Major Bleeding After Percutaneous Image-Guided Biopsies: Prevention and Management

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All three authors have no conflicts of interest to declare.
Outline

1. To review the prevalence and risk factors for major bleeding during percutaneous image-guided biopsy procedures.
2. To review pre-procedural major bleed prevention strategies, including abnormal coagulation parameter monitoring and anti-coagulant management.
3. To review optimal strategies for intra-procedural management of major bleeding.
4. To review appropriate post-biopsy monitoring procedures.
Definition and Incidence

- Major bleeding is defined as a bleed requiring blood transfusion or intervention for hemostasis.

- Following percutaneous biopsy of solid organs, the incidence of major bleeding ranges from 0.1-8.3%.

Major Bleeding:
Procedural Risk Factors

- Location of biopsy is one of the most significant predictors of bleeding risk.
- The Society of Interventional Radiology has classified biopsy procedures into the following risk categories:

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Medium Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial aspiration and biopsy (ie bone, thyroid)</td>
<td>Intrabdominal biopsy</td>
<td>Renal biopsy</td>
</tr>
<tr>
<td></td>
<td>Chest wall biopsy</td>
<td></td>
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<td></td>
<td>Retroperitoneal biopsy</td>
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<tr>
<td></td>
<td>Lung biopsy</td>
<td></td>
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<tr>
<td></td>
<td>Transabdominal liver biopsy</td>
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<tr>
<td></td>
<td>Spinal biopsy</td>
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</table>

Major Bleeding: Procedural Risk Factors

- Deep biopsies (ie retroperitoneal) and biopsies of highly vascular organs/lesions (ie kidney) increase risk of major bleeding.

- Additionally, risk also increases with the use of cutting needles, larger gauge biopsy needles, and the number of needle passes.

Major Bleeding: Patient Risk Factors

- The attending radiologist must be aware of patient risk factors for major bleeding prior to performing the biopsy. Appropriate risk stratification of patients pre-procedurally can optimize the biopsy approach and patient safety.

- Much research has been done to elucidate patient predictors of major bleeding in percutaneous liver and renal biopsies.
Major Bleeding: Patient Risk Factors

- A retrospective review of 629 liver biopsies revealed mycobacterioses, prophylactic prebiopsy platelet substitution, acute hepatic failure, same day heparin administration, advanced cirrhosis, steroid use and lymphoma to all be significant predictors of major bleeding on multivariate regression analysis.

- A meta-analysis of renal biopsies revealed high serum creatinine (>175 umol/L), acute kidney injury, female gender and increasing age as significant predictors of major bleeding.

Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedure: an evidence based review. Transfusion 2005;45(9):1413-25.
Pre-Procedural Screening

- A careful history and physical examination should be performed prior to the biopsy.

- Care must be taken to identify any prior bleeding events, known bleeding disorders, liver disease, renal disease, family history of bleeding disorders, and current medications as well as over the counter/herbal supplements.

Guideline Recommendations on Coagulation Parameter Screening

- For low risk biopsies:
  - Only patients receiving warfarin or with suspected liver disease require INR screening.
  - aPTT in those receiving unfractionated heparin.
- For moderate risk biopsies:
  - All patients should receive INR screening.
  - aPTT in those receiving unfractionated heparin.
- For high risk biopsies:
  - All patients should receive INR screening
  - aPTT in those receiving unfractionated heparin.
  - All patients should have platelets and hematocrit levels checked.

Guideline Recommendations on Coagulation Parameter Correction

- For low risk biopsies:
  - INR >2 should receive FFP or vitamin K until INR <2.
  - Platelet transfusions in those with less than 50000/umol.

- For moderate and high risk biopsies:
  - INR should be corrected with FFP or vitamin K to <1.5.
  - aPTT should be corrected to <1.5 times upper limit of normal.
  - Platelet transfusions in those with less than 50000/umol.

Utility of Coagulation Parameters?

• Despite emphasis in societal guidelines, little evidence routine INR screening and reversal

• A large meta-analysis demonstrated INR screening does not predict major bleeding in open surgical and image-guided biopsies.

• Similarly, routine correction of INR with FFP in surgical populations has not been shown to reduce the risk of major bleeding.

