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Retrospective Study

Major complications after ultrasound-guided liver biopsy: An annual audit of a Chinese tertiary-care teaching hospital

Wei-Lu Chai, Dan-Lei Lu, Zhong-Xia Sun, Chao Cheng, Zhuang Deng, Xin-Yan Jin, Tong-Long Zhang, Qiong Gao, Yu-Wei Pan, Qi-Yu Zhao, Tian-An Jiang

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Abstract

BACKGROUND
As ultrasound-guided percutaneous liver biopsy (PLB) has become a standard and important method in the management of liver disease in our country, a periodical audit of the major complications is needed.

AIM
To determine the annual incidence of major complications following ultrasound-guided PLB and to identify variables that are significantly associated with an increased risk of major complications.

METHODS
A total of 1857 consecutive cases of PLB were included in our hospital from January 2021 to December 2021. The major complication rate and all-cause 30-d mortality rate were determined. Multivariate analyses were performed by logistic regression to investigate the risk factors associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB.

RESULTS
In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases). Two cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. Fibrinogen less than 2 g/L [odds ratio (OR): 17.226; 95% confidence interval (CI): 2.647-112.102; \( P = 0.003 \)], post-biopsy hemoglobin level (OR: 0.963; 95%CI: 0.942-0.985; \( P = 0.001 \)), obstructive jaundice...
(OR: 6.698; 95%CI: 1.133-39.596; \( P = 0.036 \)), application of anticoagulants/antiplatelet medications (OR: 24.078; 95%CI: 1.678-345.495; \( P = 0.019 \)) and age (OR: 1.096; 95%CI: 1.012-1.187; \( P = 0.025 \)) were statistically associated with the incidence of major complications after PLB.

CONCLUSION
In conclusion, the results of this annual audit confirmed that ultrasound-guided PLB can be performed safely, with a major complication rate within the accepted range. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

Key Words: Liver; Percutaneous; Biopsy; Ultrasound; Complication

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Core Tip: Ultrasound-guided percutaneous liver biopsy has become a standard and important method in the management of liver disease. This annual audit confirmed that ultrasound-guided percutaneous liver biopsy is safely performed, with a major complication rate within the accepted range and in line with previously published data. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

INTRODUCTION
Image-guided liver biopsy is a widely accepted technique and a standard diagnostic procedure that is usually performed to assess diffuse liver disease by nontargeted biopsy or to diagnose a specific hepatic abnormality by targeted biopsy\[1, 2\]. Ultrasound is the main imaging modality for percutaneous liver biopsy (PLB) because of its real-time multiplanar scanning capabilities and lack of radiation exposure. Generally, the most common type of liver biopsy is ultrasound-guided PLB, which is a safe and effective procedure; however, this procedure does have risks\[1-3\].

Complications following PLB vary widely and have been examined in both prospective and retrospective studies; the reported rate of PLB-related major adverse events was 0.70%-1.06%. The literature suggests that the mortality directly related to PLB ranges from 0.01% to 0.20%, and the all-cause mortality rate is approximately 0.2%-6\[2-6\]. The most commonly reported and concerning severe complication of PLB is hemorrhage, and the frequency of moderate to severe bleeding varies from 0% to 5.3\%\[7, 8\].

A recent investigation emphasized that coagulation status and patient-related factors contributed to a high risk of major complications following PLB\[7\]. The practice guidelines recommended that there should be local and national audits on liver biopsy to ensure that the complication rates were within the accepted range\[2\]. As ultrasound-guided PLB has become a standard and important method in the management of liver disease in our country, a periodical audit on its application and complications is needed to ensure that the complication rate is within the accepted range and to further optimize the procedure. Therefore, we carried out this study to determine the annual incidence of major complications following ultrasound-guided PLB in a Chinese tertiary-care teaching hospital and to identify significant variables associated with an increased risk of major complications.

