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Acute and Delayed Bleeding Requiring Embolization after Image-Guided Liver Biopsy in Patients with Cancer

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Abstract

Purpose—To report incidence of acute versus delayed presentations of bleeding requiring embolization after focal liver biopsy, in correlation with angiographic findings and treatment success rates. The available literature will be reviewed as well.

Materials and Methods—HIPAA-compliant, institutional review board approved retrospective review of 2180 consecutive patients undergoing 2335 targeted liver biopsies at a tertiary care cancer center. Hepatic arterial embolization episodes within 30 days from biopsy were identified via Radiology PACS. Electronic medical record review was performed for indication of embolization and post-embolization clinical course.

Results—The incidence of post-biopsy bleeding requiring embolization was 0.5% (12/2335 biopsies). In those with bleeding, 1/12 (8%) had no hepatic arterial findings at angiography. Angiographic hepatic arterial findings resolved after embolization in 11/11 patients (100% technical success). Bleeding ceased after embolization in 10/12 patients (83% clinical success). Complications were seen in 2/12 (17%) patients: cholecystitis and hepatic infarct respectively. Delayed presentation of bleeding (defined as >24 hours post-biopsy) occurred in 5/12 (42%) patients; the longest latency was 12 days.

Conclusion—The overall incidence of bleeding requiring embolization in our population was 0.5%. This complication rate compares favorably to the 0% to 4.2% (median 0.29%) rate quoted in

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the available, heterogeneous, literature on this topic. Delayed presentation occurred in almost half of patients. Arterial embolization carries excellent technical and clinical success rates.

Keywords

Image-Guided Biopsy; Hemorrhage; Embolization, Therapeutic; Radiology, Interventional

Introduction

Patients with cancer in the United States are living longer [1, 2]. Surveillance imaging performed during survivorship will detect suspicious liver lesions prompting biopsy for diagnostic and prognostic purposes. Additionally, as “personalized medicine” becomes a reality, tumor biopsy is becoming increasingly important to allow molecular analysis of tumor cells. Bleeding is the main clinically significant complication of this procedure. Significant bleeding may necessitate arterial embolization. An understanding of the risks associated with imaging guided needle biopsy is essential for medical and surgical oncologists to weigh the costs and benefits in deciding whether or not to recommend a biopsy, for interventional radiologists to present accurate risk estimates to their patients and for patients to determine whether or not to proceed with a recommended procedure. We hope that our experience will help provide data useful in those pursuits.

Materials and Methods

Patient Population

Institutional Review Board approval was obtained. All patients were contained within a single electronic medical record system belonging to the institution, a tertiary care dedicated cancer hospital providing longitudinal patient care. The electronic medical record and PACS systems were retrospectively queried for all patients who underwent imaging guided percutaneous liver biopsy followed within 30 days by arterial embolization between January 2004 and December 2010. Demographic and laboratory data were obtained. Tumor biology, number of passes, and needle gauge, were not consistently documented in the retrospective cohort and this information could not be ascertained for all patients. Patients in whom embolization was performed to treat a tumor, or to treat bleeding related to subsequent biliary drainage were excluded from this analysis. For the patients who did have hepatic embolization performed for bleeding related to their biopsy, biopsy and embolization technique and images were reviewed, and clinical presentation and course was assessed.

Biopsy Technique

Pre-biopsy bloodwork was performed within 30 days for all patients. The institutional permissive coagulation parameters were INR <1.5 and platelet count >50,000. The institutional guidelines regarding holding anticoagulants were consistent with the Society of Interventional Radiology guidelines on this topic. Patients outside of these parameters either underwent transfusion or biopsy at the discretion of the operator. Imaging guidance and post-biopsy imaging (CT/ultrasound), biopsy device (needle gauge, coaxial vs bare introduction), and type of biopsy (core vs. fine needle) were determined based on clinical indication and operator preference. All patients had some type of post-procedure imaging;

nearly all had post procedure CT images through the level of the biopsy. Post-biopsy monitoring lasted at least 2 hours. Signs and symptoms of hemorrhage at any time after biopsy (pain, hypotension, tachycardia) prompted consideration for CT to evaluate for hemorrhage or other adverse event.

