

A Study on the Safety of Liver Biopsy Inpatients with Von Willebrand's Disease

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Abstract

Objectives: Liver biopsy remains the gold standard for diagnosis of chronic liver diseases. Outpatient percutaneous biopsy is generally safe with a mortality rate of 0.17% and hospitalization rate for bleeding of 3%. Von Willebrand disease (vWD) syndrome is the most common inherited hematological disorder with a prevalence of 1% - 3% globally. We sought to study whether vWD increases the risk of bleeding for liver biopsies. **Methods:** All patients (n = 120) who underwent outpatient percutaneous liver biopsies from 1997 to 2007 were analyzed. Demographics, PT/INR, platelet count, vW antigen and ristocetin induced platelet aggregation were studied. **Results:** No vWD patients had major bleeding that required transfusion, hospitalization or surgery but 9 (75%) had minor local bleeding and all had ecchymosis, which resolved spontaneously within 24 hours. **Conclusions:** Patients with vW factor deficiency can undergo percutaneous liver biopsy without major bleeding. Minor bleeding may occur at a slightly higher rate. vWD is not a contraindication to percutaneous liver biopsy.

Keywords

Liver Biopsy, vW Disease, Safety, Complications

1. Introduction

Direct visual documentation of liver disease in its entirety, from aberrant architecture to cytopathology, made

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possibly through biopsy, is an invaluable tool in the clinical armamentarium of the hepatologist. This modality is currently in ubiquitous use for the diagnosis, staging, prognosis and management of a range of infectious, metabolic, autoimmune conditions as well as peri- and post-transplant surveillance. Although newer non-invasive-liver assessment modalities such as transient elastography and MR elastography are making their debut in clinical practice, such novelties are unlikely to replace completely liver biopsy as the gold standard, in the foreseeable future [1]. This invasive procedure is still the mainstay along with its associated hazards, affecting morbidity & mortality. Performance of outpatient percutaneous liver biopsies is drifting away from clinicians towards interventional radiologists for enhanced safety and reduced complications.

Transjugular liver biopsy as compared with percutaneous liver biopsy (PCLB) in an outpatient setting is by far a safer approach in patients with coagulopathies [2]-[4]. Von Willebrand's disease (vWD) is the most common inherited bleeding disorder, affecting 1 - 3 percent of the global population [5]. There are no data published to date, on the safety of PCLB in patients with vWD.

The objective of our study was to evaluate the safety of PCLB in vWD. We performed a retrospective analysis of PCLBs for hemorrhagic complications (local hematoma, intraabdominal hemorrhage, hemorrhagic shock requiring hospitalization, blood transfusion requirements and surgical intervention). Outpatient PCLBs are generally regarded safe with a mortality rate of 0.17% and hospitalization rate for bleeding of 3% [6] [7]. However, there is paucity of published evidence on the risk of hemorrhage and the spectrum of hemorrhagic complications in patients with different types of vWD undergoing PCLB.

2. Objectives

The objectives of our study were to determine the prevalence of vWD in patients undergoing liver biopsy as well as the safety of liver biopsy in these patients who had vWD.

3. Methods

A retrospective study of patients (n = 120) who underwent PCLB in an outpatient setting, as part of a community-based practice from 1997 to 2007, was performed following appropriate institutional board review and approval.

The following medications were withheld for at least 5 days pre-PCBL: anti-platelet drugs (ASA, clopidogrel or NSAIDs) or anti-coagulants (warfarin, unfractionated heparin, LMWH or Xa inhibitors) and subsequently resumed 48 hours post-PCBL when it was deemed clinically safe.

Specific patient populations known to confound the study results were excluded, such as those with:

- Prior known coagulation diathesis (Hemophilia, factor VIII deficiencies)
- Familial history of significant bleeding diathesis
- AV malformations
- Collagen vascular diseases
- Congestive heart failure
- Chronic kidney disease or those on dialysis

A single clinician used a uniform standard technique to carry out the PCBLs [8]. Patients were placed in supine position semi-reclined at 30 degrees and sonography was used to locate the optimal biopsy site [9]. Using an aseptic technique the skin, underlying intercostal spaces as well as the liver capsule were infiltrated with 2% lignocaine. PCBL was performed using a spring-loaded Tru-Cut liver biopsy needle (Max-Core, BARD®) which was entered in the mid-axillary line, through 7th or the 8th intercostal space. No more than 3 passes were made, each lasting less than 1 sec through the liver parenchyma, with a cooperative patient holding breath in full expiration.

Post-PCBL, patients were instructed to turn over in a right lateral position for 2 hours and monitored for adverse events.

