Complications of Percutaneous Liver Biopsy in Children

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To determine the frequency and nature of complications after liver biopsy and whether risk factors could be identified to predict these complications, the medical records of all patients (age, 1 week to 28 years) who underwent a percutaneous liver biopsy at Children's Hospital over a 6-year period (1981-1986) were reviewed. Data were collected from 469 (97%) of 483 eligible charts. Twenty-one patients (4.5%) experienced major complications including bile leak (n = 3, 0.6%), prolonged drainage of ascitic fluid (n = 1, 0.2%), pneumothorax (n = 1, 0.2%), bleeding requiring transfusion (n = 13, 2.8%), and death (n = 3, 0.6%). A subgroup of patients (n = 37) with cancer or bone marrow transplantation was found to be at a nearly fivefold greater risk for transfusion than patients with other diagnoses (P = 0.02). All three deaths in previously stable patients occurred in this same high-risk group of patients with cancer or bone marrow transplantation (P < 0.001). Two deaths resulted from disseminated intravascular coagulation and one from bleeding.

Diagnosis, age, number of percutaneous passes, and prebiopsy coagulation studies were not predictive of subsequent complications. It is concluded that bleeding that requires transfusion is the most common liver biopsy complication and that it occurs more frequently in children than previously reported. Children with cancer or those who have undergone bone marrow transplantation are at a greater risk for bleeding and death following percutaneous liver biopsy.

Percutaneous liver biopsy (PLB) plays an important role in the diagnosis of hepatobiliary disorders in the pediatric patient. The introduction of the 1-second Menghini technique has significantly decreased the morbidity and the mortality of the procedure. A number of reports have suggested a low incidence of complications following the procedure in adults and children. However, based on our anecdotal experience, we believed that complications occurred more frequently than previously reported. Therefore, we retrospectively reviewed data to determine the complications that arose after PLB performed between 1981 and 1986 and to identify risk factors for these complications, including the possible existence of groups of patients at increased risk.

Materials and Methods

The hospital charts of patients who underwent PLB at Children's Hospital Medical Center between January 1, 1981, and December 31, 1986, were retrospectively reviewed. Data were collected from 469 (97%) of 483 eligible charts. The medical record was reviewed, but data for the perioperative period could not be located for nine biopsies, and no medical record could be located for an additional five biopsies (3 patients). These biopsies are not included in this analysis. Data collected included age, sex, patient diagnosis, biopsy diagnosis, and values for preoperative studies, including prothrombin time, partial thromboplastin time, platelet count, bleeding time, and hematocrit. Intraoperative methods including biopsy site, needle type, and number of passes were also recorded. In most cases the procedures were performed by pediatric gastroenterology fellows at different stages of training under the supervision of the staff attending physician. Most of the patients were admitted to the Clinical Research Center before the procedure. No biopsies were performed on an outpatient basis. All patients were sedated, in large part to ensure that the patient remained quiet and in bed after the biopsy. The most commonly used sedation was intramuscular meperidine (1–2 mg/kg) and promethazine (0.5–1 mg/kg), 30–45 minutes before the biopsy.

Nearly all biopsies were performed through an intercostal approach, (n = 444, 95%), whereas the subcostal approach was used in 3 (1%) patients. To perform a biopsy on a focal abnormality or to avoid previously identified enlarged vascular structures, the procedure was also ultrasound-guided in 4 (1%) patients. The approach used was not specified in 18 (4%) patients. A Menghini needle was used in 439 (94%) patients. Tru-Cut or Jamshidi needles were used in 10 (3%) patients, and the type of needle was not specified in 14 (3%) patients. More than one pass was...
performed if sufficient diagnostic tissue was not recovered with the first pass or if multiple specimens were required, e.g., both enzyme analysis and microscopy. After the procedure, the patient was placed on the right side for 4 hours. Customary nursing orders after the biopsy included vital signs every 15 minutes \( \times 8 \), every 30 minutes \( \times 4 \), every 60 minutes \( \times 4 \), and then every 4 hours. A hematocrit value was obtained at 2, 4, 6, and 24 hours after the biopsy. The decision to transfuse the patient was left to the clinical judgment of the responsible physician.

Complications after the procedure were categorized as perforation (pneumothorax, bile leak, or ascitic fluid drainage), pain requiring medication, oversedation requiring monitoring of respiration, transfusion, and death. Data were analyzed by analysis of variance, Mantel-Haenszel \( \chi^2 \), and Fisher’s Exact Test as appropriate. Data are presented as mean \( \pm \) SD, and differences are considered significant at \( P < 0.05 \).

