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

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Pathway Assumptions

• The pathway considers acute bleeding in patients being treated with either DOACs or VKAs.

• In the setting of bleeding with hemodynamic compromise, standard resuscitative measures should always be performed promptly.

• All indications for anticoagulation were considered, including AF, VTE treatment/prevention, prosthetic cardiac valves, intracardiac thrombus, and the presence of a mechanical cardiac support device.

• The recommendations for restarting and withholding anticoagulant therapy refers to both DOACs and VKAs.

• The pathway algorithm assumes that the provider will seek input from the appropriate specialists when indicated and include the patient and/or family in shared decision making when possible.

Writing Committee et al. JACC 2017; j.jacc.2017.09.1085
Case

75 yo man with HTN, remote CAD, NVAF on metoprolol, rivaroxaban 20 mg QD and ASA 81 mg daily presents with syncope. He was in his usual state of health until the morning of admission when he suddenly fainted on his way from the kitchen to the bathroom. He recalls feeling urgency to move his bowels then woke up on the floor. He was able to get himself to the bathroom where he had black tarry stools. His wife called 911 and he is brought to the ED.
Assessing Bleeding Severity

DOES ≥1 OF THE FOLLOWING FACTORS APPLY?
- Bleeding at a critical site (See Table 1)
- Hemodynamic instability
- Clinically overt bleeding with hemoglobin decrease ≥2 g/dL or administration of ≥2 units RBCs

YES
Bleed is considered major

NO
Bleed is considered non-major
Assessing Bleeding Severity

- H&P
- Labs
- Vitals
- Onset /location
- Time of ingestion of last dose
- Concomitant antiplatelet
- Thrombocytopenia
- Uremia
- Liver disease
Defining Bleeding Severity

**Major bleeding if ≥1 of factors apply**
- **Bleeding in critical site**
- Hemodynamic instability
- Overt bleeding with HGB drop ≥2 g/dL or admin ≥2 u PRBCs

**Nonmajor bleeding**
- None of the factors apply
Critical Site Bleeding
Table 1

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

LOC = loss of consciousness; RPH = retroperitoneal hematoma.
Case

In the ED his BP is 110/70, HR 110, O2 sat 99%
On exam his lungs are clear, heart is tachy but regular rhythm without murmur; abdomen is soft and non tender, he has no peripheral edema, rectal exam show melena

His HGB/HCT is 7.5 g/dL/24 %. his baseline is 12g/dL/36 %. Creatinine is 1.3 mg/dL, baseline 0.8 mg/dL, LFTS are normal

INR 1.9 PT 18.7

Major bleeding if ≥1 of factors apply
• Bleeding in critical site
• Hemodynamic instability
• Overt bleeding with HGB drop ≥2g/dL or admin ≥2 u PRBCs
### Suggestions for Lab Measurement of DOACs if Specialized Tests Not Available-Table 2

<table>
<thead>
<tr>
<th>Drug</th>
<th>Clinical Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exclude Clinically Relevant* Drug Levels</td>
</tr>
<tr>
<td></td>
<td>Determine Whether On-Therapy or Above On-Therapy Levels Are Present</td>
</tr>
<tr>
<td><strong>Suggested Test</strong></td>
<td><strong>Interpretation</strong></td>
</tr>
<tr>
<td><strong>Suggested Test</strong></td>
<td><strong>Interpretation</strong></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>TT, aPTT</td>
</tr>
<tr>
<td></td>
<td>Normal TT excludes clinically relevant* levels</td>
</tr>
<tr>
<td></td>
<td>Prolonged TT does not discriminate between clinically important and insignificant levels</td>
</tr>
<tr>
<td></td>
<td>Normal aPTT usually excludes clinically relevant* levels, if a sensitive reagent is used</td>
</tr>
<tr>
<td></td>
<td>aPTT</td>
</tr>
<tr>
<td></td>
<td>Prolonged aPTT suggests that on-therapy or above on-therapy levels are present</td>
</tr>
<tr>
<td></td>
<td>Normal aPTT may not exclude on-therapy levels, particularly if a relatively insensitive aPTT reagent is used</td>
</tr>
<tr>
<td>Apixaban</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Normal PT and aPTT do not exclude clinically relevant* levels</td>
</tr>
<tr>
<td></td>
<td>PT</td>
</tr>
<tr>
<td></td>
<td>Prolonged PT suggests that on-therapy or above on-therapy levels are present</td>
</tr>
<tr>
<td></td>
<td>Normal PT may not exclude on-therapy or above on-therapy levels, particularly if a relatively insensitive PT reagent is used</td>
</tr>
<tr>
<td>Edoxaban or rivaroxaban</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Normal PT and aPTT do not exclude clinically relevant* levels</td>
</tr>
<tr>
<td></td>
<td>PT</td>
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<td></td>
<td>Normal PT may not exclude on-therapy levels, particularly if a relatively insensitive PT reagent is used</td>
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</tbody>
</table>
**Suggestions for Lab Measurement of DOACs if Specialized Tests Available-Table 3**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Suggested Test</th>
<th>Interpretation</th>
<th>Measure On-Therapy or Above On-Therapy Drug Levels</th>
<th>Suggested test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Dilute TT, ECT, ECA</td>
<td>Normal result probably excludes clinically relevant levels</td>
<td>Dilute TT, ECT, ECA</td>
<td></td>
</tr>
<tr>
<td>Apixaban, edoxaban, or rivaroxaban</td>
<td>Anti-Xa</td>
<td>Absent chromogenic anti-Xa assay activity probably excludes clinically relevant levels</td>
<td>Anti-Xa†</td>
<td></td>
</tr>
</tbody>
</table>

