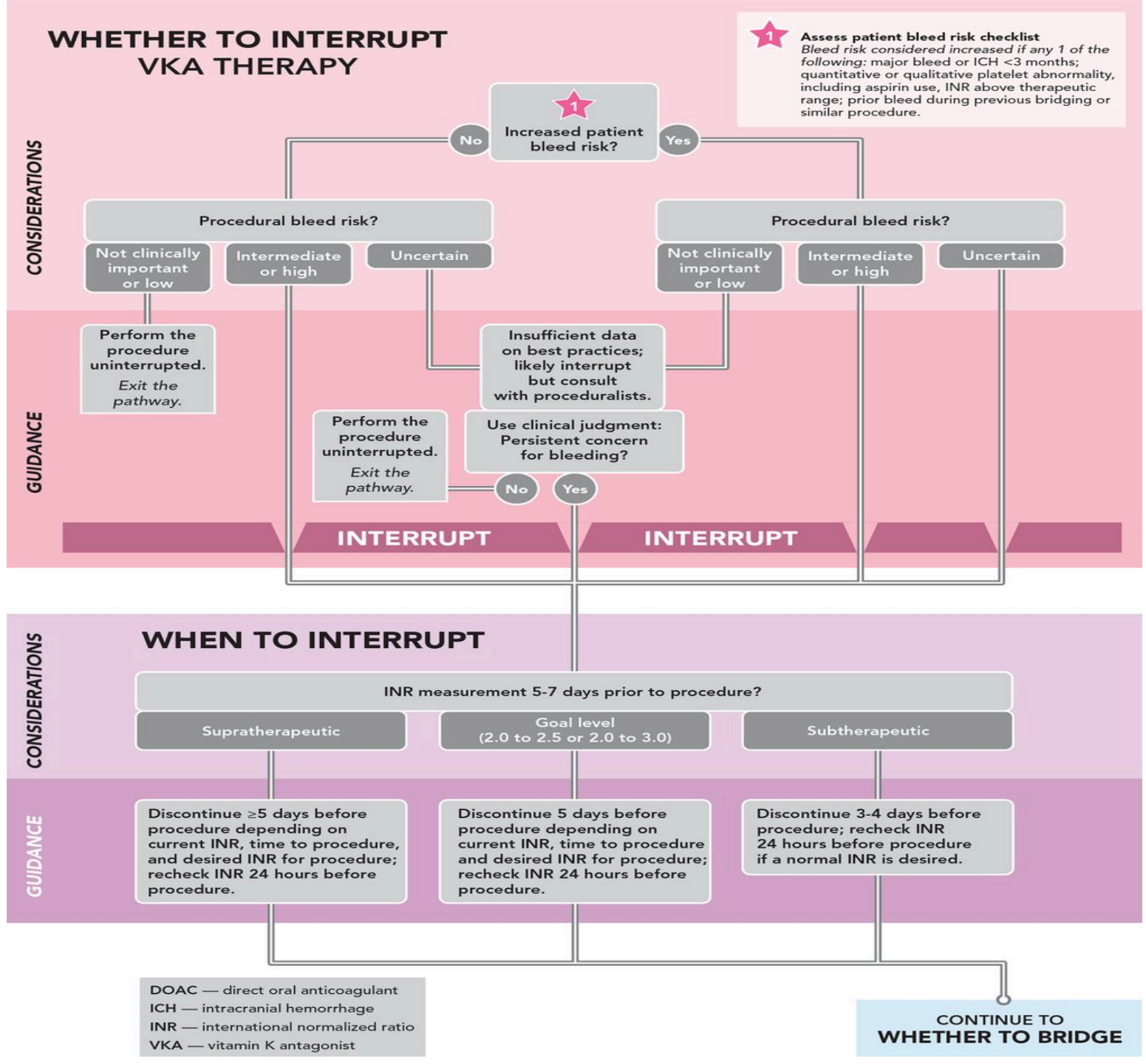
- Do not interrupt therapy with a VKA in:
  - Patients undergoing procedures with:
    - 1) no clinically important or low bleeding risk
    - 2) absence of patient-related factor(s) that increase the risk of bleeding.
- Interrupt therapy with a VKA in:
  - Patients undergoing procedures with intermediate or high bleed risk
  - Patients undergoing procedures with uncertain bleed risk and the presence of patient-related factor(s) that increase the risk of bleeding.
- Consider interrupting a VKA on the basis of both clinical judgment and consultation with the proceduralist in:
  - Patients undergoing procedures with:
    - No clinically important or low bleed risk
    - The presence of patient-related factor(s) that increase the risk of bleeding
    - Patients undergoing procedures with:
      - uncertain bleeding risk
      - The absence of patient-related factor(s) that increase the risk of bleeding.

VKA Populations

- For all patients on a VKA, an INR level should be measured 5 to 7 days before the procedure.
  - This is performed in individuals not requiring TI so that those with an INR >3.0 may be identified.
  - This is also performed in individuals requiring TI to determine the number of days that the VKA should be stopped prior to the procedure

VKA Populations

- INR of **1.5 to 1.9**, the VKA should be discontinued **3 to 4 days** prior to the procedure if a normal INR is desired OR for a shorter period of time if an elevated but sub therapeutic INR is acceptable. Recheck of INR 24 hours before procedure is desired.
- INR between **2.0 and 3.0**, the VKA should be **discontinued 5 days** prior to the procedure. Recheck INR 24 hours before planned procedure is desired.
- **INR >3.0,** the VKA should be discontinued at least 5 days prior to the procedure or longer. Depending on INR value. The INR should be rechecked within 24 hours of the procedure, particularly if a normal INR is desired.
- In those on a **higher VKA maintenance dose** (7.5 to 10 mg/day or higher) or for whom the **INR is known to normalize more quickly**, a shorter discontinuation time may be required prior to the procedure.



