Current Trends in Anticoagulation – Impact in IR

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Current Trends In Anticoagulation ~ Impact In Interventional Radiology

- Disclosure of conflict of interest
- How it begins
- What’s trending in anticoagulant usage
- Impact in Interventional Radiology
- Putting it all together
Objectives

At the end of this presentation you would

- be aware of the policy guidelines regarding hemostasis
- review the coagulation cascade and its impact on procedures
- distinguish what's trending in terms of anticoagulation
- be aware of the recommendations/guidelines on hemostasis from SIR
I do not have any affiliation (financial or otherwise) with a pharmaceutical, biotechnology, medical device, or research equipment/supply industry.

I am a Registered Nurse at the University Health Network (UHN), Toronto, and work in the Joint Department of Medical Imaging (JDMI).
Let’s start from this point

**Bleeding** - A major complication of IR procedures

**Policy (UHN)**
- Invasive procedures must have adequate protection against bleeding,
- minimizing the risk of discontinuing antiplatelet or anticoagulant therapies,
- exposing the patient to blood products

*Policy and Procedural Manual Clinical - Peri-procedural Hemostasis (Nov. 2014)*
A procedure begins

- A puncture is made through the skin
- A blood vessel is punctured
- This initiates the coagulation cascade

Now, what is this cascade all about??
The coagulation cascade

- Helps understand the coagulation status of patients
- Assists in determining the possibility of post procedural bleeding
- Helps to unravel the complexities of coagulation
## Components of the coagulation cascade

<table>
<thead>
<tr>
<th>Factor/number</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>Forms clot (fibrin)</td>
</tr>
<tr>
<td>Tissue factor</td>
<td>Co-factor of VIIa (formerly known as factor III)</td>
</tr>
<tr>
<td>Calcium</td>
<td>Required for coagulation factors to bind to phospholipid (formerly known as factor IV)</td>
</tr>
<tr>
<td>Antihemophilic factor A</td>
<td>Co-factor of IX</td>
</tr>
<tr>
<td>Christmas factor</td>
<td>Activates X: forms complex with factor VIII</td>
</tr>
<tr>
<td>Stuart-Prower factor</td>
<td>Activates II: forms prothrombinase complex with factor V</td>
</tr>
<tr>
<td>Plasma thromboplastin antecedent</td>
<td>Activates IX</td>
</tr>
<tr>
<td>Hageman factor</td>
<td>Activates factor XI, VII and prekallikrein</td>
</tr>
<tr>
<td>Fibrin-stabilizing factor</td>
<td>Crosslinks fibrin</td>
</tr>
<tr>
<td>von Willebrand factor</td>
<td>Binds to VIII, mediates platelet adhesion</td>
</tr>
<tr>
<td>Factors IV,V,VI, Fletcher factor, Protein C &amp; S, FitzGerald factor</td>
<td>All participates in the cascade</td>
</tr>
</tbody>
</table>
The main role of the tissue factor pathway is to generate a "thrombin burst", a process by which thrombin, the most important constituent of the coagulation cascade in terms of its feedback activation roles, is released very rapidly.
Coagulation Tests Done

- **Platelet count**
  known or suspected thrombocytopenia

- **PT/International Normalized Ratio (INR)**

  **Interpretation of PT/INR and PTT in Patients with a Bleeding or Clotting Syndrome**

<table>
<thead>
<tr>
<th>PT/INR RESULT</th>
<th>PTT RESULT</th>
<th>EXAMPLES OF CONDITIONS THAT MAY BE PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged</td>
<td>Normal</td>
<td>Liver disease, decreased vitamin K, decreased or defective factor VII, chronic low-grade disseminated intravascular coagulation (DIC), anticoagulation drug (warfarin) therapy, bile duct obstruction</td>
</tr>
<tr>
<td>Normal</td>
<td>Prolonged</td>
<td>Decreased or defective factor VIII, IX, or XI, von Willebrand disease (severe type), presence of lupus anticoagulant, Christmas disease, hemophilia</td>
</tr>
<tr>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Decreased or defective factor I, II, V or X, severe liver disease, acute DIC</td>
</tr>
</tbody>
</table>

- **Activated Clotting Time – post procedure**

  *used when high doses of heparin is used during procedure and rapid result is needed to monitor patient The ACT is measured in seconds: the longer the time to clot, the higher the degree of clotting inhibition.*
Did you that ~~~~ All these affect blood coagulation