## Results

The age of the study population ranged between 1 week and 28 years with a median of 2.6 years. Eight patients were more than 20 years old. Figure 1 shows the age distribution of the study population.

Preoperative diagnoses included hepatomegaly or hepatosplenomegaly \( (n = 113) \), cholestasis \( (n = 94) \), chronic hepatitis \( (n = 74) \), suspected or confirmed enzymopathy, e.g., glycogen storage disease \( (n = 100) \), cancer or status post–bone marrow transplantation (CA/BMT) \( (n = 37) \), suspected Reye’s Syndrome \( (n = 41) \), suspected rejection in liver transplant patients \( (n = 25) \), follow-up for neonatal hepatitis \( (n = 24) \), and other diagnoses \( (n = 53) \). Some patients had more than one underlying diagnosis, resulting in 561 diagnoses in 469 patients. Most patients in the CA/BMT group had hematologic malignancies and/or had undergone bone marrow transplantation. None of the patients with CA/BMT had a significant tumor load at the time of PLB. Most frequently, these patients were being evaluated for graft-versus-host disease, drug-induced hepatopathy, or viral hepatitis. In our series an etiopathologic diagnosis of the liver abnormality was obtained in 33 (89%) of the 37 CA/BMT patients.

Preoperative evaluation included determination of hematocrit (in 98% of the patients), prothrombin time (97%), partial thromboplastin time (97%), bleeding time (80%), and platelet count (90%). It was our general policy not to perform PLBs on patients with abnormal preoperative coagulation studies (platelet count < 50,000, prothrombin time > 3 seconds prolonged, or bleeding time > 9 minutes); however, from our retrospective chart review we determined that not all patients had normal or corrected preoperative coagulation studies before PLB. Despite this, no preoperative laboratory study, including prothrombin time (range, 9.3–16 seconds; mean, 11.5 \( \pm \) 1.6 seconds; normal, 10.7–12.9 seconds), partial thromboplastin time (range, 18.8–90 seconds; mean, 31.6 \( \pm \) 7.3 seconds; normal, 24.1–35.5 seconds), bleeding time (range, 1–21 minutes; mean, 4.0 \( \pm \) 2.3 minutes; normal, 1–9 minutes), or platelet count (range, 18,000–938,000; mean, 348,000 \( \pm \) 169,000; normal, 135,000–466,000) was predictive of any subsequent complication including bleeding. In addition, the number of biopsy passes (range, 1–6; mean, 1.7 \( \pm \) 0.82) did not correlate with subsequent complications.

Table 1 summarizes the minor complications after PLB including skin hematoma, oversedation requiring monitoring of respiration, and pain. These minor complications occurred in 55 patients (11.7%). There was no correlation between these complications, including sedation-related complications, and patient age. In addition, inadequate tissue for pathological diagnosis was a complication in 11 (2.3%) patients.

As shown in Table 2, 21 patients experienced ma-

![Figure 1](image-url)
Table 2. Major Complications After PLB

<table>
<thead>
<tr>
<th>Complication</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile leak</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Ascitic fluid leak</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Bleeding requiring transfusion</td>
<td>13</td>
<td>2.8</td>
</tr>
<tr>
<td>Death</td>
<td>3</td>
<td>0.6</td>
</tr>
</tbody>
</table>

NOTE. Twenty-one patients (4.5%) experienced major complications after PLB. The most common major complications were bile leak at the biopsy site, symptomatic pneumothorax diagnosed by chest radiograph, ascitic fluid leak at the biopsy site, bleeding requiring transfusion, and death.

Major complications after PLB including bile leak, pneumothorax, ascitic fluid leak, bleeding requiring transfusion, and death. Of the 13 patients who were transfused, 8 had a decrease in hematocrit within 4 hours after the biopsy and 5 had changes in vital signs consistent with blood loss before a decrease in hematocrit. Patients who were transfused because of bleeding received a mean of 10 mL/kg of packed red blood cells (range, 4-86). Patients in two diagnosis groups (CA/BMT and suspected rejection following liver transplantation) were at increased risk for transfusion. Of the 37 patients in the CA/BMT group, 4 (10.8%) required a previously unplanned transfusion within the 72 hours of the PLB; 3 of these patients died. Of the 25 patients in the post-liver transplantation group, 4 (16%) received a previously unplanned transfusion within the 72 hours of the PLB. All transplant patients were in the immediate posttransplant period and had ongoing blood loss separate from the PLB; therefore, it could not be determined to what degree, if any, the PLB necessitated the transfusion. These patients were excluded from statistical evaluation. Thus, only CA/BMT was conclusively associated with a significant increased risk for unplanned transfusion (10.8% in the CA/BMT patients vs. 2.2% in nontransplant, non-CA/BMT patients; relative risk, 4.9; 95% confidence limits, 1.3-19.0; \( P = 0.02 \)).

