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

Sean A. Kennedy MD

Lazar Milovanovic BASc

Mehran Midia MD, FRCPC

McMaster University

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%.

Gupta S et al. Quality improvement guidelines for percutaneous needle biopsy. J Vasc Interv Radiol 2010;21(7):969-975.

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:

Low Risk	Medium Risk	High Risk
Superficial aspiration and biopsy (ie bone, thyroid)	Intrabdominal biopsy Chest wall biopsy Retroperitoneal biopsy Lung biopsy Transabdominal liver biopsy Spinal biopsy	Renal biopsy

Patel IJ et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol 2012;23(6):727-36.

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.

Gupta S et al. Quality improvement guidelines for percutaneous needle biopsy. J Vasc Interv Radiol 2010;21(7): 969-975.

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 mycobacteriosis, 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-analaysis 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.
Terjung B et al. Bleeding complications after percutaneous liver biopsy: An analysis of risk factors. Digestion 2003;67(3):138-45.

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.

Patel IJ et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol 2012;23(6):727-36.

Guideline Recommendations on Coagulation Parameter Screening

- For low risk biopsies:
  - Only patients receving 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.

Patel IJ et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol 2012;23(6):727-36.

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.

Patel IJ et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol 2012;23(6):727-36.

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.

Ewe K. Bleeding after liver biopsy does not correlate with indices of peripheral coagulation. Dig Dis Sci 1981;26(5):1161-80.
Yang L et al. Is FFP clinically effective? An update of a systematic review of randomized controlled trials. Transfusion 2012;52(8):

Pre-Procedural Medication Management

Agent	Lab Monitoring	Reversal Agent	Last Dose – Procedure Interval	Post-Procedure Management
Warfarin	INR	Vitamin K +- FFP; 3 or 4-factor PCCs	Depends on INR, usually 1-8 days	Restart 24 hrs post procedure if hemostasis maintained
Dabigatran	None – aPTT or thrombin time for substantial residual effect	None – consider factor VIII inhibitor bypass activity or recombinant VIIa, hemodialysis	CrCl: ≥50 ml/min – 1-2 days CrCl: <50 ml/min – 3-5 days	Restart 12-24 hrs post procedure if hemostasis maintained
Rivaroxaban	None - Prothrombin time or anti-factor Xa antibody to rule out substantial residual effect	None – consider PCCs	Normal renal function: ≥1 day CrCl: 60 – 90 ml/min – 2 days CrCl: 30 – 59 ml/min – 3 days CrCl: 15 – 29 ml/min – 4 days	Restart 12-24 hrs post procedure if hemostasis maintained
Apixaban	None – anti-factor Xa antibody to rule out substantial residual effect	None – consider charcoal hemoperfusion or PCCs	CrCl: ≥60 ml/min – 1-2 days CrCl: 50 – 59 ml/min – 3 days CrCl: <30 – 49 ml/min – 5 days	Restart 12-24 hrs post procedure if hemostasis maintained

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

Baron TH et al. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013;368(22):2113-24)

Pre-Procedural Medication Management

Agent	Lab Monitoring	Reversal Agent	Last Dose – Procedure Interval	Post-Procedure Management
Desirudin	aPTT, thrombin time, ecarin clotting time – normal value rules out clinically relevant residual effect	None	2 hrs	Restart 12-24 hrs post procedure if hemostasis maintained
Aspirin	None – consider platelet function tests	Platelet transfusion	Low or moderate risk: None High risk: 5 days	Restart 24 hrs post procedure if hemostasis maintained
Thienopyridine agents (clopidogrel, ticlopidine, prasugrel, ticagrelor)	None – consider platelet function tests	Consider platelet transfusion (limited efficacy)	Clopidogrel/ ticagrelor – 5 days Prasugrel – 7 days Ticlopidine – 10 – 14 days	Restart 24-48 hrs post procedure if hemostasis maintained

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

Baron TH et al. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013;368(22):2113-24)

Pre-Procedural Medication Management

Agent	Lab Monitoring	Reversal Agent	Last Dose – Procedure Interval	Post-Procedure Management
Unfractionated Heparin	aPTT	Protamine sulfate	IV: 2-6 hrs, subcut: 12-24 hrs	Restart 12-24 hrs post procedure if hemostasis maintained
LMWH	None common – anti-factor Xa antibody levels in select pts	Protamine sulfate (partial reversal only)	Low or moderate risk: 1 dose High risk: 24 hours	Restart 12-24 hrs post procedure if hemostasis maintained
Fondaparinux	None currently	None – may use recombinant Factor VIIa in high risk pts with major bleed	36-48 hrs	Restart 12-24 hrs post procedure if hemostasis maintained

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

Baron TH et al. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013;368(22):2113-24)

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.

Rockey DC et al. American Association for the Study of Liver Diseases. Liver biopsy. Hepatology 2009;49(3):1017-44.

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.

Whittier WL, Korbert SM. Timing of complications in percutaneous renal biopsy. J Am Soc Nephrol 2004;15(1):142-7.

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.