ISTH recommends consideration of reversal for patients with serious bleeding and DOAC level > 50 ng/ml and severe bleeding; > 30 ng/ml is high risk bleeding and invasive procedure.

Writing Committee et al. JACC 2017; j.jacc.2017.09.1085
Assessing Bleed Severity and Managing Bleeds—Figure 2

[Diagram showing decision-making process for assessing and managing bleeds.]

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Assessing Bleed Severity and Managing Bleeds—Figure 2

- 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

Stop OAC
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- Consider surgical/procedural management of bleeding site

Suggest administering reversal agent* (See Figure 3)

Did the above measures control the bleed?

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Case

In the ED he receives 3 u lactated ringers and 2 u PRBCs. His BP is in the 90s. He continues to have melena. GI is called for urgent evaluation and he is transferred to the ICU. His last dose of rivaroxaban was at 6 am this morning with breakfast. It is now 11 am. Should he receive a reversal agent?
Guidance for Administering Reversal Agents-Figure 3

- FXa Inhibitor (apixaban, edoxaban, rivaroxaban)
- VKA (warfarin)
  - Administer 4F-PCC:
    - INR 2-4, 25 units/kg
    - INR 4-6, 35 units/kg
    - INR >6, 50 units/kg
  - Or low fixed-dose option
    - 1000 units for any major bleed
    - 1500 units for intracranial hemorrhage
    - If 4F-PCC not available, use plasma 10-15 mL/kg
- Administer 4F-PCC 50 units/kg IV
- If 4F-PCC unavailable, consider aPCC 50 units/kg IV
- Consider activated charcoal for known recent ingestion (within 2-4 hours)

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Additional Committee Recommendations

- Target HGB ≥7 g/dL (unless CAD target ≥8) g/dL
- PLTs≥ 50K ; fibrinogen ≥ 100 mg/dL
- If ≥ 3 u PRBCS-massive transfusion protocol
- Early tranexamic acid for trauma in 1st 3 hours
- Consider desmopressin or cryoglobulin if uremic platelets
- In liver disease consider thromboelastography
- Platelet transfusion should not be used routinely in those on antiplatelet therapy

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Case

The patient undergoes urgent EGD which reveals a bleeding gastric ulcer. The ulcer is cauterized. He is started on high dose PPI. His BP improves to 115/80 and heart rate decreases to 90s. HGB remains steady at 9.5 ng/dL. Should he be restarted on anticoagulation and if so, when?
Considerations for Restarting Anticoagulation—Figure 4

**Critical site?** → NO
**High risk rebleed?** → YES
**Surgery planned?** → NO

DOES ≥1 OF THE FOLLOWING CLINICAL INDICATIONS APPLY?
- PAF with CHA₂DS-VASc score ≥1
- Temporary indication of OAC: post-surgical prophylaxis, OAC after an anterior MI without LV thrombus, recovered acute stress cardiomyopathy (e.g., Takotsubo cardiomyopathy, first-time provoked DVT >3 months ago, bioprosthetic valve placement >3 months ago)