Diagnostic Angiography and Embolization

Embolization was considered in patients with symptomatic hemorrhage and/or significant findings on CT. Decision for angiography was based on clinical acuity and operator preference. Decision for embolization, selectivity of embolization and choice of embolic agent (gelfoam/coils/PVA/particles) were based on angiographic findings and operator preference.

Results

In total, 2335 percutaneous focal liver biopsies were identified for 2180 patients during the evaluation period.

Bleeding requiring embolization occurred after 12/2335 of biopsies (0.5% incidence). (Table 1a, 1b, 1c, Figures 1–3) Angiograms demonstrated hepatic arterial findings in 11/12 (92%) patients including arteriovenous fistula (5/12), pseudoaneurysm (2/12), extravasation or blush (6/12). One patient had no angiographic findings (1/12). This patient presented 12 days after biopsy with a 5.7-point hemoglobin drop and CT evidence of subcapsular and intrahepatic hematoma.

Hepatic arterial findings resolved after embolization in 11/11 patients (100% technical success). Bleeding ceased after finding-directed or empiric embolization in 10/12 patients (83% clinical success). One patient had persistent slow bleeding for 8 days after embolization and was considered a clinical failure. The other patient received a blood transfusion after embolization but did not require further treatment. The one patient (1/12) with no angiographic abnormality underwent empiric lobar embolization without complication, and had resulting in clinical success. Complications were seen in 2/12 (17%) patients: cholecystitis and hepatic infarct respectively. Delayed presentation (defined as >24 hours post-biopsy) occurred in 5/12 (42%) patients; the longest latency was 12 days. Of the remaining 7 patients, four (4/12) presented immediately while the other 3/12 presented at 3, 5, and 24 hours respectively.

In five separate outlier patients, an embolization was performed within the 30 day period but the embolization was unrelated to biopsy (spontaneous tumor hemorrhage remote to the biopsy site in 3/5 patients, bleeding related to biliary drainage catheter in 2/5 patients).

Patients who presented with delayed bleeding did not exhibit unifying clinical characteristics nor characteristics consistently diverging them from patients with acute presentation. (Table 1a, 1b, 1c) For example, the patients with delayed bleeding underwent biopsy with a variety of needle sizes for lesions of a variety of locations with various angiographic findings. (Table 1a–c)

Discussion

Personalized medicine will be driven by molecular analysis of biosamples such as tumor tissue. It will require more material than needed for conventional tumor diagnosis [3] and may require multiple biopsies over the course of treatment for research protocols or to look for new mutations to explain a change in response to therapy or a difference in response of a particular tumor relative to others in the same patient, even in the same organ [3, 4].

The risks and benefits must be weighed prior to recommending or agreeing, to undergo, any procedure; the risks must therefore be known and discussed. The incidence of hemorrhage requiring embolization in our study, one of the largest such series to date, was 0.5% [5]. This value is comparable to the relevant literature on this topic from the last thirty years where the rate of major bleeding ranges from 0% to 24% with a median of 0.29% (Table 2). Of note, the institutional guidelines followed in this study are concordant with the Society of Interventional Radiology guidelines for bleeding parameter management (INR < 1.5; Platelets > 50,000). [6]

The diagnostic yield of angiography performed with intent to embolize was 11/12 (92%). One patient (1/12) did not have angiographic findings (Table 1). Despite the lack of angiographic findings, the patient's clinical improvement after lobar hepatic arterial embolization points to a likely spasmodic culprit artery as opposed to a hepatic or portal vein laceration.

Embolization was effective and safe. Angiographic abnormalities were effectively managed with embolization in 11/11 patients (100% technical success). Bleeding ceased after finding-directed or empiric embolization in 10/12 patients (83% clinical success). Complications (cholecystitis and hepatic infarct respectively) were seen in 2/12 (17%) patients.

