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ORIGINAL RESEARCH

Analysis of Risk Factors of Bleeding Complications in Percutaneous Needle Biopsy of Liver Occupying Lesions

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Purpose: To search for risk factors for bleeding complications after percutaneous biopsy of primary or secondary space-occupying lesions of liver guided by imaging.

Methods: Consecutive 555 patients with liver space-occupying lesions who underwent ultrasound or CT-guided percutaneous biopsy in our hospital from January 2015 to January 2021 were retrospectively analyzed. Those who cannot cooperate with breath-holding and cannot successfully complete the operation, cytology, and incomplete clinical data. After screening, a total of 502 patients were enrolled, including 313 males and 189 females. Abdominal cavity or liver subcapsular hemorrhage after procedure was used as the dependent variable, and patient's gender, age, pathological results, tumor size, preoperative platelets and international normalized ratio (INR) and hemoglobin as independent variables. All independent variables were analyzed by a single factor logistic regression analysis. The independent variables with $P<0.05$ were included in the regression model and analyzed by multivariate logistic regression analysis to search for the risk factors for bleeding complications of liver space-occupying lesions.

Results: A total of 502 patients with liver space-occupying lesions undergoing percutaneous liver biopsy guided by imaging equipment were included. Twenty-six of 502 (5.2%) patients occurred abdominal cavity or liver sub-capsule bleeding after procedure. Univariate logistic regression analysis observed that liver cirrhosis, the number of punctured tissues and the depth of puncture were related to bleeding complications after puncturing. Multivariate logistic regression analysis showed that liver cirrhosis and puncture depth were risk factors for bleeding complications ($P<0.05$). The ROC curve for predicting bleeding complications after needle biopsy in patients with liver cirrhosis has a sensitivity of 94.3% and a specificity of 46.2%.

Conclusion: Liver cirrhosis and puncture depth are risk factors for bleeding complications during percutaneous biopsy of liver occupying lesions.

Keywords: percutaneous puncture biopsy, risk factors, bleeding

Introduction

Liver biopsy is the "gold standard" for diagnosing liver disease.[1] Image-guided percutaneous needle biopsy is an accurate, safe and widely used diagnostic technique.[2,3] Although the technique is minimally invasive surgery. But it is still traumatic and prone to some complications. Such as pain at puncture site, abdominal cavity or subcapsular hemorrhage, bile leakage, hypotension, arteriovenous fistula, peripheral organ injury, pneumothorax.[4–7]

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Among them, bleeding is the most serious complication after liver biopsy, and when the amount of bleeding is large, the patient's life is endangered.[4–6] At present, there have been a large number of literature reports on the clinical application and complication analysis of percutaneous biopsy of liver lesions.[8–12] However, there are very few studies on the risk factors of bleeding complications after percutaneous biopsy of liver primary or secondary space-occupying lesions. This study collected the clinical data of patients with liver space-occupying lesions who underwent percutaneous needle biopsy in our hospital, and analyzed the risk factors related to hemorrhage. The results are reported as follows.

Materials and Methods

Clinical Data

A retrospective analysis of 555 patients undergoing ultrasound or CT-guided liver biopsy in the Affiliated Cancer Hospital of Guizhou Medical University from January 2015 to January 2021. Inclusion criteria: imaging examinations suggest that liver space-occupying lesions require needle biopsy to confirm or differential diagnosis; clinical data is complete; tissue biopsy is performed with 18G needle biopsy needle. Exclusion criteria: Those who cannot cooperate with breath-holding and cannot successfully complete the operation, cytology, and incomplete clinical data. After screening, a total of 502 patients were enrolled, including 313 males and 189 females. The median age is 57 years (range: 1–86 years). The study was approved by the Affiliated Cancer Hospital of Guizhou Medical University ([2020] 13). Informed consent was obtained. Parent or legal guardian of patients under 18 years of age provided informed consent, and that this study was conducted in accordance with the Declaration of Helsinki.

The tumor size is defined as the largest diameter of the tumor recorded in the imaging examination. The diagnosis of liver cirrhosis is evaluated according to the diagnostic criteria of liver cirrhosis in the 2019 liver cirrhosis diagnosis and treatment guidelines.[13] Bleeding is defined as bleeding after puncture or diagnostic abdominal puncture with uncoagulated blood, or bloody fluid in the drainage tube of the abdominal cavity after puncture. Negative pathological results are defined as descriptive language that cannot clarify the nature of the pathology.

