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Ultrasound-Guided Thrombin Injection for the Treatment of Bleeding Following Kidney and Liver Biopsies

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The purpose of this study was to describe the technique and outcomes of percutaneous thrombin injection into the superficial aspect of actively bleeding liver and kidney biopsy tracks identified with color Doppler ultrasound with the aim of hemorrhage termination. After percutaneous thrombin injection, 15/16 (94%) patients did not require further intervention. Ultrasound-guided thrombin injection into the superficial site of active bleeding is an effective technique for terminating bleeding in the immediate post-procedure period following kidney and liver biopsies and should be considered if active bleeding persists on color Doppler after ≥30 minutes of compression and observation.

Key Words—complication; hemorrhage; kidney biopsy; liver biopsy; thrombin

Percutaneous liver and kidney biopsies provide critical diagnostic information and are relatively safe to perform.1–5 The efficacy and safety are primarily due to refined techniques and real-time imaging under ultrasound guidance.6–13 Thus, most renal and hepatic biopsies have a low complication rate.1,2,8 Although rare, post-biopsy hemorrhage, which typically occurs shortly after biopsy, may require intervention and can be fatal.1,14 Doppler sonography is a valuable tool for detecting biopsy-associated vascular complications, including active extravasation. Active bleeding is detected as linear color flow along the biopsy needle path and has been referred to as a “patent track” sign.15 A patent track can be identified immediately after the biopsy and monitored over time. Typically the patent track will resolve spontaneously or with compression. When it does not resolve, the patient is at increased risk of developing a significant hematoma, pain, hypotension, and reduction in serum hemoglobin concentration. Most techniques aimed at stopping post-biopsy hemorrhage rely on angiographic embolization and occur after signs and symptom develop when the patient is being observed in the post procedure recovery area.

Early detection of persistent active hemorrhage offers an opportunity to intervene before clinical manifestations arise and before large hematomas develop. A previous case report described successful treatment of a patient with active extravasation following renal biopsy using ultrasound-guided injection of thrombin in the patent track.16 We have used a similar technique in selected patients following liver and kidney biopsies. The purpose of this study was to analyze the technical aspects and outcomes associated with our procedures.
Materials and Methods

An imaging database search (Montage, Nuance) identified 16 patients (7 male and 9 female, average age 50 ± 17 years) that had undergone liver or kidney biopsy with active extravasation treated by ultrasound-guided thrombin injection. These patients were treated between September 2010 and May 2019. Institutional Review Board (IRB) approved chart review with waiver of consent. Percutaneous renal and liver biopsies were performed under sonographic guidance by a fellowship trained attending radiologist or a radiology resident or abdominal imaging fellow under the supervision of an attending radiologist. All biopsies were performed using free-hand technique. After percutaneous kidney or liver biopsy was performed, the area of the biopsy was surveyed for a perirenal or perihepatic hematoma using grayscale ultrasound and a patent biopsy track using color Doppler. We recorded the biopsy indication, needle gauge, number of passes, duration of manual compression prior to thrombin injection, amount of thrombin injected, location of injection, and initial and delayed success of injection.

In most cases, firm compression was applied after identification of a hematoma or patent biopsy track, and after compression, the biopsy area was again surveyed. Ultrasound-guided thrombin injection was performed in patients with patent biopsy tracks that persisted despite prolonged compression.

All statistical analysis was performed with GraphPad Prism version 8 (GraphPad Software, LaJolla, CA). Unless specified otherwise, all data are represented as mean ± standard deviation.

Results

The study included 4 patients who had undergone a liver biopsy and 12 who had undergone a renal biopsy. Focal lesions were biopsied in 1/4 livers and 1/12 kidneys, and the remaining were random parenchymal biopsies. All kidney biopsies were performed on native kidneys. Liver biopsies were performed on 3 native livers and 1 transplant liver. A total of 3 attending physicians performed ultrasound-guided thrombin injection, and the majority of patients (13/16) were treated by one attending. All 16 patients underwent biopsy with 18-gauge needles. A 17-gauge coaxial introducer needle was used in two kidney biopsies. Two patients underwent additional kidney biopsy with 16-gauge needles. The average number of passes was 1.6 ± 0.8 and length of the throw was 2.5 ± 0.7 cm.