MATERIALS AND METHODS
Patients and design
The Quality Management Division of our hospital initiated this retrospective annual audit of severe adverse events after ultrasound-guided PLB following the Standard Operating Procedure of Data Validation, which was certified by Joint Commission International. Our institutional review board approved this audit and waived related informed consent according to the regulations of the ethics committee. A total of 1857 consecutive cases of ultrasound-guided PLB performed in a Chinese tertiary-care teaching hospital in a major metropolitan area from January 2021 to December 2021 were included. Cases of PLB combined with hepatic drainage or drug injection were also included, but cases involving targeted biopsies performed just before thermal ablation of hepatic tumors were excluded. Hematological tests, which included routine blood examination and coagulation tests within 7 d before PLB, were needed, and on the day after PLB, the level of hemoglobin was routinely examined. The data on patient demographics, laboratory tests, prebiopsy images,
PLB details (objectives, operators and techniques), pathology results, major complications and peri-biopsy management were collected from digital medical records and the picture archiving and communication system according to a predefined standardized protocol and entered into worksheets (Microsoft Office Excel 2007; Microsoft, Redmond, Wash) by ten radiology trainees.

**Ultrasound-guided PLB**

Ultrasound guidance was defined as the use of ultrasound or contrast-enhanced ultrasound to obtain real-time visualization of the whole course of PLB, which included prebiopsy imaging assessment, needle advancement and triggering and post-biopsy imaging assessment. In our center, all ultrasound-guided PLBs were performed as inpatient procedures by interventional radiologists with adequate training, and the patients were observed in the hospital overnight.

The indications for PLB in our center were as follows: (1) Determine the nature and/or grade of hepatic tumors; (2) Investigate the reason for abnormal liver function tests; (3) Determine the severity of liver damage; and (4) Obtain liver tissue for non-histological assessment (microbiology, biochemical, other).

Absolute contraindications for PLB were as follows: (1) International normal ratio (INR) > 1.5; (2) Prothrombin time (PT) prolonged 5 s; and (3) Platelet count < 50 × 10^9/L. Biliary dilatation, ascites and lack of cooperation of the patient were considered partial contraindications. Where a biopsy was performed outside guidelines or standardized protocols, multidisciplinary consultation was performed prior to biopsy, and decisions were reflected in medical records.

In our institution, discontinuation of antiplatelet medication or anticoagulants was requested (antiplatelet medication and warfarin: At least 5 d before PLB; heparin and related products: 12-24 h before PLB). After PLB, antiplatelet therapy was resumed after 2-3 d, and warfarin was restarted the following day. The risk of discontinuing anticoagulant/antiplatelet medication was strictly weighed against the potential risk of hemorrhage during PLB. Patients who used antiplatelet medications and anticoagulants were recorded, even though peri-biopsy administration strictly conformed to the above regulations.

Under local anesthesia, two passes by an 18-gauge (G) Tru-cut needle (Tru-cut; Angiotech, Gainesville, FL, United States) with a fully automatic device was the standard technique for targeted or nontargeted liver biopsy. Coaxial cutting needle biopsy with or without plugging by gelatin sponge while withdrawing the introduction was based on the clinical indication and operator’s preference. Contrast-enhanced ultrasonography with SonoVue (contrast agent, Bracco, Milan, Italy) or Sonazoid (contrast agent, GE Healthcare, United States) was an important tool for evaluating the vascularization of target lesions or the patent biopsy method, differentiating necrotic tissue from tumorous tissue and identifying hemorrhage events during the whole course of PLB. SonoVue was supplied as lyophilized powder and reconstituted with 5 mL of saline to make a homogeneous microbubble suspension; 2.4 mL of this suspension was administered per bolus, followed by a 5-mL physiologic saline flush. The Sonazoid was supplied as 16 μL perfluorobutane microspheres and reconstituted with 2 mL of distilled water to make a homogeneous microbubble suspension; 0.12 μL (0.015 mL)/kg of this suspension was administered per bolus, followed by a 5-mL physiologic saline flush. A total of 18 operators in our center performed ultrasound-guided PLB, and 5 of them had more than 10 years of experience in abdominal intervention.

The following pertinent variables were investigated and collected: platelet count; PT; fibrinogen; prebiopsy hemoglobin level; comorbidity; application of anticoagulant/antiplatelet medication; operator’s experience; biopsy technique; objective of biopsy; number of passes to obtain adequate tissue specimens; post-biopsy application of hemostatic medication; location of target; miltipleion; maximum diameter of target; post-biopsy hemoglobin level; repeat biopsy; and histological diagnosis. Exploratory analyses were conducted to identify any statistically significant variables that might be implicated in major complications.