It is interesting that so many of the patients who bled and required embolization presented with delayed bleeding. We defined "delayed presentation" as more than 24 hours post-biopsy in keeping with the literature on this topic [7]. Among patients with bleeding requiring embolization, delayed presentation was seen in 5/12 patients (42%) with the longest latency lasting 12 days. The diagnosis was established immediately in 4/12 cases (33%), and within 24 hours in 7/12 patients (59%). Specific to delayed bleeding episodes, Terjung *et al* [8] reported an incidence 70% (439/629 patients), which continues to be the highest reported rate of delayed bleeding in this setting. At our institution, the standard monitoring period is approximately 2 hours post-biopsy. Piccinino studied this duration and reported that 61% of complications are found within two hours after biopsy and 96% within 24 hours [9].

Limitations

Retrospective reviews carry certain limitations. We report only on patients who underwent embolization at our institution, a tertiary care, cancer hospital in a major metropolitan area. It is possible that some of our patients who bled after discharge presented to, and were treated at, their local hospital. Further, we do not know the number of patients who bled enough to require transfusion, but did not get embolized. Our general practice is to embolize

patients if we are aware that they have bled significantly. However, it is conceivable that a patient who re-presented after discharge post biopsy might have been managed by the referring service without notifying the Interventional Radiology service of the admission or the complication. It is possible as well that the number of patients receiving intervention may potentially be underestimated due to patient wishes for DNR or supportive care. For example, in their study of 15,181 patients (including focal and non-focal biopsies), Atwell [10] found that all three patients who died due to hemorrhagic complications after liver biopsy had care withheld or withdrawn at the request of the family.

Still, despite these limitations, we have found these data to be useful in our practice when helping patients and referring clinicians weigh the risks and benefits of proceeding with imaging guided needle biopsy of the liver.

Conclusions

The overall incidence of bleeding requiring embolization in our population was 0.5%. This complication rate compares favorably to the 0% to 4.2% (median 0.29%) rate quoted in the available, heterogeneous, literature on this topic. Delayed presentation occurred in almost half of patients. Arterial embolization carries excellent technical and clinical success rates.

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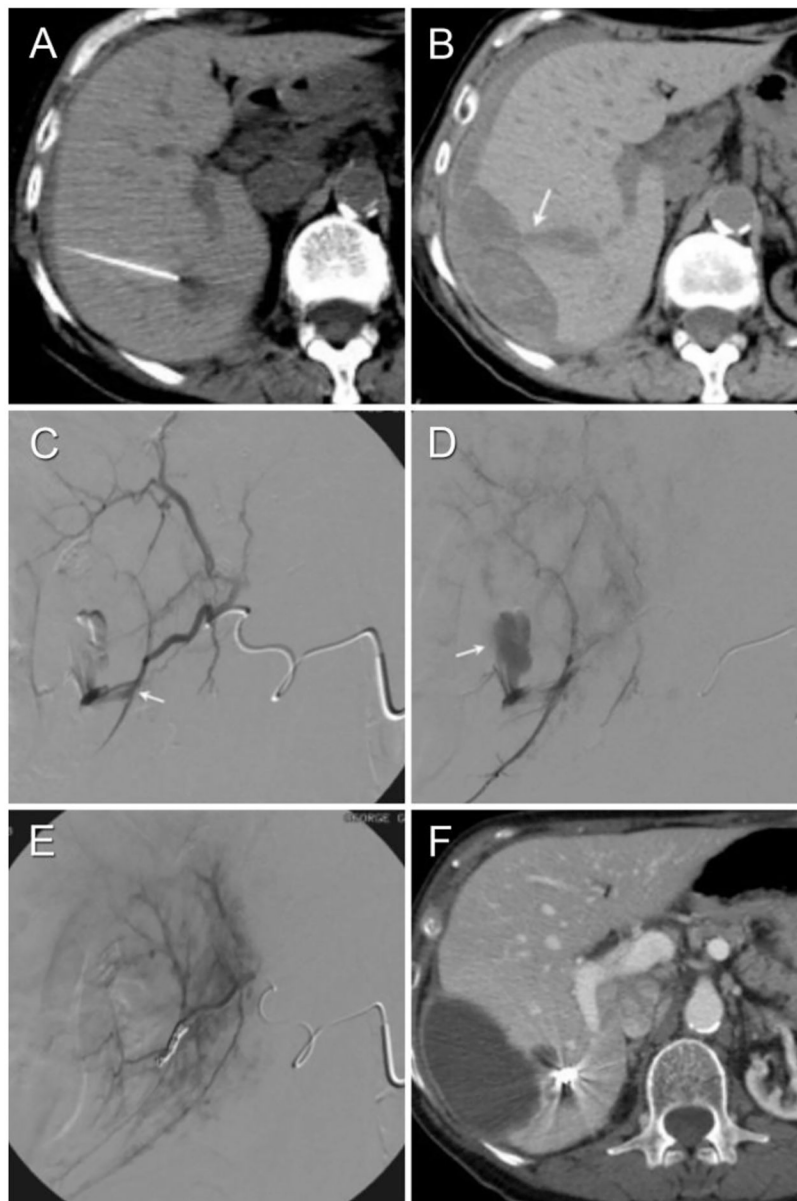