Figure 1 illustrates the site of thrombin injection. Patent biopsy tracks were readily identified in all subjects after percutaneous biopsy of the kidney (Figure 2) or liver (Figure 3). Perinephric (Figure 2C) or perihepatic (Figure 3D) hematomas were documented in 12/16 (75%) patients.
Compression time was reported in the radiology report after identification of a patent track in 15/16 (94%), lasting on average 27 ± 13 minutes.

Human thrombin (concentration 1000 U/mL) was delivered in 1000 U (1 mL) aliquots in 14/16 cases. In the remaining cases, it was delivered in aliquots of 400–500 U. Spinal needles were used for all of the injections and the needle gauge was 25, 22, and 20 in 1, 13, and 2 cases, respectively. In 14/16 cases, the thrombin was injected at the organ capsule directly at the site of where the patent biopsy track exited the organ. In 3/16 cases, a pseudoaneurysm was confirmed with ultrasound; two of these cases the pseudoaneurysm alone was targeted and in one the pseudoaneurysm and biopsy track organ exit site were both targeted. The average total thrombin delivered was 2,300 ± 1500 U (range = 400–5000 U).

Thrombin injection terminated Doppler detectable hemorrhage in 15/16 patients (94%). In one patient, two discrete patent tracks developed following a native kidney biopsy. The larger was successfully thrombosed with thrombin injection, but the smaller track was patent with a suspected associated pseudoaneurysm. Angiography confirmed a persistent pseudoaneurysm and arteriovenous fistula, which were both treated with coil embolization.

Discussion

Complications after kidney and liver biopsies can be life threatening, but are rare. A meta-analysis investigating complications after native kidney biopsy surveyed 34 studies (9474 biopsies) and reported that transfusion was required in only 0.9% of cases.17 Mirroring these findings, a meta-analysis of complications following percutaneous liver biopsy examined 51 studies (12,481 patients), and found that only 45 patients developed bleeding that required transfusion.18 Despite rarity, post-biopsy hemorrhage poses a diagnostic and therapeutic quandary, which is compounded by frequent lack of post-procedural imaging in asymptomatic patients.19 Furthermore, when imaging is obtained, a hematoma alone is not a reliable predictor of a complication that requires intervention, particularly after renal biopsies.20
Transarterial embolization provides definitive treatment for hemorrhage after liver and kidney biopsy and is an attractive adjunct to medical resuscitation in patients with bleeding. Angiographic embolization, typically reserved for patients with clinical evidence of bleeding, offers the ability to confirm the presence of active extravasation, visualize the source of bleeding, identify presence of pseudoaneurysm and arteriovenous fistula, and subsequently perform targeted embolization. It is highly effective at treating severe acute renal hemorrhage, be it iatrogenic or otherwise. A study, which incorporated various embolic materials, including metallic coils, polyvinyl alcohol (PVA) particles, gel-foam, and n-butyl cyanoacrylate (NBCA) iodized oil found that transarterial embolization is highly effective and technical success was reported in all 40 embolization procedures. Angiographic embolization for post liver biopsy hemorrhage is also highly effective.

Although angiographic techniques are highly effective, non-angiographic techniques are also effective, and offer a potentially less invasive alternative for preventing hemorrhage-related morbidity associated with renal or liver biopsy. For example, introduction of hemostatic matrix, such as gelatin matrix, via coaxial needles used for percutaneous kidney and liver biopsies has been reported to be an effective measure to prevent hemorrhage. It has been demonstrated that percutaneous “plugging” of biopsy tracks with PVA foam may help prevent post liver biopsy hemorrhage. But this technique is used prophylactically, is only possible when coaxial needles are employed, and is not designed to treat active hemorrhage.

Figure 3. Forty-three-year-old female with alcoholic cirrhosis status post liver transplant presents with elevated transaminases. Serial sonographic images of a transplanted liver were obtained and thrombin injection terminated patent liver biopsy track blood flow. A, Core needle biopsy of liver parenchyma. B, Flow within a patent biopsy track indicated with color Doppler at 19 minutes following the biopsy. C, Spectral analysis confirms a venous signal. D, Biopsy track flow termination after injection of a 1000 U thrombin aliquot. Cursors are measuring a perihepatic hematoma.
Percutaneous approaches for addressing post-biopsy complication are, in general, straightforward and cost-effective. Ultrasound-guided percutaneous microwave ablation has been shown to successfully control hemorrhage after liver biopsy. Although intriguing, access to percutaneous microwave ablation equipment may be limited compared to alternative techniques. Direct intraoperative gelatin-thrombin hemostatic matrix injection into patent renal biopsy tracks without ultrasound guidance was shown to be efficacious in two cases of hemorrhage refractory to angioembolization. Thrombin is a particularly attractive agent for addressing vascular complications given its position in the clotting cascade.