Consideration for DOACS

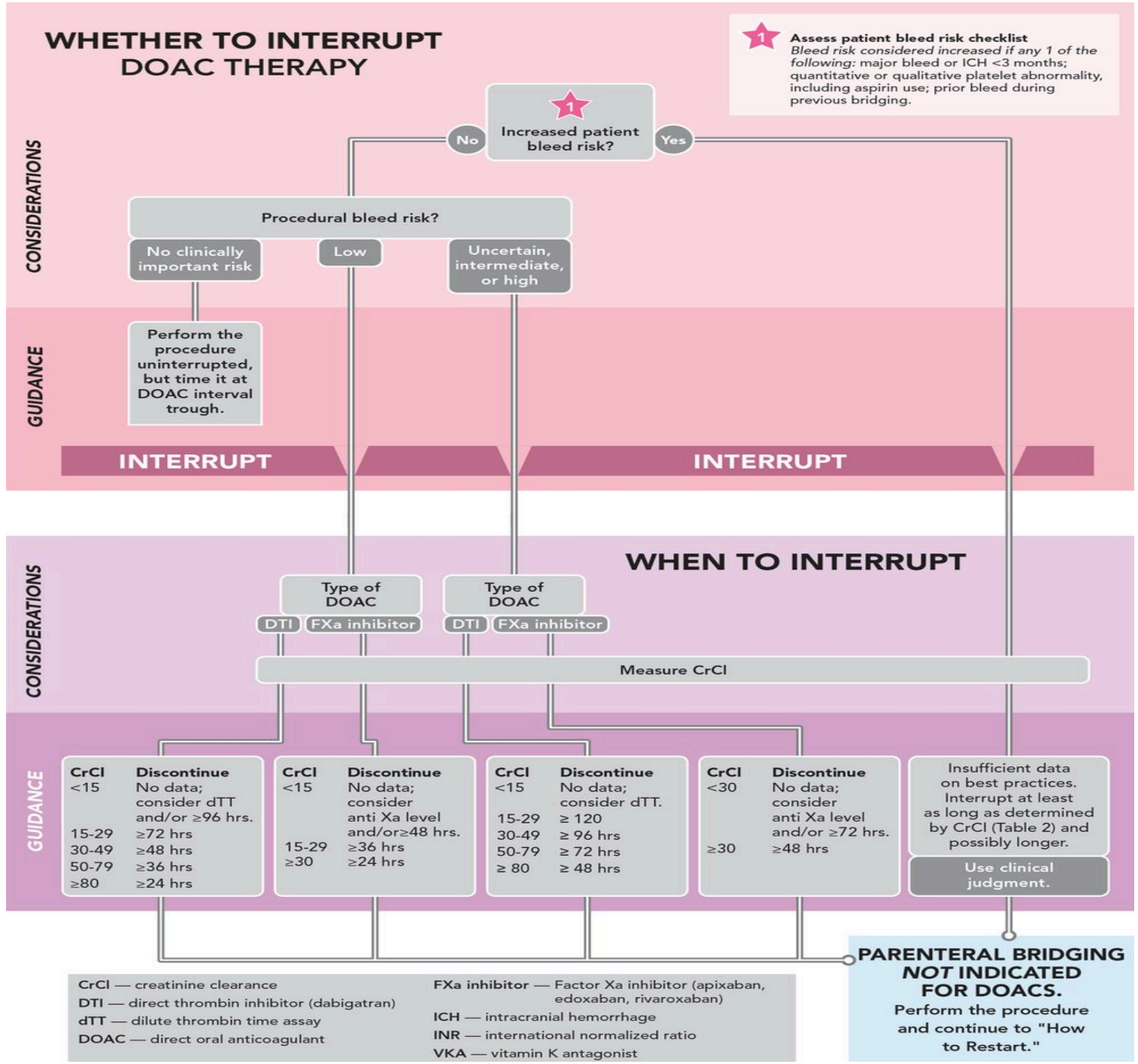
- DOAC who require TI of anticoagulant therapy, it is imperative that **renal function** be assessed to determine the anticipated duration of anticoagulant effect once the agent has been discontinued (**~4 to 5 drug half-lives**).
- Due to Pharmokinectics some low risk procedures can be done during troughs of the dosing of the DOACS. Requiring only missing one dose or none at all.
- Little data exist to provide guidance on periprocedural management of DOACs in patients with stage V chronic kidney disease (CrCl <15 mL/min or on dialysis), consideration should be given to specific laboratory testing (e.g., dilute thrombin time for dabigatran and agent-specific calibrated chromogenic anti-factor Xa activity for apixaban, edoxaban, and rivaroxaban) in patients taking these agents. Consulting with a Hematologist familiar with test for interpretation of results and recommendations.

	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.	

[illegible] procedural bleeding risk and 4 to 5 drug half-lives for uncertain, intermediate, or high procedural bleeding risk (46,60–67).
[illegible]

Guidance Statement for interruption of a DOAC peri procedurally

- Interrupt therapy for low bleed-risk procedures in:
  - Patients treated with any of the approved DOACs for a duration based on the estimated CrCl .
- Interrupt therapy for intermediate, high, or uncertain bleed-risk procedures in:
  - Patients treated with any of the approved DOACs for a duration based on the estimated CrCl



Peri procedural DOAC use with Neuroaxial Procedures.

- Use of anticoagulants in the setting of neuraxial anesthesia raises the risk of a spinal or epidural hematoma, which could be catastrophic.
- Currently available DOACs carry a black box warning regarding their use in the setting of neuraxial anesthesia.
- The American Society of Regional Anesthesia and Pain Management has developed guidelines regarding the periprocedural management of antiplatelet and anticoagulant medications around interventional pain procedures. Their guidelines recommend discontinuing a DOAC prior to neuraxial procedures (**for 4 to 5 days for dabigatran and 3 to 5 days for factor Xa inhibitors**), with **reinitiation 24 hours postprocedure**.
- If a patient is at an elevated thrombotic risk, considering a drug-free interval of 2 to 3 half-lives prior to the procedure or considering bridging parenteral anticoagulation with LMWH may be reasonable to keep the risk of a spinal hematoma low.