Figure 1. 69-year-old female with history of breast and ovary cancer presents with multiple liver lesions. (Patient #8 in Tables 1a–c) (A) Non-enhanced interventional CT shows target lesion and biopsy needle vector and tip. There is a thin crescentic subcapsular hematoma laterally. (B) Follow-up non-enhanced CT performed 3 hours post-biopsy demonstrates enlarged subcapsular hematoma. (C,D) Diagnostic arteriogram demonstrates extravasation from right posterior hepatic artery branch. (E) Post-embolization arteriogram demonstrates coil mass and no further extravasation (technical success). (F) Contrast-enhanced axial CT performed 4 weeks post-biopsy demonstrates expected evolutionary changes of subcapsular hematoma, as well as radiodense coil mass. Note the location of the coil mass relative to needle tip in Figure 1a.

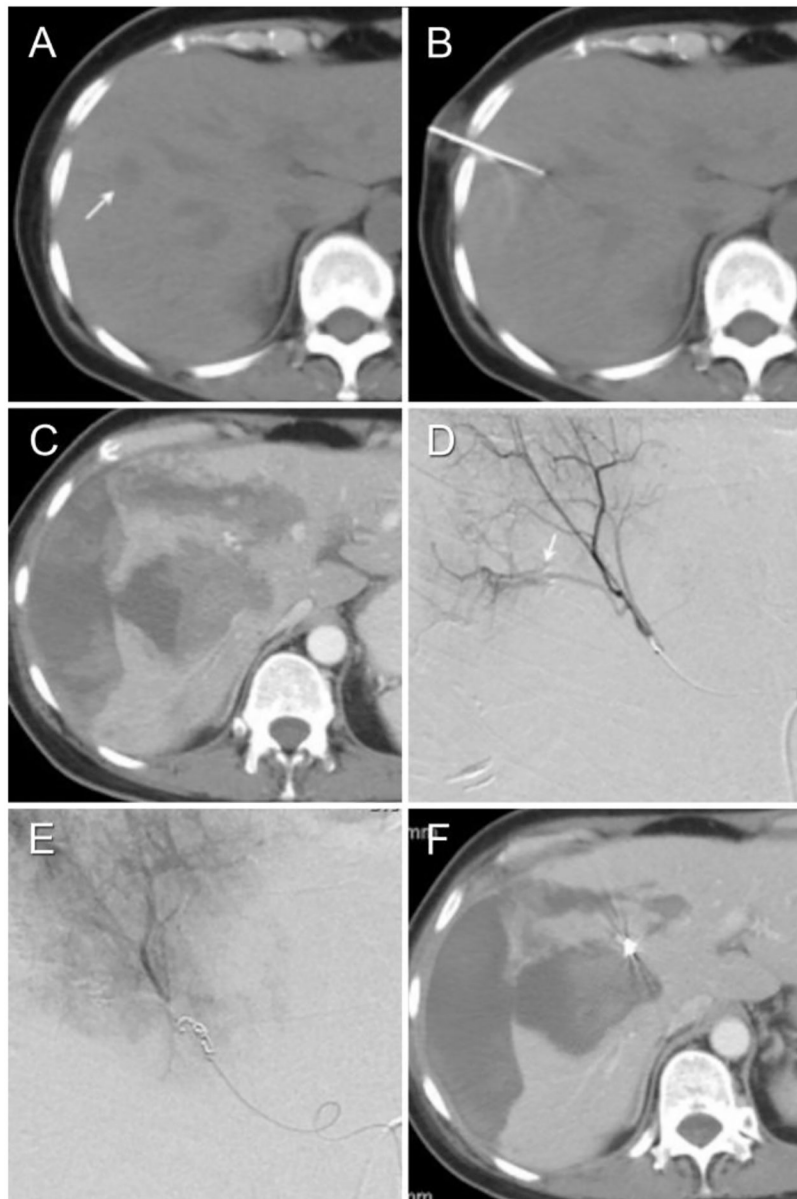


Figure 2.

A 55-year-old female with history of leukemia presents with new liver lesions. (Patient #1 in Tables 1a–c). (A) Pre-biopsy non-enhanced axial CT shows target lesion. (B) Non-enhanced interventional CT shows target lesion and biopsy needle vector and tip. (C) Contrast-enhanced axial CT on day 2 post-biopsy to evaluate for dyspnea and dropping hematocrit demonstrates a large peri-hepatic and intrahepatic hematoma. (D) Diagnostic arteriogram shows arterio-venous fistula but no extravasation. (E) Post-embolization arteriogram after intra-arterial injection of 100 µm PVA to stasis followed by two 3 mm microcoils. The arteriovenous fistula is no longer evident (technical success). (F) Contrast-enhanced axial CT on day 7 post-biopsy week later demonstrates expected evolutionary changes of subcapsular hematoma, as well as radiodense coil mass.