**Definitions**

This audit focused on the identification of major complications, especially mortality directly related to ultrasound-guided PLB. The major complication in this study was defined according to the Quality Improvement Guidelines for Percutaneous Needle Biopsy of the Society of Interventional Radiology, including bleeding requiring transfusion or intervention, prolonged hospitalization, requiring major therapy, unplanned increase in level of care and permanent adverse sequelae or death. The main complications following PLB are liver hematoma (symptomatic or asymptomatic), pain, vasovagal reactions, hemothorax, hemoperitoneum, pneumothorax, hemobilia, bile leakage, organ perforation (gallbladder, colon) and arteriovenous fistula. Clinically significant hemorrhage is the most common and is defined as a decrease in hemoglobin level of more than 2.0 g/dL and a change in vital signs with radiologic evidence of bleeding necessitating blood transfusion. An acute major complication was defined as one that occurred less than 24 h after PLB, and a delayed major complication was defined as one that occurred more than 24 h after PLB. Overall all-cause mortality was also calculated by 30 d after PLB. All the included factors of both the major complication group and the no major complication group were compared, and the independent predictors for the occurrence of major complications after PLB were identified. Clinical, radiological and technical variables were investigated statistically for their association with all-cause 30-d mortality following PLB.

**Data analysis**

The differences in categorical variables between the major complication group and the no major complication group were presented as percentages and were compared using the \( \chi^2 \) or Fisher’s exact test, as appropriate. Normally distributed variables were expressed as the mean ± standard deviation and were compared with the Student’s \( t \) test. Nonnormally distributed variables were expressed as medians (quartile 1, quartile 3) and were compared by nonparametric tests (Mann-Whitney \( U \) test). Multivariate analyses were performed by a forward step (likelihood ratio) multivariable logistic regression model to investigate the risk factors associated with major complications and all-cause 30-d mortality.
following ultrasound-guided PLB. All statistical tests were two-sided. A P value less than 0.05 was considered statistically significant. All analyses were performed using SPSS software (version 20.0, SPSS Inc., Chicago, IL, United States).

RESULTS

A total of 1857 biopsies were performed and included; 1108 (59.7%) patients were male. The mean age of the patients was 55.1 ± 17.8 years. Biopsy pathology revealed hepatocellular carcinoma (278, 15.0%), intrahepatic cholangiocarcinoma (225, 12.1%), secondary hepatic tumors (518, 27.9%), liver abscesses (91, 4.9%), chronic liver disease (393, 21.2%) and others (352, 18.9%). Demographic, clinical, procedural and pathological characteristics of the patients in the major complication and no major complication groups are listed in Table 1.

In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB, 9 of which were associated with clinically severe hepatic hemorrhage and 1 of which was associated with hemothorax. More than one complication might occur in 1 patient. Among 9 cases of severe hepatic hemorrhage, 1 case was combined with severe infection, 2 cases with hemoperitoneum and 1 case with hemothorax. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases), and 2 cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. No patients experienced pneumothorax. Eight of ten major complications (80%) occurred acutely within 24 h.

Except for blood transfusion, 4 patients received emergency laparotomy, 1 patient who had delayed artery pseudoaneurysm after liver biopsy required transcatheter embolization, 2 patients who had post-biopsy active bleeding underwent ultrasound-guided microwave ablation and local thrombin injection, and 1 patient who had hemoperitoneum underwent percutaneous drainage of fluid collection.