Now you have decided to TI what to do next?

- Minimize perioperative thrombotic risk while the OAC is being withheld.
- Minimize perioperative bleeding risk.
- DOACs have short half-lives that obviate the need to administer an alternative anticoagulant during TI in the majority of situations. In contrast, the anticoagulant effect of a VKA takes longer to dissipate once it is stopped and longer to become therapeutic when restarted.
- Patients on a VKA who have a higher risk of thromboembolic events may benefit from bridging using parenteral agents in the periprocedural setting.

How do you assess one's thrombotic risk?

- The timing of OAC interruption and the decision to bridge with a parenteral anticoagulant is based on the patient's estimated risk of thromboembolism, there are no validated assessment schemes to determine this risk.
- Extrapolating risk for a thrombotic event as a function of the period of interruption based on the annual risk may be attractive but has not been validated.
- The CHA_2DS_2-VASc score can be used to assess an individual patient's thrombotic risk overall. Although not well validated the higher the score the more apparent the risk of thrombosis becomes more apparent. As thrombotic risk increases the need for bridging becomes more apparent.

TI with bridging for Patients on DOACs

- The short-half lives of DOACs, bridging with a parenteral agent is rarely, if ever, needed prior to procedures.
- Reinitiation of these agents after the procedure, however, may need to be delayed owing to the risk of post procedural bleeding.
- Reinitiation might also be delayed depending upon:
  - The need for additional procedures
  - The patient's ability to tolerate oral medications.
    - A short-acting parenteral anticoagulant (e.g., unfractionated heparin [UFH]) may be needed either between procedures or post-procedure, when thrombotic risk remains high.

Interruption and Bridging for Patients on a VKA.

- Patients at low Thrombotic Risk
  - **For patients who are at low risk for thromboembolism (<5%/year), with a CHA_2DS_2-VASc score ≤4 or and no prior history of ischemic stroke, TIA, or SE, discontinue the VKA prior to the procedure and resume once the bleeding risk becomes acceptable, without bridging.**
- Patients at moderate thrombotic risk
  - **Appropriateness for bridging in those on a VKA at moderate risk for thromboembolism (5% to 10%/year) with a CHA_2DS_2-VASc score of 5 to 6 or history of prior ischemic stroke, TIA, or peripheral arterial embolism (3 or months previously)**
- If increased risk of bleeding, interruption of the VKA without bridging is recommended.
- If no significant bleed risk:
  - **In patients with prior stroke, TIA, or SE, consider use of a parenteral anticoagulant for periprocedural bridging (use clinical judgment, likely bridge);**
  - **In patients with no prior stroke, TIA, or SE, the use of a parenteral anticoagulant for periprocedural bridging is not advised (use clinical judgment, likely do not bridge).**

Interruption and Bridging for Patients on a VKA.

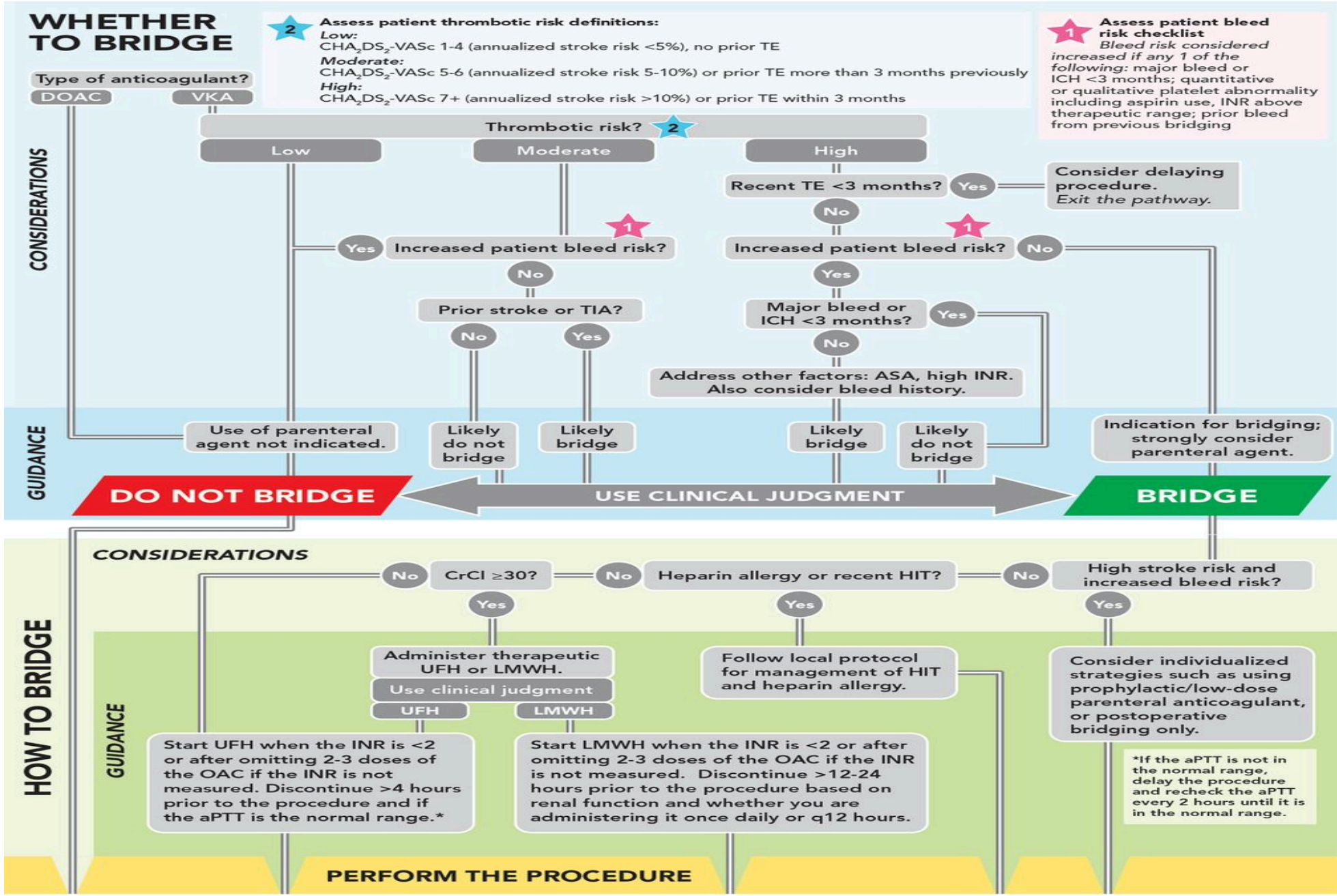
- Determining appropriateness for bridging in those on a VKA at high risk for thromboembolism:
  - **For patients who are at high risk of stroke or systemic embolism (>10% per year) with a CHA_2DS_2-VASc score of 7 to 9 or recent (within 3 months) ischemic stroke, TIA, or SE, parenteral bridging anticoagulation should be considered.**
  - Those with a recent (within 3 months) thrombotic event, the elective procedure should ideally be delayed, if possible, to move beyond this timeframe
  - For those with a recent (within 3 months) intracranial hemorrhage, the procedure should be performed either with no bridging or with post procedural bridging only.