In 328 patients who were not transfused, a 4-hour post-PLB hematocrit value was recorded on the chart. The ratio of hematocrit value 4 hours after PLB to that before PLB was 0.97 ± 0.08, indicating a mean blood loss of 3%. However, 15 (4.6%) patients who were not transfused had a ≥15% blood loss as measured by decrease in hematocrit. Three of these 15 were patients with CA/BMT. Therefore, of 37 patients with CA/BMT, 7 (18.9%) either required transfusion or had blood loss of ≥15% after PLB.

The mortality rate in our study was 0.6%. All three deaths occurred in patients with CA/BMT (8.1%). No deaths occurred in patients with other underlying diagnoses (\( P < 0.001 \)). Two patients died of sepsis and disseminated intravascular coagulation (DIC). Another patient died as a result of intrabdominal bleeding (hemoperitoneum) without evidence of DIC.

Discussion

McGill et al.,\(^6\) in a 20-year study of 9212 adult patients undergoing PLB, reported 10 fatal and 22 nonfatal hemorrhages (0.11% and 0.24%, respectively). The risk of bleeding was higher in patients with malignancy for both fatal and nonfatal hemorrhage (0.4% and 0.57%, respectively). Perrault et al.,\(^4\) reported a morbidty rate of 5.9% including pain and hypotension but no mortality after PLB in 1000 adult patients.

In one of the earliest descriptions of PLB in pediatrics, Hong and Schubert reported no significant complications in 36 biopsies.\(^7\) In a subsequent study of 210 children (age, 1 week to 15 years), Walker et al.,\(^7\) reported no mortality, no patients needing transfusions, and only “minor” complications (pneumothorax, bowel perforation, and gall bladder perforation) in 3 patients. Ament reported in abstract form a complication rate of 4% including bleeding, pneumothorax, and pain in 584 patients who underwent PLB in 25 centers.\(^9\) More recently, Lichtman et al. reported no deaths in 184 biopsies in children <1 year old.\(^10\) Three children (1.6%) had a decrease in hemoglobin concentration for which two children (1.1%) were given transfusion.\(^10\)

In our patient population, bleeding requiring transfusion was the most common major complication, occurring in approximately 1 in 45 (2.2%) non-transplant, non-CA/BMT patients. This is 10 times greater than the incidence of bleeding seen in adults.\(^6\) The transfusion rate for children <1 year old was 1.8% (3/167), which was similar to the results observed in infants by Lichtman et al. (2/184).\(^10\) A type II or \( \beta \) error might account for the lower frequency of bleeding in previous smaller studies in children.\(^7\) A lower threshold for transfusion in our study would also explain our increased transfusion rate; however, all patients who were transfused in our study experienced shock, active bleeding at the biopsy site, or a decrease in hematocrit value (mean, 7.05% ± 3.21%; range, 3.1%-13.2%).

Whereas bleeding was not predicted by abnormal preoperative laboratory evaluation, patients with abnormal or uncorrectable preoperative coagulation study results are often referred for open liver biopsy; consequently, these patients would not be included in our study. Normal results in preoperative coagulation studies do not afford complete protection from postoperative bleeding. The lack of correlation between bleeding after liver biopsy and indices of coag-
ulation was previously reported by Ewe. McGill et al. also reported no correlation between bleeding after PLB and laboratory indices of coagulation. Recently, McVay and Toy reported no increased risk of bleeding after PLB in patients with mild hemostatic abnormalities.

Because transient bacteremia may be associated with PLB, we speculate that post-PLB bacteremia may lead to sepsis, DIC, and death in CA/BMT patients with immunosuppression. We further speculate that transient endotoxemia may result in poor clot formation and increased bleeding after PLB. In view of the increased risk of sepsis in these patients, the use of broad-spectrum antibiotic coverage for PLB in immunosuppressed patients should be prospectively studied. Liver biopsy is often extremely helpful in these patients in differentiating viral hepatitis, drug-induced hepatopathy, and graft-versus-host disease. However, when possible, other tissue specimens (rectal, esophageal, or skin) may be preferred to liver to help in the diagnosis of graft-versus-host disease. When a liver biopsy is indicated in pediatric patients with CA/BMT, we would give strong consideration to an open or laparoscopic biopsy in view of the increased risk of bleeding.

We conclude that complications after PLB, especially bleeding, occur more frequently than previously reported in the pediatric population. Additionally, patients with CA/BMT are at a significantly increased risk of complications after PLB.

References

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