Univariate correlates of the occurrence of major complications following ultrasound-guided PLB were age, patients with obstructive jaundice, prebiopsy hemoglobin level, fibrinogen less than 2 g/L, prebiopsy application of anticoagulants/antiplatelet medications, post-biopsy application of hemostatic medication and post-biopsy hemoglobin level. The objective of PLB, operator experience, biopsy technology, characteristics of targets, number of specimens and histological diagnosis were not contributing factors for major complications (Table 1). Multivariable analysis revealed that obstructive jaundice [odds ratio (OR): 6.698; 95% confidence interval (CI): 1.133-39.596; P = 0.036], fibrinogen less than 2 g/L (OR: 17.226; 95%CI: 2.647-112.102; P = 0.003), prebiopsy application of anticoagulants/antiplatelet medication (OR: 24.078; 95%CI: 1.678-345.495; P = 0.019), post-biopsy hemoglobin level (OR: 0.963; 95% CI: 0.942-0.985; P = 0.001) and age (OR: 1.096; 95%CI: 1.012-1.187; P = 0.025) were statistically associated with an increased risk of major complications after PLB (Table 2). The patients with obstructive jaundice had a 6.7-fold increased risk of major complications. The patients with a fibrinogen level less than 2 g/L had a 2.1% risk of major complications compared with 0.3% for the patients with a fibrinogen level greater than 2 g/L. Although strictly followed by the recommendations on the peri-biopsy administration of anticoagulants or antplatelet medications, the risk of major complications was also significantly increased compared with the patients who had not used anticoagulants or antiplatelet medications. The post-biopsy hemoglobin level was a meaningful indicator for the occurrence of major complications, and the older patients were more likely to develop major complications following PLB. For all-cause 30-d mortality after PLB, the prebiopsy hemoglobin level (OR: 0.963; 95%CI: 0.928-0.999; P = 0.042) and post-biopsy hemoglobin level (OR: 0.958; 95% CI: 0.930-0.987; P = 0.005) were deemed statistically meaningful predictors (Table 2).

DISCUSSION

Ultrasound-guided PLB plays an increasingly important role in the management of liver disease or abnormal liver function tests[1-3] as well as in patients with a diagnostic dilemma[9]. It is important to maintain the safety of liver biopsy and control the potential risks as the volume of liver biopsies increases worldwide. The results of this annual audit of 1857 liver biopsies in Chinese tertiary-care teaching hospitals confirmed that the incidence of major complications (0.53%) following ultrasound-guided PLB was low and in line with published data from other parts of the world[2-8].

The reported morbidity and mortality associated with PLB varies extensively[10]. An American multicenter study included 2740 liver biopsies for patients with advanced chronic liver disease. The rate of serious adverse events was 1.1%, and the bleeding rate was 0.58%[4]. The analysis of elective PLBs collected from the National Health Service of England showed that death within 7 d directly related to liver biopsy occurred in approximately 1 in 10000 biopsies, and the major hemorrhage rate was 0.6%[5]. From Australian audits on percutaneous core liver biopsies, major complications occurred in 12 patients (1.0%); 7 patients had an abnormal baseline coagulation profile[11]. A systematic review concluded that the rate of major bleeding after liver biopsy ranged from 0.1% to 4.6%[7]. In accordance with these previous large-scale reports, the major complication rate, the overall all-cause 30-d mortality and the biopsy-related mortality from our study were within the expected parameters, and post-biopsy hemorrhage accounted for the main source of adverse events.