Specific Recommendations regarding Bridging

- The parenteral anticoagulant may be started 24 hours following the first missed dose of warfarin.
- To use UFH rather than an LMWH as the bridging agent depends upon:
  - Renal function (based on CrCl), if CrCl is <30 mL/min, UFH is preferred over an LMWH. Although there is protocol for LMWH with CrCL 15-30 mL/min.
  - Parenteral bridging setting (inpatient versus outpatient)
  - Patient comfort with self-injections
  - Insurance coverage

Recommendations regarding Bridging

- Although UFH or a LMWH is most commonly used for bridging, for those with an active or remote history of heparin-induced thrombocytopenia, non heparin anticoagulants should be used and selected in accordance with hospital policy and consideration of renal and hepatic function.
- Start parenteral anticoagulant therapy when the INR is no longer therapeutic (e.g., <2.0 in those with NVAF).
- Discontinue UFH ≥4 hours prior to the procedure; the residual anticoagulant effect may be measured by the activated partial thromboplastin time.
- Discontinue LMWH at least 24 hours prior to the procedure; the residual anticoagulant effect may be measured by an LMWH-specific antifactor Xa assay.



aPTT – activated partial thromboplastin time assay; **ASA** – acetylsalicylic acid (aspirin); **DOAC** – direct oral anticoagulant; **HIT** – heparin-induced thrombocytopenia; **ICH** – intracranial hemorrhage; **INR** – international normalized ratio; **LMWH** – low-molecular-weight heparin; **OAC** – oral anticoagulation; **TE** – thromboembolic event; **TIA** – transient ischemic attack; **UFH** – unfractionated heparin; **VKA** – vitamin K antagonist

Post procedural Reinitiation of Anticoagulant Therapy.

- Restarting OAC in the postprocedural setting may place the patient at significant risk for bleeding. In patients managed with TI of anticoagulation, recent studies have documented an overall major bleed risk of 1.2% to 1.3% without bridging, with even higher rates in patients bridged with parenteral anticoagulation.
- Post procedural bleed risk depends on:
  - The timing of anticoagulation reinitiation
  - The type of procedure performed
  - Intra procedural findings, changes to the planned procedure, or complications
  - The anticoagulant used.
- Post procedural bleed risk will reflect the preprocedural bleed risk of the procedure typically; however, details of the particular procedure that the patient underwent may shift that risk in 1 direction or the other.

Guidance Statement for restarting anticoagulation postprocedure

- Ensure procedural site hemostasis.
- Consider bleeding consequences, especially with high bleed-risk procedures such as open cardiac surgical, intracranial, or spinal procedures.
- Consider patient-specific factors that may predispose the patient to bleeding complications (e.g., bleeding diathesis, platelet dysfunction, antiplatelet medications).
- In most situations, a VKA can be restarted in the first 24 hours after the procedure at the patient's usual therapeutic dose.

Indications for Post procedural Parenteral Bridging and Unique Post procedural Indications