Following discharge from hospital, all patients included in the study returned to be tested for vWD and subtypes.

4. Results

Of the 120 patients who underwent PCBL, 12 (10%) were found to have vWD, of which 6 patients had type I

vWD (low levels of vW factor levels) and 6 patients had type II vWD (qualitative defect in vW factor), but none had type III. The prevalence of vWD in our cohort of patients was much higher (10%) than the general population (3%), with a similar distribution between type I and II (**Table 1**).

There was no major bleeding (requiring transfusion) but 9/12 patients in the vW disease group experienced minor bleeding which settled with pressure. All vW patients also experienced transient post procedural pain lasting <24 hours in addition to biopsy site ecchymosis (**Table 2**).

5. Discussion

PCLB is generally regarded as a safe diagnostic modality. Complications of liver biopsy are extremely rare but potentially hazardous [10]. The majority of complications (60%) occur within two hours, and 96% occur within 24 hours following the procedure [11] [12]. Less than 3% of patients following the procedure require inpatient care related to adverse event [7] [13]. A third of patients are known to experience significant pain during the procedure itself but clinically significant bleeding following the liver biopsy occurs only in 1% - 2%, usually apparent within 4 hours post-procedure [6]. Intra-peritoneal hemorrhage is the most disastrous form of bleeding requiring expeditious surgery, others such as intra-parenchymal & biliary, which are self contained by surrounding tissue usually amenable to angiographic embolization [14]-[16]. Unfortunately, fatalities have occurred from uncontained and missed intra-peritoneal hemorrhage in up to 0.01% - 0.3% of patients post-PCBL [6] [17]-[19].

vWD has traditionally been regarded as a general risk factor for bleeding during invasive procedures [20]. Liver biopsies have been performed safely in patient populations with coagulation defects such as thrombocytopenia and hemophilia following clotting factor replacements or substitutes [21]. However, there is paucity of

Table 1. Patient demographics, diagnosis, liver disease severity (MELD), vW disease type and RIPA.

Patient Number	Age	Ethnicity	Sex	Diagnosis	#MELD	vW Disease Type (Factor Level %)	Ristocetin Induced Platelet Aggregation (RIPA)
1	38	Caucasian	M	Chronic hepatitis B	6	I (<45%)	Hypoactive agglutination
2	46	Hispanic	M	PBC	8	IIB (Normal)	Hyperactive agglutination
3	59	Caucasian	F	Chronic hepatitis C	8	I (<45%)	Hypoactive agglutination
4	76	Caucasian	F	Chronic hepatitis C	6	IIB (Normal)	Hyperactive agglutination
5	44	Caucasian	M	Chronic hepatitis C	4	I (<45%)	Hypoactive agglutination
6	54	Caucasian	M	Chronic hepatitis C	8	IIN (Normal)	Normal agglutination
7	67	Asian	F	PBC	8	I (<45%)	Hypoactive agglutination
8	50	Caucasian	M	Chronic hepatitis C	6	I (<45%)	Hypoactive agglutination
9	43	Caucasian	F	Chronic hepatitis C	6	IIN (Normal)	Normal coagulation
10	32	Hispanic	F	Chronic hepatitis B	8	IIB (Normal)	Hyperactive coagulation
11	65	Caucasian	M	Chronic hepatitis B	8	I (<45%)	Hypoactive coagulation
12	56	Caucasian	M	Chronic hepatitis B	6	IIN (Normal)	Normal coagulation

#MELD—Model for end stage liver disease.

Table 2. Complications in patients with vW disease who underwent liver biopsy.

Complication	Patient's n (%)
Pain at the site <24 hours	12 (100)
Biopsy site ecchymosis	12 (100)
Minor biopsy site bleed	9 (75)
Major bleeding requiring transfusion	0 (0)
Hemobilia	0 (0)

data on the safety of PCLB in vWD (most common inherited bleeding disorder in our population [5], the specific extent of bleeding diathesis encountered in different subtypes of the disease during/post-biopsy and any associated morbidity & mortality, have not been previously described in literature.

6. Conclusion

In conclusion, our study has shown that patients with vWD can safely undergo PCBL without major bleeding requiring transfusion or need for DDAVP (desmopressin acetate) or cryoprecipitate. Minor bleeding and ecchymosis at the biopsy site may occur at a higher rate than the general population. We concur with the AGA guidelines that outpatient percutaneous liver biopsy is safe and non-threatening despite concomitant minor inherited bleeding diathesis [22]. We propose a much larger cohort to obtain better statistical validation.

Guarantor of the Article

Patrick P Basu.

Specific Author Contributions

All authors contributed equally to design, data collection and drafting of the manuscript and have all approved the final version before submission.

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