The risk factors for complications in the published literature vary considerably. In this audit, the factors influencing the incidence of major complications and mortality following ultrasound-guided PLB were explored. Patient-related factors primarily influenced the occurrence of major complications, but operator-related or procedure-related factors were not found, even though needle size and hepatic malignancy were identified as risk factors in the published literature[3,4,6-8,12,13]. Older age was deemed to be associated with a significantly higher likelihood of post-biopsy major complications. This finding was supported by several studies, which noted that patient age > 50 years or < 2 years significantly increased the risk[3,7,14].
# Table 1 Demographic, clinical, procedural and pathological characteristics of patients in the major complication and no major complication groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Major complication, $n = 10$, %</th>
<th>No major complication, $n = 1847$, %</th>
<th>$P$ value</th>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
<td>8, 80.0</td>
<td>1100, 59.6</td>
<td>0.189</td>
</tr>
<tr>
<td>Female</td>
<td>2, 20.0</td>
<td>747, 40.4</td>
<td></td>
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<tr>
<td><strong>Age, median (Q1, Q3)</strong></td>
<td>65.0 (54.5, 76.3)</td>
<td>58.0 (47.0, 67.0)</td>
<td>0.156</td>
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<td><strong>Comorbidity</strong></td>
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<td>Cardiovascular and cerebrovascular diseases</td>
<td>2, 20.0</td>
<td>238, 12.9</td>
<td>0.504</td>
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<tr>
<td>Extensive ascites</td>
<td>0, 0</td>
<td>35, 1.9</td>
<td>0.660</td>
</tr>
<tr>
<td>Obstructed jaundice</td>
<td>3, 30.0</td>
<td>137, 7.4</td>
<td>0.007</td>
</tr>
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<td><strong>Laboratory test</strong></td>
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<tr>
<td>Platelet count &lt; 50 × 10^9/L</td>
<td>0, 0</td>
<td>15, 0.8</td>
<td>0.922</td>
</tr>
<tr>
<td>Prebiopsy hemoglobin level, median (Q1, Q3)</td>
<td>112.5 (76.5, 126.3)</td>
<td>125.0 (112, 139)</td>
<td>0.027</td>
</tr>
<tr>
<td>Fibrinogen &lt; 2 g/L</td>
<td>5, 50.0</td>
<td>228, 12.3</td>
<td>&lt; 0.001</td>
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<td>PT prolonged 5 s</td>
<td>1, 10.0</td>
<td>63, 3.4</td>
<td>0.255</td>
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<td><strong>Objectives of PLB</strong></td>
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<tr>
<td>Focal liver lesions</td>
<td>8, 80.0</td>
<td>1346, 72.9</td>
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<td>Diffuse liver disease</td>
<td>2, 20.0</td>
<td>501, 27.1</td>
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<td>Prebiopsy application of anticoagulants/antiplatelet medication/Y</td>
<td>2, 20.0</td>
<td>79, 4.5</td>
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<td>462, 26.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Operator/10-yr experience</td>
<td>6, 60.0</td>
<td>665, 36.0</td>
<td>0.115</td>
</tr>
<tr>
<td><strong>Biopsy technique</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bare introduction Tru-cut (18G)</td>
<td>6, 60.0</td>
<td>922, 49.9</td>
<td>0.525</td>
</tr>
<tr>
<td>Coaxial introduction Tru-cut (18G)</td>
<td>4, 40.0</td>
<td>925, 50.1</td>
<td></td>
</tr>
<tr>
<td><strong>Location of targets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>6, 75.0</td>
<td>1046, 73.0</td>
<td>0.659</td>
</tr>
<tr>
<td>Left</td>
<td>1, 12.5</td>
<td>301, 21.0</td>
<td></td>
</tr>
<tr>
<td>Hilar</td>
<td>1, 12.5</td>
<td>86, 6.0</td>
<td></td>
</tr>
<tr>
<td>The maximum diameter of targets, median (Q1, Q3)</td>
<td>2.8 (1.7, 6.3)</td>
<td>3.3 (2.1, 5.9)</td>
<td>0.514</td>
</tr>
<tr>
<td>Multilesion/Y</td>
<td>4, 44.0</td>
<td>848.0.2</td>
<td>0.336</td>
</tr>
<tr>
<td>Post-biopsy hemoglobin level, median (Q1, Q3)</td>
<td>81.0 (65.3, 107.8)</td>
<td>114.7 (109.0, 126.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Repeat biopsy/Y</td>
<td>0, 0</td>
<td>30, 1.6</td>
<td>0.685</td>
</tr>
<tr>
<td>Number of specimens, median (Q1, Q3)</td>
<td>2 (2.0, 2.3)</td>
<td>2 (2.0, 2.0)</td>
<td>0.553</td>
</tr>
<tr>
<td><strong>Histological analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCC</td>
<td>0, 0</td>
<td>278, 15.1</td>
<td>0.094</td>
</tr>
<tr>
<td>ICC</td>
<td>3, 30.0</td>
<td>222, 12.0</td>
<td></td>
</tr>
<tr>
<td>Secondary hepatic tumor</td>
<td>2, 20.0</td>
<td>516, 27.9</td>
<td></td>
</tr>
<tr>
<td>Liver abscess</td>
<td>1, 10.0</td>
<td>90, 4.9</td>
<td></td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0, 0</td>
<td>393, 21.3</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>4, 40.0</td>
<td>348, 18.8</td>
<td></td>
</tr>
</tbody>
</table>

