

Perioperative Management of Patients on DOAC Therapy – Major Orthopedic Injury

Statement of Problem:

- 1) Lack of institutional guidelines regarding perioperative management of anticoagulation for patients on DOAC therapy undergoing major orthopedic interventions including timing of cessation, ideal monitoring, and timing of resumption
- 2) Conflicting aims between perioperative management guidelines of anticoagulants for patients undergoing surgical interventions and literature supporting early surgery for major traumatic orthopedic injuries.

Goals:

- 1) Standardize perioperative management of anticoagulation for those who will undergo major orthopedic interventions.
- 2) Minimize postoperative complications while balancing length of stay as well as institutional and patient cost.

Background:

It is estimated that up to 1/3 of patients who present with hip/femur fractures are receiving anticoagulant treatment for various other medical reasons. There is a striking absence of generally adopted guidelines by trauma or orthopedic associations regarding anticoagulants in patients presenting with hip/femur fractures.

Several interventions are described in the literature to reverse DOAC effect. One option is delaying surgery and waiting for the anticoagulant effect to wear off (“watch and wait”). However, it is known that time to surgery correlates directly with morbidity and mortality in the setting of hip and femur fractures [1], [2], [3]. Another approach is to wait two half-lives between the last dose and surgery (corresponding to 25% residual anticoagulant effect). Pharmacologic reversal is possible using plasma products such as PCC or aFVII or drug specific antidotes. However, these medications are expensive and pose a thrombosis risk ranging from 1.8-9.1% [4]. As a final option, surgery may proceed disregarding anticoagulant effect (“non-reversal”).

Some studies in have shown a 3.4-fold increase risk for intraoperative transfusion requirement for patients with femur fractures on DOACs [5] as well as a 15% greater blood loss and transfusion rates of up to 40% with hip-fracture patients on DOACS [6]. Interestingly, both of these studies recommended early surgical intervention based on argued decreased time to surgery and cost-savings. A recent systematic review and meta-analysis found no differences in mortality, Hgb drop, or transfusion requirements for hip fracture patients on DOACs who underwent time reversal vs those who did not [7]. However, those patients in the “non time reversed” group underwent surgery at a mean time of 24.8 hours.

The 2018 EHRA Practical Guide on NOACs in AF recommend reversal for “Immediate procedures” [8]. However, for “urgent procedures” (specifically fixation of fractures) the recommendation is to defer surgery for at least 12 hours, ideally 24 hours after last dose. Otherwise, procedures should proceed according to elective protocols. This is consistent with recommendations from both the Association of Anesthetists and the British Committee of Standards for Hematology [9], [10].

Based on the aforementioned evidence and guidelines, it is our recommendation to defer major orthopedic surgical interventions for 24hours from last oral dose on those patients on DOAC therapy.

Clinical Practice Guideline:

Emergent/Immediate: Reversal

- Use the “Oral Anticoagulant Reversal (PCC (Kcentra), coagulation factor Xa (Andexxa), idarucizumab (Praxbind)” power-plan
 - For apixaban/rivaroxaban/edoxaban: Reversal with PCC
 - Kcentra 50 units/kg IV Once (max 5000 units)
 - For dabigatran:
 - Idarucizumab 2.5 gram IV every 5 minutes x 2 doses

Urgent: (including fracture fixation)

- Preferred: Defer surgery until 24 hours after last dose (if last dose unable to be obtained from history, use time of indicative Xa level)
 - Optional: Can consider reversal (as above) if significant clinical concern to delaying surgery, and indication for DOAC is atrial fibrillation, or low risk VTE
 - Do not reverse if prosthetic valve or high risk VTE

Elective:

- Low bleeding risk procedure: hold DOAC one day prior & restart one day after
- High bleeding risk procedure: hold DOAC two days prior & resume 2 days after
- Renal impairment: additional day for low/mod, additional 2 days high-risk

Note: there are currently no indications for Xa levels monitoring outside of the initial use to determine DOAC use. We do not recommend trending Xa levels to assess for clearance.

Definitions:

Surgery Type – per EHRA Guidelines [8]

- Emergent/Immediate: life, limb, or organ saving intervention. Typically cardiac, vascular, and neurosurgical emergency procedures.
- Urgent: interventions for acute onset or clinical deterioration of potentially life-threatening conditions, conditions that may threaten the survival of limb or organ, fixation of fractures, relief of pain, or other distressing symptoms.

Thrombosis

- High thrombosis risk: VTE within 3 months, severe inherited thrombophilia (Protein C/S, antithrombin, APL)
- Moderate thrombosis risk: VTE 3-12 months, recurrent VTE, non-severe thrombophilia (Factor V Leiden), active cancer
- Low thrombotic risk: VTE > 12 months

Bleeding Risk - per ISTH Guidance Statement [11]

- High bleeding risk (>2% risk major bleed):
 - Major surgery with extensive tissue injury

- Cancer surgery, especially solid tumor resection
- Major orthopedic surgery, including shoulder replacement surgery
- Reconstructive plastic surgery
- Urologic or gastrointestinal surgery, especially anastomosis surgery
- Transurethral prostate resection, bladder resection, or tumor ablation
- Nephrectomy, kidney biopsy
- Colonic polyp resection
- Bowel resection
- Percutaneous endoscopic gastrostomy (PEG) placement, endoscopic retrograde cholangiopancreatography (ERCP)
- Surgery in highly vascular organs (kidneys, liver, spleen)
- Cardiac, intracranial, or spinal surgery
- Any major operation (procedure duration >45 min)
- Neuraxial anesthesia
- Low bleeding risk (0-2% risk of major bleed):
 - Arthroscopy
 - Cutaneous/lymph node biopsies Foot/hand surgery
 - Coronary angiography^d
 - Gastrointestinal endoscopy +/- biopsy Colonoscopy +/- biopsy
 - Abdominal hysterectomy
 - Laparoscopic cholecystectomy
 - Abdominal hernia repair
 - Hemorrhoidal surgery
 - Bronchoscopy +/- biopsy
- Minor bleeding risk
 - Minor dermatologic procedures
 - Cataract procedures
 - Minor dental procedures
 - Pacemaker or defibrillator implantation

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