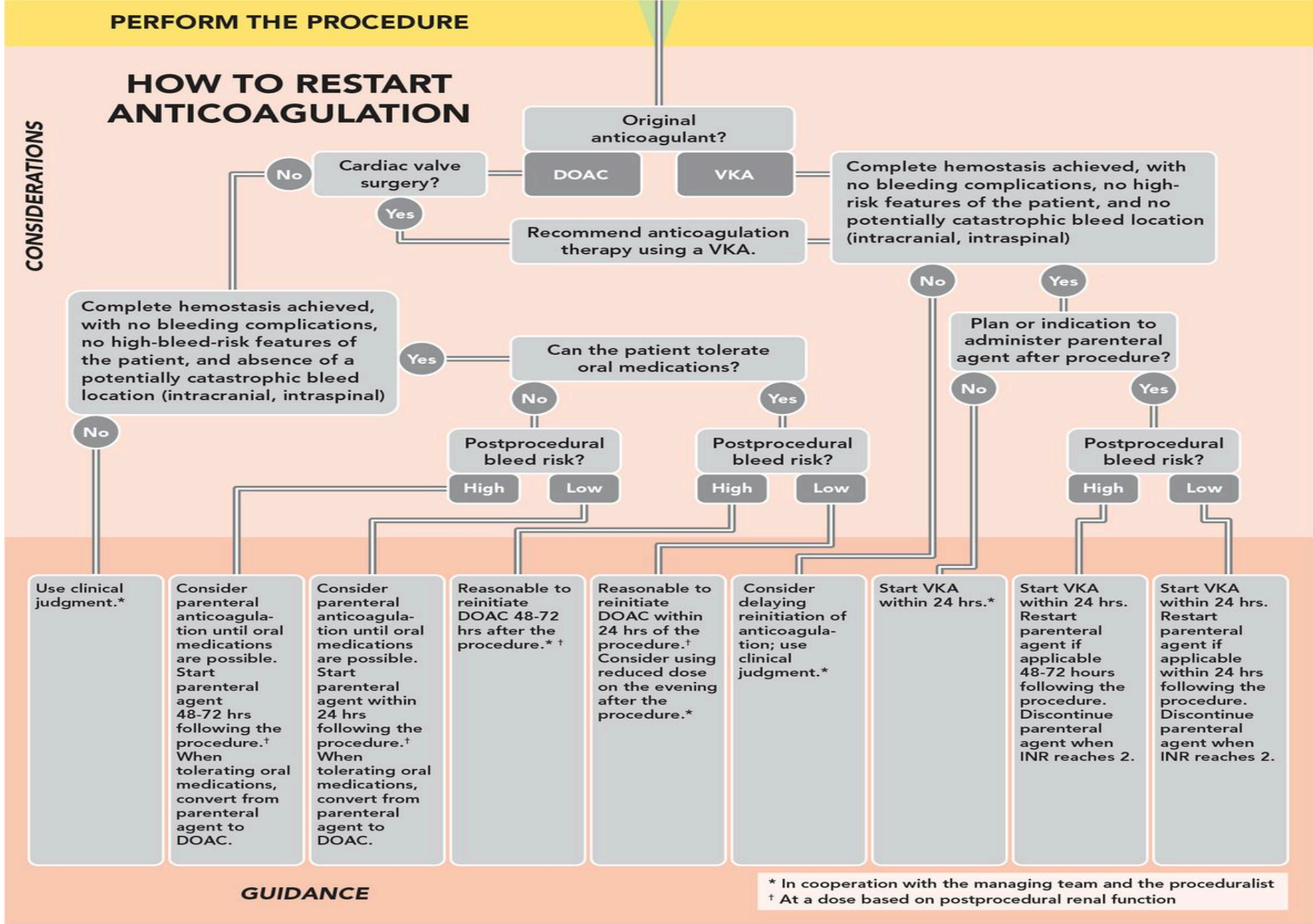
- Postprocedural bridging with a parenteral agent can be considered in patients with moderate or high risk of stroke or thromboembolic event.
- VKA therapy should be resumed (in most cases at the patient's usual therapeutic dose) without use of parenteral anticoagulation in cases associated with high risk for bleeding.

Use of Parenteral Anticoagulation Postprocedure in Patients With Moderate or High Thrombotic Risk: Clinical Factors and Monitoring

- Establish that **hemostasis has been achieved**, procedure-specific bleeding complications have been considered, patient-specific bleeding factors have been evaluated, and the proceduralist and the primary managing service are involved in the decision to restart anticoagulation.
- Following procedures with a **lower postprocedural risk of bleeding**, therapeutic parenteral anticoagulation, if indicated, can be started within the **first 24 hours** after the procedure in collaboration with the proceduralist and care team.
- Following procedures with a **higher postprocedural risk of bleeding**, therapeutic parenteral anticoagulation should be delayed for at least **48 to 72 hours** after the procedure.
- When VKA therapy is reinitiated, careful monitoring of the INR during bridging is required to mitigate bleed risk.
- LMWH or UFH should be discontinued when the INR is within goal range (≥2.0).

Guidance Statement for restarting DOAC therapy postprocedure

- Establish that hemostasis has been achieved, procedure-specific bleeding complications have been considered, patient-specific bleeding factors have been evaluated, and the proceduralist and primary managing service have been involved in the decision to restart anticoagulation.
- Following procedures with **low post procedural bleed risk** where TI is indicated, it is reasonable to resume **DOAC therapy at full dose on the day following the procedure.**
- Following **high post procedural bleed-risk procedures**, it is reasonable to wait at least **48 to 72 hours before resuming DOAC therapy** at full dose if complete hemostasis has been achieved.
- DOAC dosing should reflect post procedural renal function.
- Bridging therapeutic anticoagulation with a parenteral agent is generally **not required**



DOAC — direct oral anticoagulant
INR — international normalized ratio
VKA — vitamin K antagonist