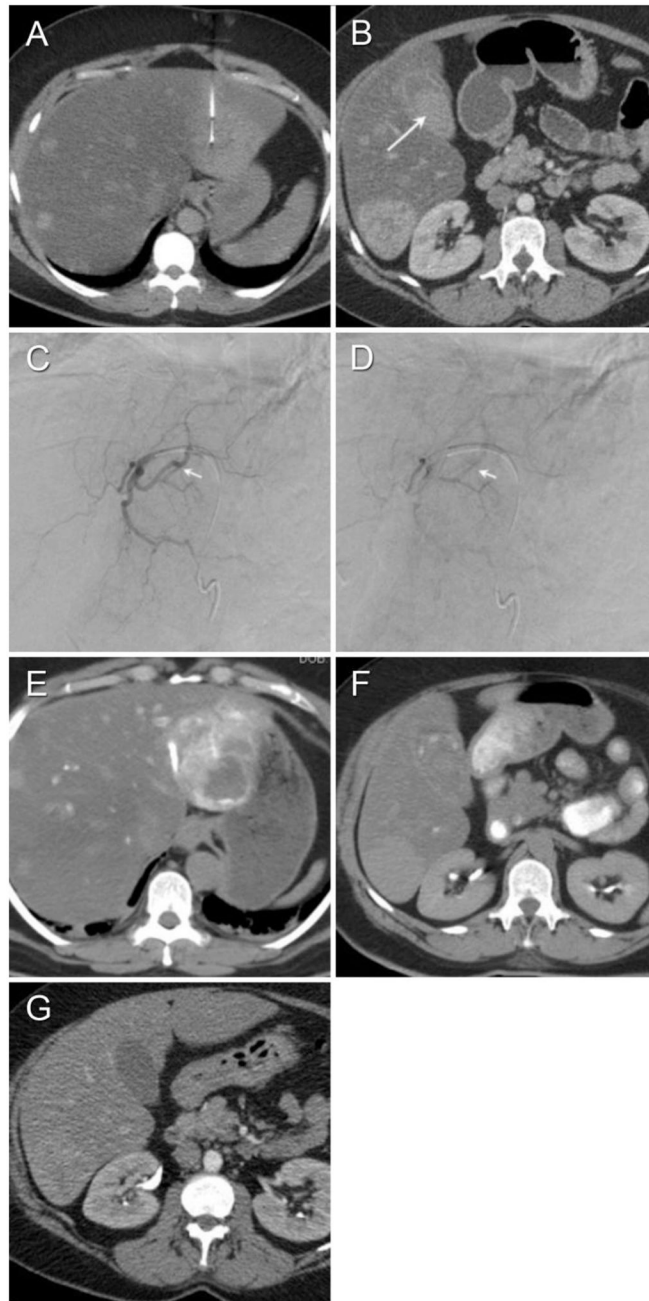


Figure 3.

A 51-year-old female with presents with multiple liver lesions (Patient #10 in Tables 1a–c). (A) Non-enhanced interventional CT shows target lesion and biopsy needle vector and tip. (B) Contrast-enhanced axial CT on day 4 post-biopsy to evaluate severe right upper quadrant pain demonstrates hyperdense gallbladder contents compatible with hemorrhage. (C, D) Diagnostic arteriogram performed on day 14 post-biopsy for severe persistent pain shows arterio-venous fistula without active extravasation. The left hepatic artery was embolized to stasis with 6 cc 100–300 μ m embospheres and 1 cc 100 μ m PVA (not shown). (E, F) Non-enhanced post-embolization CT hyperdensity of the tumor (indicating successful

embolization of the tumor) as well as the lumen of the gallbladder, duodenum and stomach (indicating hemobilia with enterogastric reflux). (G) Contrast-enhanced axial CT performed 21 days post-biopsy shows interval evolution and near-complete resolution of subcapsular hematoma.

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Clinical-Interventional debriefing analysis for all patients with major hemorrhage after focal liver biopsy. HCC= hepatocellular carcinoma.

Table 1a.

Patient	Age (yrs)	Gender	Biopsy indication (Resulting diagnosis)	Underlying liver disease	Hgb/Hct/Plt/PTT/INR	Tumor Size (cm)	Couinaud Segment
1	55	F	Leukemia, new liver lesion (no malignant cells)	None	8.9/26.5/276/34.2/1.1 morning of procedure	1.2	VIII