Apparatus

Color Doppler ultrasound (Philips IU22, Philips, Netherlands), convex array probe, frequency 2–5MHz; 64 rows of 128-slice spiral CT (Somatom Definition AS, Siemens, Germany); automatic coaxial biopsy gun system (16G with Shaft puncture needle, 18G disposable biopsy gun, COOK company, USA).

Needle Biopsy

Preoperative Preparation

Complete imaging examination, blood routine and coagulation function for all patients before operation, imaging examination to confirm liver space-occupying lesions, blood routine examination of patients' platelet count and hemoglobin, and coagulation function examination INR. Ultrasound-guided needle biopsy: The patient is in a supine position, and the location of liver lesions is located by ultrasound. Select the best puncture path, local disinfection of the puncture point, and drape. Local anesthesia at the puncture point with 5% lidocaine. The coaxial needle is inserted into the lesion and the needle core is pulled out. Use an 18G disposable biopsy gun to enter the lesion through the coaxial cannula, click the switch to puncture the material. The biopsy tissue was fixed in formalin solution and sent for pathological examination, followed by ultrasound examination for bleeding.

CT-Guided Needle Biopsy

The patient lies on a CT examination bed, sticks the self-made grid on the right upper abdomen, performs CT scan to observe the location and size of the lesion, selects the puncture approach plane, determines the needle angle, measures the distance between the puncture point and the lesion along the puncture approach, and calculates the needle depth. Sterilize the puncture point area and insert the puncture trocar percutaneously to the expected depth. After the CT scan confirms that the needle tip is located in the mass (Figure 1), remove the needle core. The coaxial technique uses a disposable biopsy gun to cut the diseased tissue, put it in formalin solution for fixation, and send it for medical examination. Routine scanning of the puncture site after the operation to observe whether there is hemorrhage in the abdominal cavity or under the liver capsule.

After Biopsy

After the operation, all patients were bed rest for 24 hours, routine intramuscular and intravenous use of hemagglutinin 1KU, and ECG monitoring for 24 hours.

Statistics

Use SPSS 20.0 statistical software for statistical analysis. The enumeration data is expressed as a percentage (%),

Figure 1 CT-guided needle biopsy.

and the chi-square test is used to compare the differences between groups. The measurement data line kolmogorov-Smirnov detects normality, and the normal data is represented by the mean ± standard deviation, and the *t*-test is used to compare the differences between groups. Those that did not conform to the normal distribution were represented by the median (interquartile range), and Mann–Whitney U was used to compare the differences between groups. All variables were first subjected to single-factor Logistic regression analysis, and P<0.05 was used as the inclusion standard. The consistent variables were included in the regression model to perform multivariate Logistic regression analysis to calculate the diagnostic odds ratio (OR). P<0.05 indicates that the difference is statistically significant.

Results

The Basic Situation of Patients with Liver Space-Occupying Lesions

All the included 502 patients were punctured and collected in a coaxial manner. The positive rate of pathological diagnosis was 96.8%. There were 176 cases of primary liver lesions (54 cases of hepatocellular carcinoma, 62 cases of cholangiocarcinoma, and 60 cases of benign lesions); 310 cases of metastases; 16 cases of negative tumors. The incidence of bleeding after puncture was 5.2% (26/502), of which 18 cases (3.6%) had a small amount of hemorrhage under the liver capsule (Figure 2), without special treatment, and 8 cases (1.6%) had abdominal hemorrhage. 5 cases of abdominal hemorrhage were treated with sodium chloride sodium chloride injection, hemocoagulase intravenously and intramuscularly to stop bleeding. The vital signs and status of the patients were closely monitored, and the changes in hemoglobin were rechecked. The patient's condition was controlled on the second day. No further aggravation.

Two patients developed significant abdominal distension, abdominal pain, and blood pressure drop. Afterwards, the bleeding was controlled by interventional embolization. One case died due to ineffective rescue. In this group of cases, complications such as pain at the puncture point, cholangitis, biliary heart reflex, and pneumothorax can still be observed.

Logistic Regression Analysis of Predictive Factors of Bleeding During Liver Biopsy

According to whether bleeding complications occurred, patients were divided into bleeding group and no bleeding group. Single factor Logistic regression was used to analyze the patient's gender, age, lesion type, pathological results, tumor size, location, whether it is located under the liver capsule, presence or absence of cirrhosis, puncture guidance method, number of punctured tissues, puncture depth, preoperative platelet and Preoperative INR and hemoglobin factors. It can be seen that there are statistically significant differences in the presence or absence of liver cirrhosis, the number of punctured tissues, preoperative INR and the depth of puncture between the two groups (P<0.05), see Table 1.

Figure 2 A small amount of bleeding under the capsule after ultrasound-guided needle biopsy.