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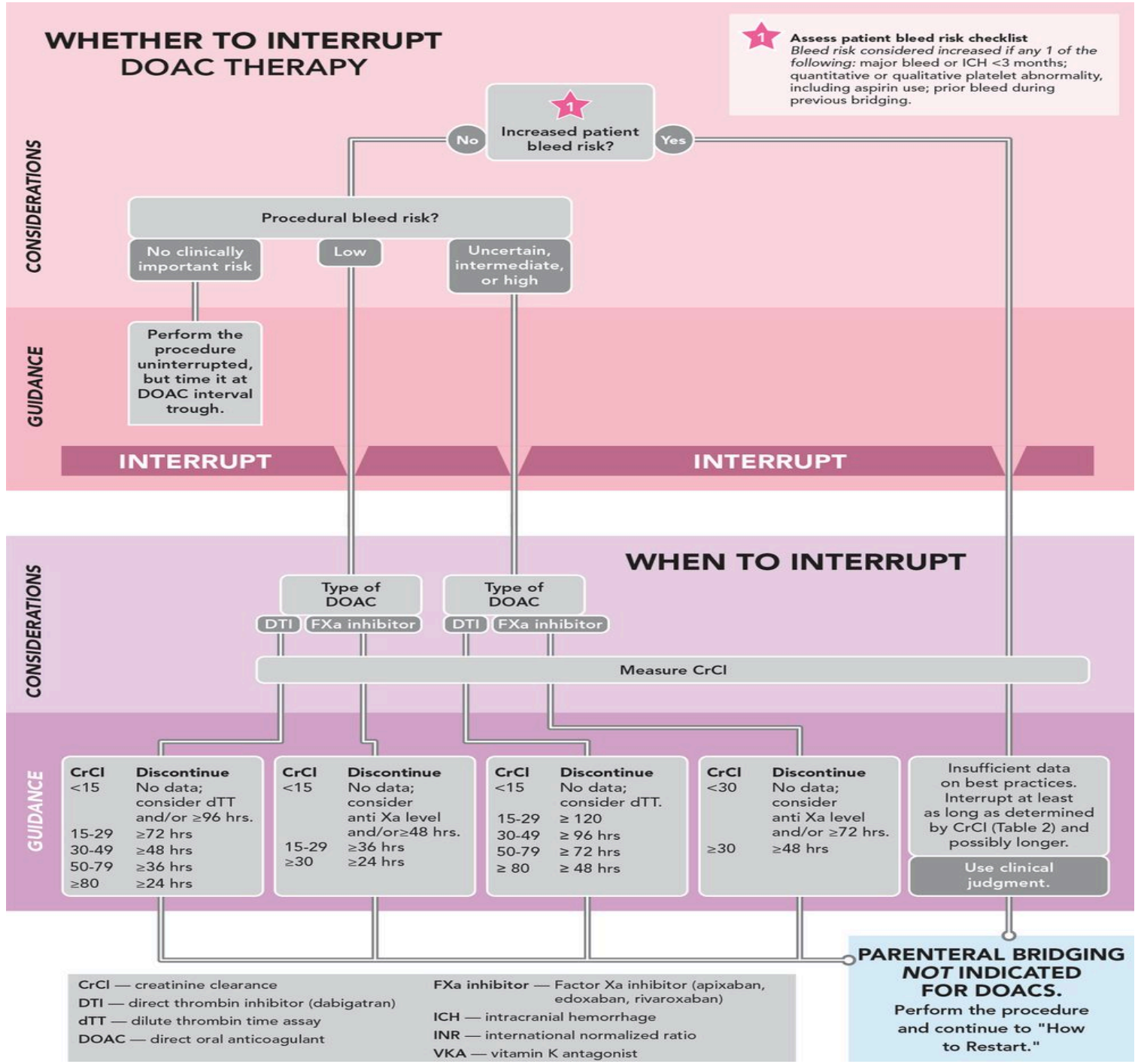