HCC: Hepatocellular carcinoma; ICC: Intrahepatic cholangiocarcinoma; PLB: Percutaneous liver biopsy; PT: Prothrombin time; Q: Quartile; Y: Yes.
The results of this annual audit confirmed that ultrasound-guided PLB can be safely performed in our hospital, with a major complication rate within the accepted range and in line with previously published data. This study highlighted the

**Table 2 Risk factors related to increased risk of major complications and all-cause 30-d mortality**

<table>
<thead>
<tr>
<th>Risk factors for major complication</th>
<th>( \beta )</th>
<th>OR (95%CI)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructed jaundice</td>
<td>1.902</td>
<td>6.698 (1.133-39.596)</td>
<td>0.036</td>
</tr>
<tr>
<td>Fibrinogen &lt; 2 g/L</td>
<td>2.846</td>
<td>17.226 (2.647-112.102)</td>
<td>0.003</td>
</tr>
<tr>
<td>Prebiopsy application of anticoagulants/antiplatelet medications</td>
<td>3.181</td>
<td>24.078 (1.678-345.495)</td>
<td>0.019</td>
</tr>
<tr>
<td>Postbiopsy hemoglobin level</td>
<td>-0.037</td>
<td>0.963 (0.942-0.985)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td>0.091</td>
<td>1.096 (1.012-1.187)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Risk factors for all-cause 30-d mortality

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>( \beta )</th>
<th>OR (95%CI)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prebiopsy hemoglobin</td>
<td>-0.038</td>
<td>0.963 (0.928-0.999)</td>
<td>0.042</td>
</tr>
<tr>
<td>Postbiopsy hemoglobin</td>
<td>-0.043</td>
<td>0.958 (0.930-0.987)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

CI: Confidence interval; OR: Odds ratio.

Practice guidelines recommend that liver biopsy should be performed for biliary obstruction only when there is doubt about the diagnosis and the benefit to the patient outweighs the risk, such as biliary peritonitis, septicemic shock and death[3]. Our study also demonstrated that the risk of major complications was significantly higher in patients with obstructive jaundice. This may be ascribed to the nature and location of the biopsy targets; they were more likely to be tumors of biliary origin and developed adjacent to the hepatic vessels. Therefore, it should be carefully assessed during the liver biopsy procedure to prevent adjacent vessel puncture.

As the level of prebiopsy platelet count and PT/INR were strictly evaluated and controlled, the level of fibrinogen appeared to be more of a limiting issue for the following major complications. In the majority of studies, the hemorrhagic complication rates increased as the INR increased and platelet counts decreased[2,3,15-17]. A previous study suggested that the fibrinogen level, platelet count < 30 × 10^9/L and elevated INR were the best routine coagulation parameters for the prediction of new onset of major bleeding[7,17,18]. The function of fibrinogen has not been verified in the cohort of liver biopsies in situations where the platelet count and PT/INR were within the recommended range. The cutoff level of fibrinogen in this analysis was the lower limit of the reference value of fibrinogen tested in our hospital, which varied between different laboratories. Therefore, patients with consumptive coagulopathy and low fibrinogen are at high risk of post-biopsy bleeding.

Although we strictly followed the recommendations on the peri-biopsy administration of anticoagulants or antiplatelet medications, the patients with a history of anticoagulants or antiplatelet medications had a major complication rate that was comparable to that of patients who had not received these drugs. For anticoagulants or antiplatelet medications interfering with coagulation status or platelet function, especially under the development of new relevant drugs, a predominantly increased frequency of bleeding was identified and demonstrated by several large-scale reports[3,19]. As with all clinical decisions, the risks of discontinuing the coagulants or antiplatelet medications should be carefully balanced with the benefit of liver biopsy. If appropriate, consultant advice may be needed.

The post-biopsy hemoglobin level was associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB. Major hemorrhage, which is the most common severe complication of liver biopsy, is defined as a decrease in hemoglobin level of more than 2.0 g/dL and a change in vital signs with radiologic evidence of bleeding[7,20]. Therefore, the change in hemoglobin strongly predicts ongoing blood loss. The risk of all-cause mortality at 30 d after PLB increased as the prebiopsy hemoglobin level decreased, which has not been reported before. By case review, the deaths were combined with hematological disease, autoimmune disease or late malignancy; the level of hemoglobin was much lower compared with controls. Whether these comorbidities influenced the incidence of post-biopsy all-cause mortality was understudied.