Thrombin is a serine protease responsible for converting fibrinogen to fibrin and has demonstrated utility in several applications involving vascular complication. Thrombin has been shown to be effective in endoscopic management of bleeding gastric varices, catheterization-related arterial perforation, and for percutaneous management in post aortic repair endoleak. Percutaneous thrombin injection is also an effective treatment for vascular access-related femoral artery pseudoaneurysm, and has been reported to be sufficient for treating intrarenal and extracapsular pseudoaneurysm. In these cases, intervention via thrombin injection relied on targeting of a specific abnormality.

In some cases, after percutaneous solid organ biopsy, a patent biopsy track can be used to detect active extravasation and serve as a potential target for thrombin-mediated intervention. In the majority of cases, the patent biopsy track will resolve spontaneously and require no intervention. A patent track that persists for 5 minutes after percutaneous liver biopsy was found to be strongly predictive of clinically significant post biopsy bleeding. If a patent color flow track is identified after native kidney biopsy there is a reported increased risk for major complications, particularly in the setting of low glomerular filtration rate. An association has also been identified between a patent biopsy track (referred to as the color Doppler “line sign”) and hematomas in patients following radiofrequency ablation of liver and kidney tumors. Furthermore, a case report documents successful termination of bleeding using ultrasound guided thrombin injection into the site of active arterial hemorrhage after a renal mass biopsy. In the current study, we describe ultrasound-guided thrombin injection of patent biopsy tracks after kidney or liver biopsies in a series of 16 patients. Injecting 2 or 3 aliquots of 1000 U human thrombin in 1 mL volumes at the superficial aspect of a patent biopsy track was sufficient for terminating liver and kidney post-biopsy hemorrhage in 15 patients. A perinephric pseudoaneurysm, if identified, can also be targeted to terminate hemorrhage.

These results suggest that ultrasound guided thrombin injection offers a simple and relatively non-invasive approach for management of hemorrhage when a track is identified. However, there are limitations to our analysis. Assessing the efficacy of the technique proposed in the current study is somewhat limited given the relatively small number of patients studied, and this reflects the few circumstances when intervention was needed after a percutaneous liver or kidney biopsy. Without having a control group, it is uncertain how many patients would have had spontaneous resolution of hemorrhage and no clinical symptoms without intervention. We chose to inject in the perinephric or perihepatic space immediately adjacent to the biopsy track to avoid the possibility of direct intravascular injections. This approach required
higher doses of thrombin than what is typically required for peripheral pseudoaneurysms. It is possible that subcapsular injections would have been equally successful with lower doses of thrombin. Subcapsular injections would be necessary in patients with perihepatic ascites, but we did not encounter any such cases in this patient cohort. Finally, this technique also requires relatively precise needle positioning to be effective and may not be possible when sonographic visualization is limited.

Our results show that the majority of patients (15/16) with persistent post biopsy hemorrhage can be treated immediately with thrombin injection when the hematoma is small and before clinical symptoms develop. Based on our experience with thrombin injections, we have developed an algorithm for post-biopsy hemorrhage management (Figure 4). Post biopsy Doppler is performed in all cases after 5 minutes of compression. If a patent biopsy track is identified, continued firm intermittent compression for up to 30 minutes should be performed with periodic reassessment of hematoma and biopsy track patency. If a patent track persists after prolonged compression, then ultrasound-guided serial injection of 1000 U aliquots of thrombin should be performed to the superficial aspect of the biopsy track until Doppler detectable hemorrhage resolves. We believe that this approach will prevent more severe complications associated with post-liver or kidney biopsy hemorrhage. Escalation to endovascular or surgical treatment should be considered for biopsy tracks that remain patent after targeted thrombin injection.

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References