### Pre-Procedural Medication Management

<table>
<thead>
<tr>
<th>Agent</th>
<th>Lab Monitoring</th>
<th>Reversal Agent</th>
<th>Last Dose – Procedure Interval</th>
<th>Post-Procedural Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>INR</td>
<td>Vitamin K +- FFP; 3 or 4-factor PCCs</td>
<td>Depends on INR, usually 1-8 days</td>
<td>Restart 24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>None – aPTT or thrombin time for substantial residual effect</td>
<td>None – consider factor VIII inhibitor bypass activity or recombinant VIIa, hemodialysis</td>
<td>CrCl: ≥50 ml/min – 1-2 days&lt;br&gt;CrCl: &lt;50 ml/min – 3-5 days</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>None - Prothrombin time or anti-factor Xa antibody to rule out substantial residual effect</td>
<td>None – consider PCCs</td>
<td>Normal renal function: ≥1 day&lt;br&gt;CrCl: 60 – 90 ml/min – 2 days&lt;br&gt;CrCl: 30 – 59 ml/min – 3 days&lt;br&gt;CrCl: 15 – 29 ml/min – 4 days</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Apixaban</td>
<td>None – anti-factor Xa antibody to rule out substantial residual effect</td>
<td>None – consider charcoal hemoperfusion or PCCs</td>
<td>CrCl: ≥60 ml/min – 1-2 days&lt;br&gt;CrCl: 50 – 59 ml/min – 3 days&lt;br&gt;CrCl: &lt;30 – 49 ml/min – 5 days</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
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INR - international normalized ratio, aPTT - activated partial thromboplastin time, FFP – fresh frozen plasma; PCC – prothrombin complex concentrates; LMWH – low molecular weight heparin; CrCl – creatinine clearance

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<tr>
<td>Desirudin</td>
<td>aPTT, thrombin time, ecarin clotting time – normal value rules out clinically relevant residual effect</td>
<td>None</td>
<td>2 hrs</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Aspirin</td>
<td>None – consider platelet function tests</td>
<td>Platelet transfusion</td>
<td>Low or moderate risk: None</td>
<td>Restart 24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Thienopyridine agents (clopidogrel, ticlopidine, prasugrel, ticagrelor)</td>
<td>None – consider platelet function tests</td>
<td>Consider platelet transfusion (limited efficacy)</td>
<td>Clopidogrel/ ticagrelor – 5 days Prasugrel – 7 days Ticlopidine – 10 – 14 days</td>
<td>Restart 24-48 hrs post procedure if hemostasis maintained</td>
</tr>
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<tr>
<td>Unfractionated Heparin</td>
<td>aPTT</td>
<td>Protamine sulfate</td>
<td>IV: 2-6 hrs, subcut: 12-24 hrs</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>LMWH</td>
<td>None common – anti-factor Xa antibody levels in select pts</td>
<td>Protamine sulfate (partial reversal only)</td>
<td>Low or moderate risk: 1 dose High risk: 24 hours</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>None currently</td>
<td>None – may use recombinant Factor VIIa in high risk pts with major bleed</td>
<td>36-48 hrs</td>
<td>Restart 12-24 hrs post procedure if hemostasis maintained</td>
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Intraprocedural Bleed Management

- Careful image-guided delineation of vascular structures prior to biopsy is critical in preventing bleeds.

- Continuous monitoring of vital signs throughout the procedure is important to identify significant bleeds.
Intraprocedural Bleed Management

- In the event of an obvious bleed, biopsy via a coaxial technique enables the physician to perform rapid biopsy tract embolization.

- Ultrasound directed physical compression can also be used to stop bleeding.
Post-Procedural Monitoring

- All patients should be monitored post-biopsy to ensure hemodynamic stability and rule out major bleeding.

- Unfortunately, little high quality evidence exists to guide specific durations and practice patterns around post-biopsy monitoring.
Post-Procedural Monitoring

- Current guidelines recommend liver biopsy patients are monitored for 3-6 hours post-biopsy.

- Following this, patients should be sent home with someone who can watch them for at least 24 hours to ensure continued stability.

Post-Procedural Monitoring

- Appropriate duration of monitoring in renal biopsy patients is even less clear.

- <8 hours of post-biopsy observation has been shown to miss up to 33% of major complications, including bleeding.

- Cases of delayed major bleeding have been reported as late as 15 days post-renal biopsy.

Conclusion

- Major bleeding following percutaneous image-guided biopsies is not uncommon.

- The radiologist performing the biopsy must consider various risk factors pre-procedurally.

- Rapid identification of bleeding events intra-procedurally and careful post-biopsy monitoring are critical towards ensuring patient safety.