Table 1 Single Factor Logistic Regression Predicts the Influence of Bleeding Risk Factors

Variable	OR value	95% Confidence Interval	P value
Gender	0.863	0.377–1.977	0.727
Age	0.976	0.946–1.006	0.110
Type of lesion:			
Hepatocellular carcinoma	3.304	0.829–13.169	0.090
Cholangiocarcinoma	0.633	0.102–3.931	0.624
Metastatic cancer	0.699	0.189–2.585	0.591
Benign	0.368	0.056–2.420	0.298
Pathological results	0.555	0.098–3.144	0.506
Tumor size	1.054	0.957–1.159	0.285
Tumor location			
Left lobe	0.778	0.216–2.805	0.701
Right lobe	0.607	0.215–1.717	0.347
Is it under the envelope	0.835	0.342–2.038	0.692
With or without cirrhosis	0.07	0.03–0.166	0.000
Guide way	1.877	0.694–5.073	0.215
Number of punctured tissues	0.64	0.429–0.956	0.029
Puncture depth	1.044	1.005–1.085	0.028
Preoperative platelets	0.998	0.993–1.002	0.276
Preoperative INR	25.658	2.259–291.63	0.009
Preoperative hemoglobin	0.992	0.976–1.008	0.304

The index of P<0.05 in the univariate logistic regression analysis was included in the regression model. Further multivariate logistic regression analysis showed that liver cirrhosis and puncture depth were risk factors for bleeding complications, as shown in Table 2. The sensitivity of liver cirrhosis to predict bleeding after liver biopsy was 30.3%, and the specificity was 97.9%. The ROC curve draws the value of predicting bleeding complications of liver cirrhosis (area under the curve=0.641; P=0.00, Figure 3).

Discussion

Complications of percutaneous needle biopsy guided by imaging equipment for liver lesions mainly include pain, bleeding, bile leakage, hypotension, arteriovenous fistula, peripheral organ damage, and bile-cardioreflex.[4–7,14] The most common complication is pain at the puncture site. Most patients have mild symptoms and do not need any treatment. A few symptomatic pains can be relieved. The second is bleeding, the incidence rate of foreign research reports is 0.13%-5.30%.[3–6,11] Domestically, it is 0.87%-6%.[10,15,16] The incidence of bleeding in this study was 5.2%. Most of them are a small amount of subcapsular bleeding at the puncture site. After hemostatic treatment, absolute bed rest and close monitoring of vital signs, most bleeding can be controlled. A small number of severe bleeding can endanger the life of the patient.

It has been reported in the literature that significant prolongation of PT and the use of anticoagulant drugs are related risk factors for hepatic biopsy bleeding.[4,17,18] Multiple puncture needles, thick needle cutting biopsy, and liver biopsy in elderly patients have a high incidence of bleeding.[19,20] Patients with poor breathing coordination

Table 2 Multivariate Logistic Regression Analysis Analysis of Imaging Bleeding Complications

Factor	β Value	Wald χ^2 Value	P value	OR Value	95% Confidence Interval
Puncture depth	0.052	5.318	0.021	1.053	1.008–1.101
Number of punctured tissues	−0.363	2.723	0.099	0.695	0.452–1.071
With or without cirrhosis	−2.655	31.411	0.000	0.07	0.028–0.178
Preoperative INR	2.33	2.972	0.085	10.279	0.727–145.386