2	44	F	Lymphoma, enlarging liver lesion (lymphoma)	None	13.5/40/107/45.4/1.09 morning of procedure	6.1	VIII
3	45	F	Remote history of breast cancer; new liver lesions (breast cancer metastasis)	Diffuse liver metastases with pseudocirrhosis	12.1/36.9/151/31.9/1.05 4 days before procedure	6.1	II
4	59	M	Hepatitis B, cirrhosis with multiple liver lesions (granulomatous process)	Hepatitis B and cirrhosis	12.7/39.1/138/31.4/1.33 22 days before procedure	3	V
5	63	F	Breast cancer with liver lesions (breast cancer metastasis)	None	9.0/27/140/24.1/0.99 12 days before procedure	1.5	IVa
6	65	F	Lymphoma with multiple diffuse liver lesions (HCC)	Hepatitis C, idiopathic thrombocytopenic purpura	8.6/27.8/37/29.8/1.0 morning of procedure	11	V
7	56	M	Rectum cancer, liver lesions (rectum cancer metastasis)	None	8.8/28.9/344/26.2/1.12 16 days before procedure	10.2	III
8	68	F	Breast cancer, ovary cancer, multiple liver lesions (ovary cancer metastasis)	None	11.3/32.7/234/28.7/0.94 2 days before procedure	1.7	VI
9	65	M	Prostate cancer, liver lesions (prostate cancer metastasis)	Diffuse liver metastases	12.9/39.4/244/30.2/0.96 17 days before procedure	8.3	VI
10	51	F	Liver lesions, diagnosis (HCC)	Fatty liver	10.8/35.4/314/24.8/0.94 13 days before procedure	6.8	V
11	22	M	Adrenal cancer, liver lesions (adrenal cancer metastasis)	None	14.9/45.7/456/31.5/0.99 3 days before procedure	1.8	VIII
12	61	F	Hepatitis B, liver lesion indeterminate at imaging (well-differentiated hepatic neoplasm, likely adenoma)	Hepatitis B, cirrhosis, portal vein thrombus	10.2/31.1/152/30/15 1 day before procedure	3.5	V/VI