There are important limitations to our study. First, this was a single-center, annual audit initiated by the Quality Management Division of our hospital. The adverse events after PLB were retrospectively examined by reviewing the electronic medical records. The documentation was incomplete if the patient left our hospital, and the incidence may be inaccurate. A large-scale, multicenter and prospective study is warranted to validate the findings of our study, especially the administration of peri-biopsy coagulants/antiplatelet medications and the assessment of the baseline coagulation profile. Second, under the introduction of a coaxial system, the use of biopsy track plugging by gelatin sponges was based on the operator’s preference in our hospital. Therefore, the impact of this technique was unclear and under investigated. Third, the diagnostic yield of ultrasound-guided PLB in this audit was not obtained and analyzed.

**CONCLUSION**

The results of this annual audit confirmed that ultrasound-guided PLB can be safely performed in our hospital, with a major complication rate within the accepted range and in line with previously published data. This study highlighted the
administration of peri-biopsy coagulants/antiplatelet medications and coagulation parameters, especially fibrinogen levels. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

ARTICLE HIGHLIGHTS

Research background
As ultrasound-guided percutaneous liver biopsy (PLB) has become a standard and important method in the management of liver disease in our country, a periodical audit of the major complications is needed.

Research motivation
As ultrasound-guided PLB has become a standard and important method in the management of liver disease in our country, a periodical audit on its application and complications is needed to ensure that the complication rate is within the accepted range and to further optimize the procedure. Therefore, we carried out this study to determine the annual incidence of major complications following ultrasound-guided PLB in a Chinese tertiary-care teaching hospital and to identify significant variables associated with an increased risk of major complications.

Research objectives
The aim of this study was to determine the annual incidence of major complications following ultrasound-guided PLB and to identify variables that were significantly associated with an increased risk of major complications.

Research methods
A total of 1857 consecutive cases of PLB were included in our hospital from January 2021 to December 2021. The major complication rate and all-cause 30-d mortality rate were determined. Multivariate analyses were performed by logistic regression to investigate the risk factors associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB.

Research results
In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases), and 2 cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. Fibrinogen less than 2 g/L [odds ratio (OR): 17.226; 95% confidence interval (CI): 2.647-112.102; \( P = 0.003 \)], post-biopsy hemoglobin level (OR: 0.963; 95%CI: 0.942-0.985; \( P = 0.001 \)), obstructive jaundice (OR: 6.698; 95%CI: 1.133-39.596; \( P = 0.036 \)), application of anticoagulants/antiplatelet medications (OR: 24.078; 95%CI: 1.678-345.495; \( P = 0.019 \)) and age (OR: 1.096; 95%CI: 1.012-1.187; \( P = 0.025 \)) were statistically associated with the incidence of major complications after PLB.

Research conclusions
In conclusion, the results of this annual audit confirmed that ultrasound-guided PLB can be performed safely, with a major complication rate within the accepted range. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

Research perspectives
A large-scale, multicenter and prospective study is warranted to validate the findings of our study, especially the administration of peri-biopsy coagulants/antiplatelet medications and the assessment of the baseline coagulation profile.

FOOTNOTES

Author contributions: Jiang TA and Chai WL contributed to conceptualization; Chai WL, Lu DL and Jiang TA contributed to data curation; Chai WL and Sun ZX contributed to formal analysis; Jiang TA contributed to funding acquisition and resources; Chai WL, Cheng C, Jin XY, Deng Z, Zhang TL, Zhao QY and Jiang TA contributed to investigation; Chai WL and Gao Q contributed to methodology; Jiang TA, Sun ZX, Zhao QY, Lu DL and Fan YW contributed to project administration; Chai WL and Lu DL contributed software; Zhao QY, Jiang TA and Sun ZX contributed to supervision; Chai WL and Jiang TA contributed to validation; Chai WL contributed to writing the original draft; Zhao QY and Jiang TA contributed to reviewing and editing.

Institutional review board statement: Ethical approval was obtained from the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine before the study.

Informed consent statement: The requirement for informed consent was waived due to the retrospective nature of the study.

Conflict-of-interest statement: All the authors report having no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.
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REFERENCES