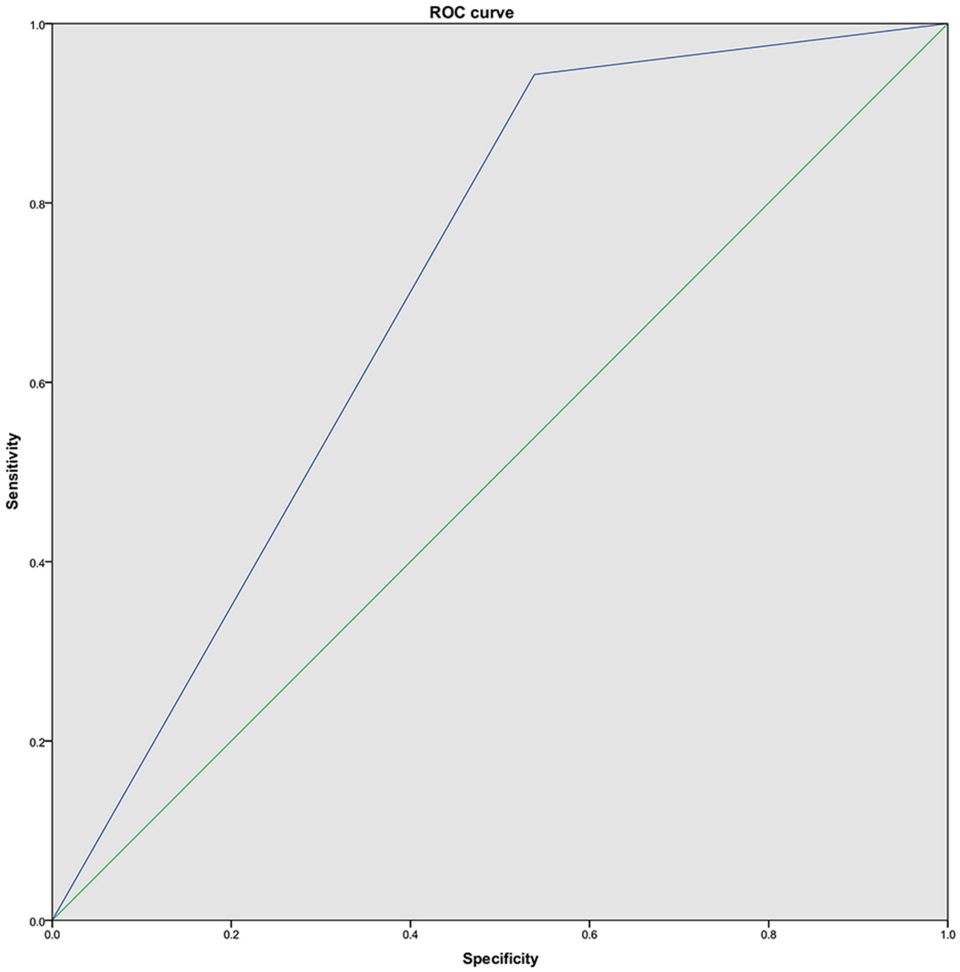

Figure 3 ROC curve of liver cirrhosis predicting bleeding complications.

have an increased risk of bleeding after liver biopsy.[10] After liver biopsy, fiber wax, tampon, gelatin sponge, etc. are implanted into the puncture needle canal to reduce the incidence of bleeding after puncture.[21] Routine intravenous infusion of hemostatic agents in postoperative patients can prevent serious complications of bleeding after puncture.[9] In this study, the surgeons of liver biopsy are all attending physicians, and all the patients involved can cooperate with breathing and hold their breath. All patients underwent biopsy with coaxial 18G biopsy needle, and hemostatic drugs were routinely used after operation.

In this study, 26 patients 5.2% (26/502), had bleeding, of which 12 patients (12/26, 46.2%) had liver cirrhosis. Among 10 patients with bleeding under the background of liver cirrhosis, 41.7% (5/12) suffered from a small amount of bleeding under the capsule, and 58.3% (7/12) suffered from abdominal hemorrhage. Single factor Logistic regression was used to analyze the influencing factors of bleeding complications after needle biopsy. It was found that liver cirrhosis, number of puncture tissues and puncture depth were statistically significant. Multiple logistic regression further confirmed that cirrhosis and puncture depth were risk factors of bleeding complications.

The incidence of bleeding complications after image-guided percutaneous biopsy of liver lesions is not high. The number of patients with liver cirrhosis background in this study is limited. Considering the potential impact of sample size, multi-center large sample data is needed to further study the risk factors of bleeding complications. And analyze the relationship between the occurrence of bleeding and the severity of bleeding under the background of different degrees of cirrhosis.

In summary, image-guided liver biopsy of primary or secondary space-occupying lesions is safe to perform on the basis of strict compliance with the operating specifications. Liver cirrhosis and puncture depth are risk factors for

postoperative bleeding complications. Needle biopsy should be carried out under the guidance of images, choose a suitable puncture path, and reduce the depth of puncture. During needle aspiration biopsy, patients with liver cirrhosis should pay attention to the higher risk of bleeding complications than those without liver cirrhosis. Hemostatic drugs can be used when necessary. Biogel or gelatin sponge can be used to block the puncture path to reduce postoperative bleeding. At the same time, after operation, we should observe closely and do a good job of rescuing after bleeding.

Abbreviations

INR, international normalized ratio; OR, odds ratio.

Ethics Approval and Consent to Participate

The study was approved by the Affiliated Cancer Hospital of Guizhou Medical University ([2020] 13). Informed consent was obtained. Parent or legal guardian of patients under 18 years of age provided informed consent, and that this study was conducted in accordance with the Declaration of Helsinki.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

There are no potential conflicts of interest to disclose.

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