Table 1b.

Clinical-Interventional debriefing analysis for all patients who underwent ultrasound-guided focal liver biopsy and developed hemorrhage requiring embolization. MAC=monitored anesthesia care. CECT=contrast enhanced computed tomography. NECT = Non-enhanced computed tomography. US-ultrasound.

Patient	Needle Size (coaxial)	Needle passes	Tissue Samples	Minimal Transparenchymal Trajectory (mm)	Imaging Guidance	Anesthesia	Imaging findings at completion of study	Time to post-biopsy hemorrhage diagnosis (hours/days)	Symptoms leading to hemorrhage diagnosis	Hemoglobin drop before embolization performed	Imaging findings at hemorrhage diagnosis
1	20-22G	3	2	26	CT	MAC	No bleeding	1 d	Dyspnea	1.9	CECT: Intrahepatic and subcapsular hematoma; hemoperitoneum; right pleural effusion
2	19.5G	1	1	22	CT	MAC	No bleeding	5 d	Pain	4.1	CECT: Perihepatic hematoma, intratumoral bleeding; hemoperitoneum
3	18G	1	1	0	CT	MAC	No bleeding	3 h	Pain, hypotension	4	NECT: Perihepatic hematoma, hemoperitoneum
4	19.5G	4	3	30	CT	MAC	No bleeding	8 d	Fever, pain	0.2	CECT: Subcapsular hematoma, right pleural effusion and ascites
5	20G(19G)	5	3	12	US	MAC	Subcapsular hematoma	Immediate	Pain, hypotension	2.3	NECT: Large subcapsular hematoma
6	20G	1	1	3	CT	MAC	No bleeding	5 h	Hypotension	2.9	CECT: Intra- and perihepatic hematoma, pseudoaneurysm, hemoperitoneum
7	18G(17G)	2	1	18	CT	MAC	Subcapsular hematoma	Immediate	Orthostatic hypotension	1.3	NECT: Perihepatic hematoma, hemoperitoneum
8	22G(20G)	4	4	43	CT	MAC	Subcapsular hematoma	Immediate	Pain, hypotension	3.6	NECT: Subcapsular and intrahepatic hematoma, hemoperitoneum
9	19.5G	1	1	15	CT/US	MAC	Free fluid in pelvis	Immediate	Hypotension	2.7	NECT: Hemoperitoneum
10	18G	2	1	0	CT	MAC	Subcapsular hematoma	4 d	Pain	3.7	NECT: Hemobilia in the gallbladder

Patient	Needle Size (coaxial)	Needle passes	Tissue Samples	Minimal Transparenchymal Trajectory (mm)	Imaging Guidance	Anesthesia	Imaging findings at completion of study	Time to post-biopsy hemorrhage diagnosis (hours/days)	Symptoms leading to hemorrhage diagnosis	Hemoglobin drop before embolization performed	Imaging findings at hemorrhage diagnosis
11	22G	2	2	3	CT	MAC	No bleeding	12 d	Pain	5.7	NECT: Subcapsular and intra hepatic hematoma
12	18G(17G)	1	2	26	CT	MAC	No bleeding	10 d	Abdominal distension, hypotension	3.5	CECT: Hemoperitoneum, extravasation, pleural effusion

Clinical-Interventional debriefing analysis for all patients who underwent ultrasound-guided focal liver biopsy and developed hemorrhage requiring embolization. PVA=polyvinyl alcohol particles. AVF = Arterial-Venous fistula. PSA = Pseudoaneurysm

Table 1c.