- Beer
- Ginger
- Spinach
- Fish oils
- Green tea
- Celery
- Cranberry
- Ginseng
- Alcohol
- Hormone replacement therapy

- Niacin
- Pomegranates
- Grape fruit
- Onion
- Soya bean products
- St. John’s wort
- Grapefruit interferes with some anticoagulant drugs
- Some antibiotics
- Beef or pork liver
# Anticoagulants now encountered in Interventional Radiology

- **Heparin or heparinized saline**
  - lock & flush for central venous catheters (CVCs). potentiates the action of antithrombin III by accelerating inhibition of factor Xa. Therapeutic response is monitored by aPTT, which is targeted at 1.5–2.5 times normal. Platelet count should be measured post administration to check for HIT. Reversal agent is Protamine

- **Sodium Citrate 4% w/v Solution**
  - flush or lock for CVCs in HIT patients – Chelates Calcium ions

- **Normal saline**
  - as a lock for CVCs

- **Warfarin**
  - antagonizes the production of the vitamin K– dependent extrinsic pathway clotting factors (II, VII, IX, X) and protein C and S in the liver. The clinical effect is measured by the INR.

- **Low Molecular Weight Heparin**
  - inhibits factor Xa, and is administered subcutaneously and often dosed by weight. LMWH is poorly reversible with protamine and therefore does not prolong the aPTT, nor does it affect the INR.

- **Fondaparinux**
  - acts as an indirect selective inhibitor of factor Xa, similar to LMWH. heparin-induced thrombocytopenia is substantially lower compared with unfractionated heparin and LMWH, excreted by the kidneys.

- **Direct Thrombin Inhibitors**
  - directly inhibits the enzyme thrombin, producing a more predictable anticoagulant response than heparin. Examples are Dabigatran, Hirudin, Argatroban. There is no known reversal drug for DTIs but a trial drug is in Phase 3 of its development,
  - Reversal of Dabigatran Anticoagulant – Idarucizumab

- **Aspirin**
  - irreversibly inhibits the cyclooxygenase enzymes, inhibits platelet aggregation

- **Clopidogrel (Plavix)**
  - Thienopyridines that irreversibly inhibit adenosine-diphosphate receptors, decreasing platelet aggregation. Usually ordered for 3 months post carotid angioplasty

- **NSAIDs (Ibuprofen, diclofenac)**
  - reversibly inhibit cyclooxygenase, inhibiting Thromboxane A2, decreasing platelet aggregation.
<table>
<thead>
<tr>
<th>Hemostatic agents used in IR</th>
<th>Fibrin sealant Tisseal, Crosseal</th>
<th>Recombinant Factor VIIa</th>
<th>Vitamin K (Phytonadione)</th>
<th>Platelets</th>
<th>Cryoprecipitate</th>
<th>Desmopressin (DDAVP)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>containing fibrinogen, factor XIII, fibronectin, and fibrinolysis inhibitors (aprotinin), and in the other is thrombin and calcium chloride. When combined, thrombin becomes activated and activates the clotting cascade and enhances conversion of fibrinogen to fibrin. Absorbed from the body within 5–10 days.</td>
<td>used in patients with hemophilia with inhibitors to factor VIII or in severe, non–hemophilia-related bleeding such as acute trauma.</td>
<td>managing elevated INRs and/or clinical bleeding in patients receiving oral anticoagulation.</td>
<td>used in the setting of thrombocytopenia or platelet dysfunction.</td>
<td>cryoprecipitate will typically increase fibrinogen level.</td>
<td>enhance the plasma levels of factor VIII and von Willebrand factor.</td>
</tr>
<tr>
<td>Gelatin (Gelfoam, Surgifoam)</td>
<td>The gelatin is able to absorb more than 45x its weight, providing a matrix for the clotting cascade in addition to providing a physical barrier. Absorbed by the body in 4–6 weeks.</td>
<td></td>
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</tr>
<tr>
<td>Fresh Frozen Plasma</td>
<td>contains plasma proteins, including coagulation factors, that can be administered to correct coagulopathies secondary to clotting factor deficiency.</td>
<td></td>
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</tr>
<tr>
<td>Protamine</td>
<td>may be used in emergency situations when rapid reversal of heparin is needed.</td>
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<tr>
<td>Desmopressin (DDAVP)</td>
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</table>
A history of congenital or acquired bleeding diathesis, unexplained bleeding tendency or abnormalities in coagulation testing is required and referred for further investigation. UHN Policy - Periprocedural Hemostasis