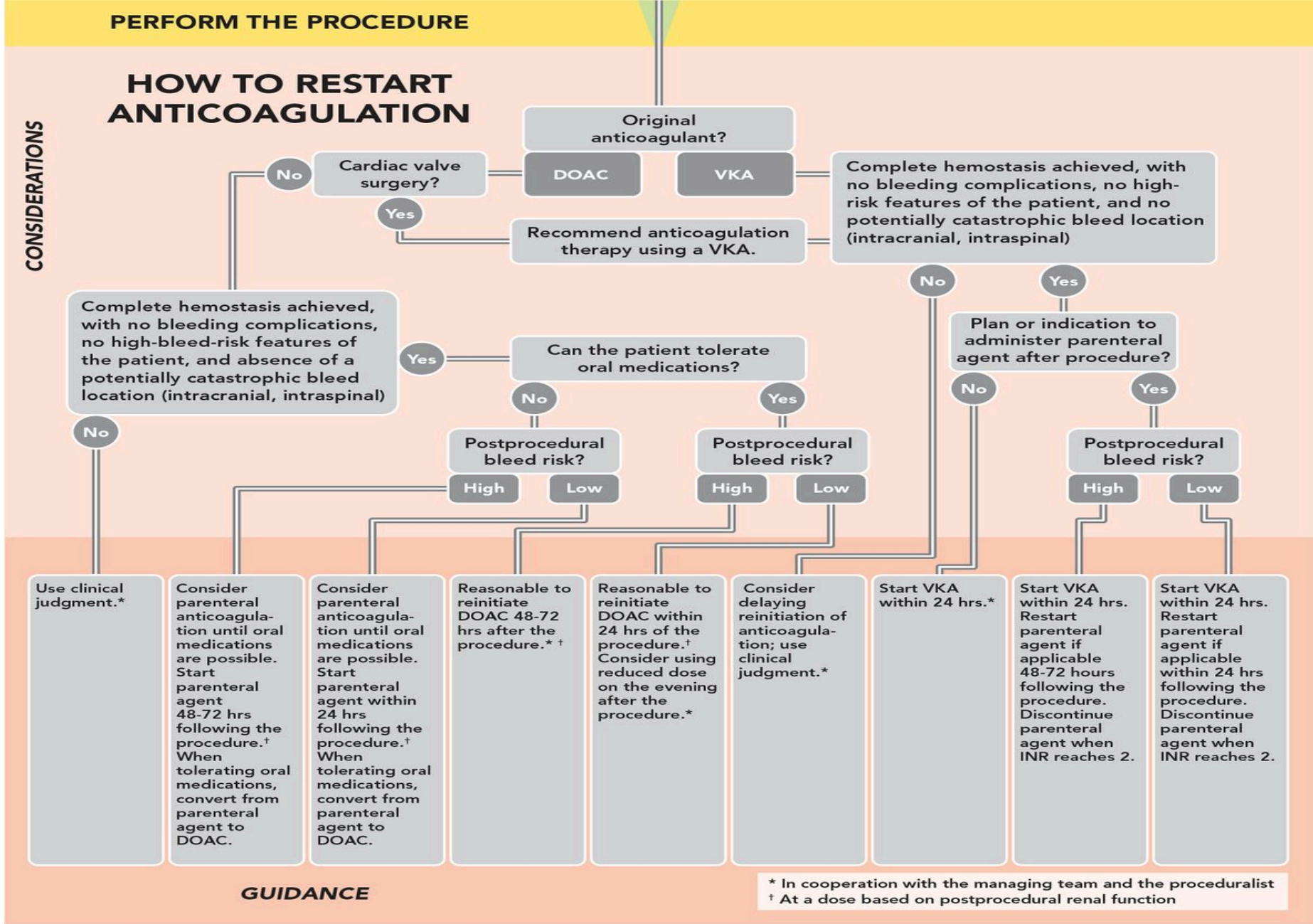

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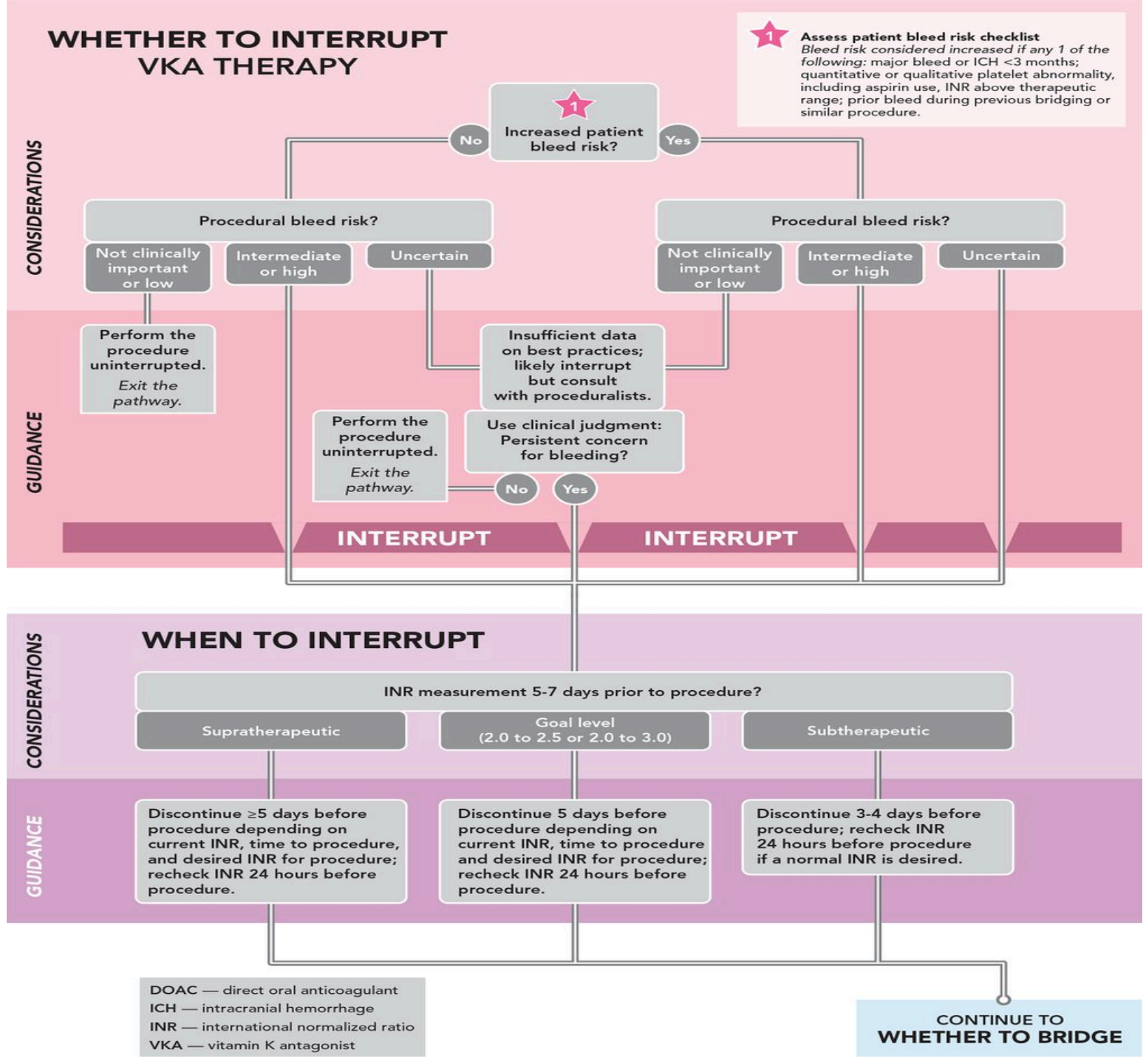