Patient	Angiography findings	Embolization materials	Catheter position	Result
1	AVF	100 µm PVA, microcoils	Segmental (focal / sub-selective not possible)	Effective
2	Extravasation	40–120 µm microspheres, PVA, microcoils	Segmental, lobar (focal / sub-selective not possible)	Effective
3	AVF, PSA	500–700 µm microspheres, microcoils	Focal sub-selective/subsegmental	Effective
4	AVF	300 µm PVA, microcoils	Focal sub-selective and segmental	Effective
5	AVF	300–500 µm PVA	Lobar	Effective
6	PSA, hypervascular tumor	50 µm PVA, microcoils	Focal sub-selective and subsegmental	Effective
7	Transient blush	Gelfoam particles and slurry	Lobar	Effective
8	AVF, Extravasation	Microcoils	Focal sub-selective	Effective
9	Transient blush	Gelfoam particles	Sectoral	Post-embolization transfusion was given for hemoglobin drop by 1 point.
10	Hepatic arterial-biliary fistula	100–300 µm microspheres, 100 µm PVA	Lobar	Persistent slow bleeding for 8 days after embolization.
11	None	50 µm PVA	Lobar	Effective
12	Extravasation	Coils, 300–500 µm PVA	Sectoral	Effective

Table 2.

Review of the literature regarding major bleeding after focal image-guided liver biopsy.

Year	Patient Population	Number of Focal Liver Biopsies	Core vs FNA/Gauge/Passes	Image Guidance/Tract Embolized?	Permissive Coagulative Parameters	Bleeding Requiring Intervention (IR/surgery)	Bleeding Requiring Transfusion	Bleeding Not Requiring Transfusion or Intervention	Overall Major Hemorrhage Rate
Luening [11]	510	510	FNA and core/14-21 gauge/3-4 passes	CT/Not specified	Inclusion parameters not specified	0	1	0	0% (0/510)
Zins [12]	72	24	Core/18 Gauge/1-2 passes	US/Gelatin and Thrombin	Inclusion parameters for focal biopsy patients not specified	1 patient died of hemorrhage; specific treatments not reported			4.2% (1/24)
Little [13]	476	296	18-20G/1-3 passes	277 US and 19 CT/Not reported	Plt >50K PT <15 PTT <45	8 US 2 CT	15 US 1 CT	0	3.4% (10/296)
Riemann [14]	321	47	Core/18g or 20g/2 Passes	US/Not reported	Quicktime >50% Plt >50K	0	1	0	0% (0/47)
Giorgio [15]	12,962	16,648	2320 19G Core; 14,328 22G FNA/ not reported	US/Not reported	Plt >45K INR <1.7 Held anticoagulants 1 week prior, aspirin 2-3 days prior	0	0	36/16,648	0% (0/16,648)
Terjung [16]	629	100	Core/Menghini (Gauge not reported)/Not reported	US/Not reported	INR <1.4 Plt >50K	1 patient died of hemorrhage; specific treatments not reported			1% (1/100)
Kim [17]	352	201	Core/10-18 Gauge/2 passes usually	US/Not specified	Inclusion parameters not specified	1	1	0	0.5% (1/20)
El-Osta [18]	155	46	Core/18g/not reported	CT vs US, exact number not specified /Not reported	Inclusion parameters not specified	0	0	0	0% (0/46)
Westheim [19]	275 Pediatric Patients	25	Not Specified/18-22 gauge/1-8 passes	US/Not specified	Inclusion parameters not specified	1	5	0	4% (1/25)
Aribas [20]	1300	1300	Core and FNA/up to 20G/Four or less	US/Not Specified	Inclusion parameters not specified	1	0	Not specified	0.08% (1/1300)
Median rate of major hemorrhage across all major studies in the last 30 years:									0.29%