YES → Suggest discontinuing anticoagulation
NO →

DOES ≥1 OF THE FOLLOWING FACTORS APPLY?
- Bleed occurred in a critical site (see Table 1)
- Patient is at high risk of rebleeding or death/disability with rebleeding
- Surgical/evasive procedure planned
- After informed discussion, patient declines or does not wish to restart OAC at this time (see Table 7)

YES → Suggest delaying restarting anticoagulation (see Figure 6)
NO → Suggest restarting anticoagulation (see Figure 5)
## Indications for Anticoagulation with High Thromboembolic Risk - Table 6

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical valve prosthesis</td>
<td>- Mechanical valve + additional thrombotic considerations: AF, CHF, prior stroke/TIA</td>
</tr>
<tr>
<td></td>
<td>- Caged-ball or tilting disc aortic valve prosthesis</td>
</tr>
<tr>
<td></td>
<td>- Stroke/TIA within 6 months</td>
</tr>
<tr>
<td>AF</td>
<td>- AF with CHADS$_2$ score $\geq 4$ (or CHA$_2$DS$_2$-VASc score $\geq 6$)</td>
</tr>
<tr>
<td></td>
<td>- Stroke/TIA within 3 months</td>
</tr>
<tr>
<td></td>
<td>- Stroke risk $\geq 10%$ per year</td>
</tr>
<tr>
<td></td>
<td>- Rheumatic valve disease or mitral stenosis</td>
</tr>
<tr>
<td>VTE</td>
<td>- VTE within 3 months</td>
</tr>
<tr>
<td></td>
<td>- History of unprovoked or recurrent VTE</td>
</tr>
<tr>
<td></td>
<td>- Active cancer and history of cancer-associated VTE</td>
</tr>
</tbody>
</table>

Writing Committee et al. JACC 2017; j.jacc.2017.09.1085
Indications for Anticoagulation with High Thromboembolic Risk

<table>
<thead>
<tr>
<th>Prior thromboembolism with interruption of anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular or left atrial thrombus</td>
</tr>
<tr>
<td>Left ventricular assist device (LVAD)</td>
</tr>
</tbody>
</table>
Restarting Anticoagulation-Figure 5
Restarting Anticoagulation—Figure 5

- 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, antiarrhythmics such as amiodarone)

Suggest restarting anticoagulation

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)

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Case-Finale

The patient continues to do well with no signs of recurrent bleeding. The team discusses anticoagulation with GI, anticoagulation service and cardiology. It is decided that he should no longer be on antiplatelet therapy in ADDITION to full dose anticoagulation for his remote chronic stable CV disease and that he will resume anticoagulation with apixaban after 2-3 weeks at follow up with PCP, provided he remains stable without recurrent bleeding.
Other Scenarios

• What if this patient reported 3 days of hematuria?
• What if this patient presented with intracranial hemorrhage?
Consider holding in non-majour bleed if:

Underlying bleeding risk changed
New ↓ hepatic or renal function
AC is supratherapeutic
Procedure needed
Baseline severe anemia requiring transfusion
Active medical issue – demand ischemia
Concern for slow critical site bleed

Reconsider concomitant antiplatelet
Factors to Consider in Delaying Restart of Anticoagulation-Figure 6

- Is the patient willing to restart OAC at this time?
  - Yes: See Table 2 for guidance on clinician/patient discussion.
  - No: Is an urgent surgical/invasive procedure planned?
    - Yes: Suggest delaying restarting anticoagulation until procedure performed.
    - No: Did bleeding occur in a critical site (see Table 1)?
      - Yes: Has sufficient time passed to consider restarting anticoagulation?
        - Yes: Suggest restarting anticoagulation (see Figure 5).
        - No: Is the patient at high risk of rebleeding?
          - Yes: Is the patient at low/moderate thrombotic risk?
            - Yes: 1. Use clinical judgment and consider patient values/preference.
              2. If indicated, start temporary anticoagulation for VTE prophylaxis.
              3. Delay OAC for a short duration and reassess.
            - No: Is there evidence of bleeding?
              - Yes: Reassess the severity of the bleed (see Figure 2).
              - No: Is there evidence of bleeding?
                - Yes: Ensure plan for follow-up on a specific date to address restarting anticoagulation.
                - No: Consider non-pharmacologic therapies.
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