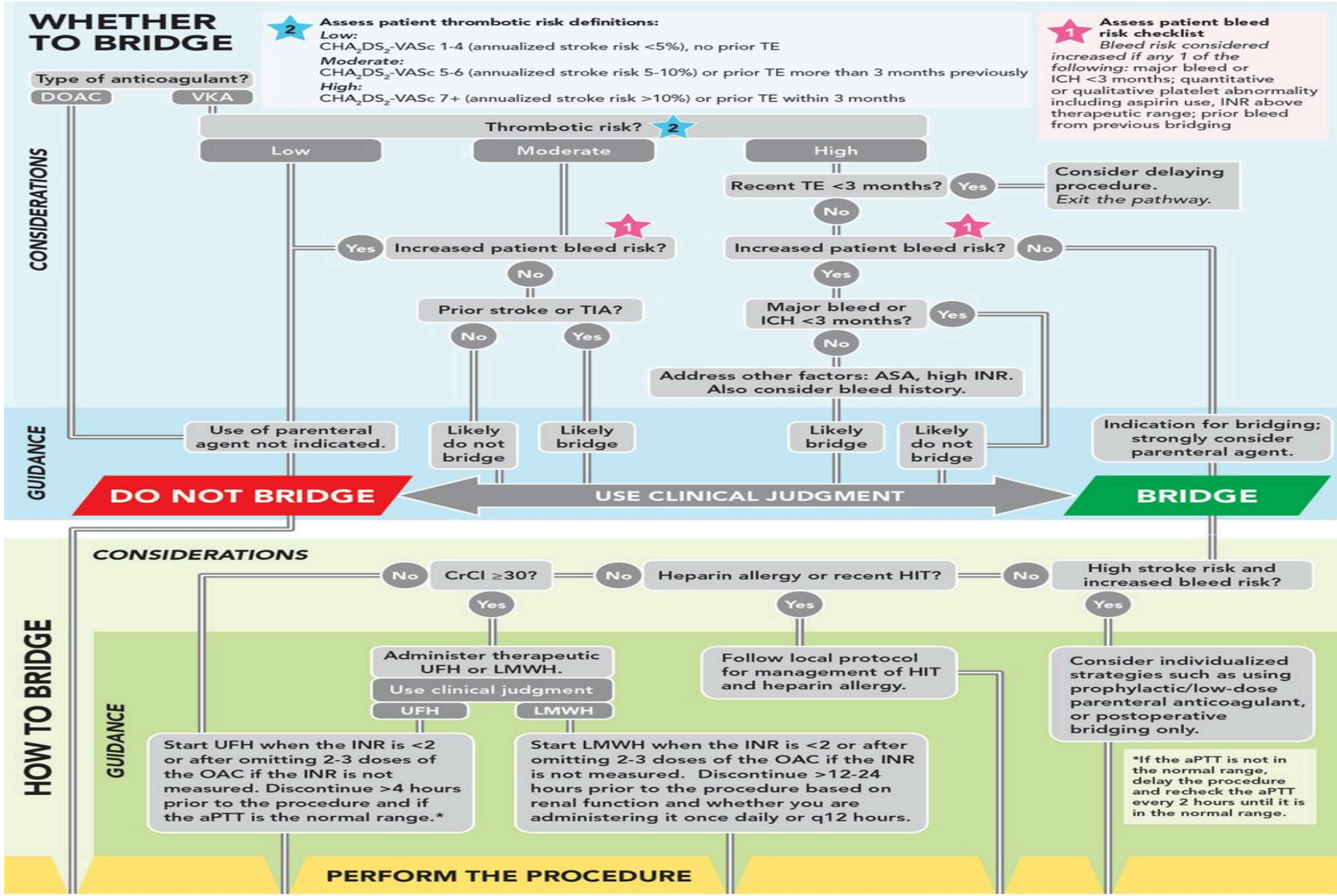

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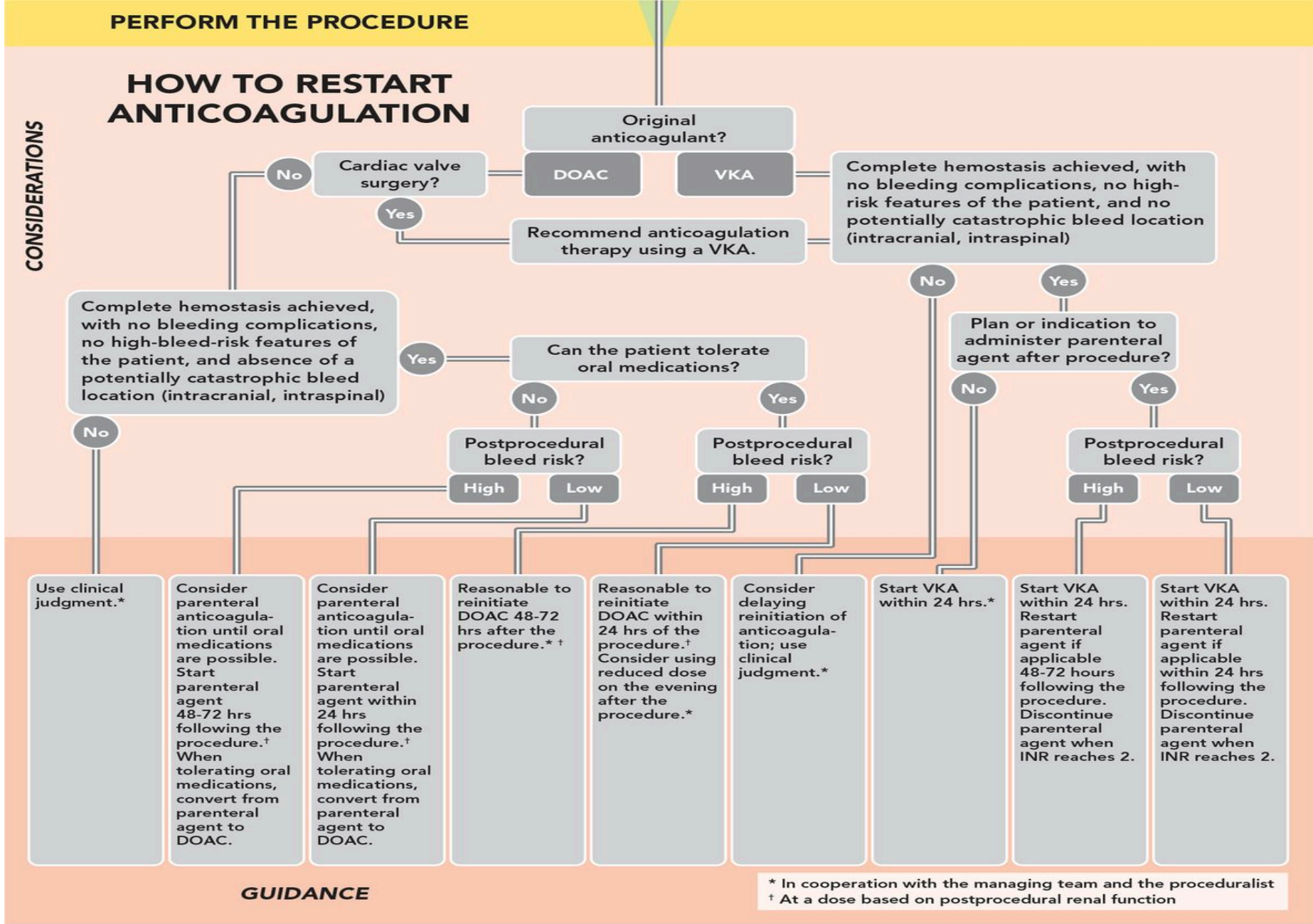

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Questions

2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation

A Report of the American College of Cardiology Clinical Expert Consensus Document Task Force

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