Assessment and preparation of the patient before imaging-guided procedures will vary according to the procedure to be performed in conjunction with a comprehensive assessment of the patient's comorbidities. SIR Standards of Practice Committee

Although image guidance is likely to make minimally invasive procedures more accurate, for example, in their ability to target lesions or to put effector devices such as needles or catheters in optimal position, by their very nature these procedures preclude the operator from direct visualization of post procedure bleeding

- **Category/Group 1**: Procedures with Low Risk of Bleeding, Easily Detected and Controllable
- **Category/Group 2**: Procedures with Moderate Risk of Bleeding
- **Category/Group 3**: Procedures with Significant Bleeding Risk, Difficult to Detect or Control
## Category / Group One - Low Risk of Bleeding

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Preprocedure Laboratory Testing</th>
<th>Management</th>
</tr>
</thead>
</table>
| **Vascular** | • INR: Routinely recommended for patients receiving warfarin anticoagulation or with known or suspected liver disease  
• Activated PTT: Routinely recommended for patients receiving intravenous unfractionated heparin.  
• Platelet count: Not routinely recommended  
• Hematocrit: Not routinely recommended | • INR >2.0: Threshold for treatment (i.e., FFP, vitamin K)  
• PTT: No consensus  
• Hematocrit: No recommended threshold for transfusion  
• Platelets: Transfusion recommended for counts <50,000/UL  
• Plavix: Do not withhold  
• Aspirin: Do not withhold  
• Low-molecular-weight heparin (therapeutic dose): Withhold one dose before procedure  
• DDAVP: Not indicated |
| **Nonvascular** | • Drainage catheter exchange (biliary, nephrostomy, abscess catheter)  
• Thoracentesis  
• Paracentesis  
• Superficial aspiration and biopsy (excludes intra-thoracic or intra-abdominal sites): thyroid, superficial lymph node  
• Superficial abscess drainage | |

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- Hematocrit: No recommended threshold for transfusion
- Platelets: Transfusion recommended for counts <50,000/UL
- Plavix: Do not withhold
- Aspirin: Do not withhold
- Low-molecular-weight heparin (therapeutic dose): Withhold one dose before procedure
- DDAVP: Not indicated
Category/Group Two – Moderate Risk of Bleeding

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Preprocedure Laboratory Testing</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>• INR: Recommended • Activated PTT: Recommended in patients receiving intravenous unfractionated heparin • Platelet count: Not routinely recommended • Hematocrit: Not routinely recommended</td>
<td>• INR: Correct if above 1.5 or 1.7 at UHN. Consider vit.K if more than 24 hours or greater prior to procedure. Consider transfusion of FFP for patients with hepatic coagulopathy • Activated PTT: No consensus (trend toward correcting for values &gt;1.5 times control, 73%) • PTT &gt; 45 seconds and patient on Heparin consider Protamine usage • Platelets: Transfusion recommended for counts &lt;50,000/uL • Hematocrit: No recommended threshold for transfusion • Plavix: Withhold for 5 days before procedure • Aspirin: Do not withhold • Low-molecular-weight heparin (therapeutic dose): Withhold one dose before procedure • DDAVP: not indicated</td>
</tr>
<tr>
<td>Vascular</td>
<td>• INR: Recommended • Activated PTT: Recommended in patients receiving intravenous unfractionated heparin • Platelet count: Not routinely recommended • Hematocrit: Not routinely recommended</td>
<td>• INR: Correct if above 1.5 or 1.7 at UHN. Consider vit.K if more than 24 hours or greater prior to procedure. Consider transfusion of FFP for patients with hepatic coagulopathy • Activated PTT: No consensus (trend toward correcting for values &gt;1.5 times control, 73%) • PTT &gt; 45 seconds and patient on Heparin consider Protamine usage • Platelets: Transfusion recommended for counts &lt;50,000/uL • Hematocrit: No recommended threshold for transfusion • Plavix: Withhold for 5 days before procedure • Aspirin: Do not withhold • Low-molecular-weight heparin (therapeutic dose): Withhold one dose before procedure • DDAVP: not indicated</td>
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<tr>
<td>Vascular</td>
<td>• INR: Recommended • Activated PTT: Recommended in patients receiving intravenous unfractionated heparin • Platelet count: Not routinely recommended • Hematocrit: Not routinely recommended</td>
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- **Vascular**
  - Angiography, arterial intervention with access size up to 7 F
  - Venous interventions
  - Chemoembolization
  - Uterine fibroid embolization
  - Trans-jugular liver biopsy
  - Tunneled central venous catheter
  - Subcutaneous port device
- **Nonvascular**
  - Intra-abdominal, chest wall, or retroperitoneal abscess drainage or biopsy
  - Lung biopsy
  - Trans-abdominal liver biopsy (core needle)
  - Percutaneous cholecystostomy
  - Gastrostomy tube: initial placement
  - Radiofrequency ablation: straightforward
  - Spine procedures (vertebroplasty, kyphoplasty, lumbar puncture, epidural injection, facet block)
## Category/Group Three – Significant Bleeding Risk
Discontinuation of Anticoagulants / Antiplatelet Medications

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</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>• INR: Routinely recommended</td>
<td>• INR: Correct if above 1.5 (95% consensus)</td>
</tr>
<tr>
<td>Trans-jugular intrahepatic porto-systemic shunt</td>
<td>• Activated PTT: Routinely recommended in patients receiving intravenous unfractionated heparin infusion. No consensus on patients not receiving heparin</td>
<td>• Activated PTT: Stop or reverse heparin for values &gt;1.5 times control</td>
</tr>
<tr>
<td>Nonvascular</td>
<td>• Platelet count: Routinely recommended</td>
<td>• Platelets &lt;50,000: Transfuse</td>
</tr>
<tr>
<td>Renal biopsy</td>
<td>• Hematocrit: Routinely recommended</td>
<td>• Hematocrit: No recommended threshold for transfusion</td>
</tr>
<tr>
<td>Biliary interventions (new tract)</td>
<td></td>
<td>• Plavix: Withhold for 5 days before procedure</td>
</tr>
<tr>
<td>Nephrostomy tube placement</td>
<td></td>
<td>• Aspirin: Withhold for 5 days</td>
</tr>
<tr>
<td>Radiofrequency ablation: complex</td>
<td></td>
<td>• Fractionated heparin: withhold for 24 hours or up to two doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DDAVP: Not indicated</td>
</tr>
</tbody>
</table>
Important to note
Patients on DTIs
ex.Dabigatran, Rivaroxaban, Apixaban

Patients receiving oral Direct Thrombin Inhibitors

- Routine blood tests are not informative in these patients
- Consult Hematology prior to start of procedure
- Creatinine clearance should be done as DTIs excreted by kidneys
- Hold DTI as directed if CrCl < 30 and not > 50 in last 2 to 5 days
Bleeding disorders: Hemorrhagic diatheses

Excessive bleeding can result from

1. increased fragility of vessels,
2. platelet deficiency or dysfunction,
3. derangement of coagulation,
4. combinations of these
### History

- **Vessel Wall Abnormality**
- **Thrombocytopenia**
- **Defective Platelet Function**

<table>
<thead>
<tr>
<th>Vessel Wall</th>
<th>Reduced Platelet Count</th>
<th>Defective Platelet Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated Intravascular Coagulation</td>
<td>Generalized diseases of bone marrow</td>
<td>Hemophilia Factor VIII deficiency</td>
</tr>
<tr>
<td>Cushing Syndrome (excessive Corticosteroid production)</td>
<td>Immunologic destruction, ex. HIT, may occur in approx. 5% of patients receiving heparin</td>
<td>Von Willebrand Disease VIII-vWF complex deficiency</td>
</tr>
<tr>
<td>Drug Reactions ex. vasculitis</td>
<td>Dilutional, massive blood transfusions or bad storage of blood</td>
<td>Christmas Disease Factor IX deficiency</td>
</tr>
<tr>
<td><strong>Platelet count, bleeding time, INR are usually normal.</strong></td>
<td><strong>Platelet count decreased, INR may be normal</strong></td>
<td><strong>Platelet count may be normal, INR increased</strong></td>
</tr>
</tbody>
</table>
Note that ****

Needs to be mentioned

- CBC is required on all patients 30 days prior to procedure
- INR is required on all patients 30 days prior to procedure if not receiving heparin, no liver disease, no suspicion of coagulopathy or sepsis
- aPTT or heparin level is required on patients receiving UFH, bivalirudin or argatroban (DTIs)
- Serum creatinine is required on patients receiving LMWH or fondaparinux, oral DTIs e.g. dabigatran or oral Xa inhibitors e.g. rivaroxaban
Platelet aggregation
Coagulation Cascade
References

- Discussion with Pharmacy personnel
- Discussions with Interventional Radiologists
- Policy & Procedure Manual, University Health Network
- Recommendations/Guidelines, Society of Interventional Radiologists
- Online Google resources