Original Article

Effectiveness of ultrasound-guided percutaneous transhepatic puncture for the diagnosis of low-level alpha-fetoprotein liver cancer patients

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Background: Globally, liver cancer is the most frequent fatal malignancy. The aim of the present study was to explore the effectiveness of ultrasound (US)-guided percutaneous transhepatic puncture in patients with low-level alpha-fetoprotein (AFP) liver cancer.

Methods: A total of 300 patients with primary liver cancer (PLC) (with AFP level ≤200 ng/mL and who underwent fine-needle aspiration) who were admitted to Central South University Xiangya School of Medicine Affiliated Haikou Hospital from January 2016 to December 2020 were selected to participate in the present study. Data, such as the expression of AFP and the biological characteristics of cells related to follow-up information, were retrospectively analyzed.

Results: Patients with AFP content <50 ng/mL accounted for 27% of total patients. Patients with tumors <20 mm accounted for 11% of total patients. There were 88 patients with 0–50 ng/mL AFP, 75 patients with 51–100 ng/mL AFP, 57 patients with 101–150 ng/mL AFP, and 83 patients with 200 ng/mL AFP. The sensitivity of detection was ≥90%, specificity was 100%, PPV was 100%, and NPV was ≥90%. In the present study, 34 patients with tumors <20 mm in size underwent US-guided percutaneous transhepatic puncture. The sensitivity of the treatment was 93.33%, 100% specificity, 100% PPV, and 64.35% NPV. The sensitivity of US-guided percutaneous transhepatic puncture was 97.65%, 100% specificity, 100% PPV, and 55.42% NPV in 266 patients with tumor size >20 mm. Implantation and metastasis accounted for 5% of complications, and gastrointestinal bleeding accounted for 7%. Among the adverse reactions, nausea and vomiting accounted for 15%, diarrhea accounted for 10%, and bone marrow suppression accounted for 8%.

Conclusions: US-guided percutaneous transhepatic puncture has high sensitivity, high specificity, and is relatively safe, with a low complication rate in patients with low-level AFP liver cancer, and has certain clinical diagnostic value.

Keywords: Liver cancer; alpha-fetoprotein (AFP); fine-needle aspiration; effectiveness; complications

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Introduction

Primary liver cancer (PLC) is a common malignant neoplasm worldwide. The incidence of PLC continues to increase due to the growing burden of global liver diseases (1). Because of its asymptomatic nature, liver cancer is usually diagnosed at late and advanced stages, at which time it is generally too late for surgical resection owing to tumor size, location of the tumor, or poor liver function, resulting in a short life expectancy (2). Therefore, disease monitoring and accurate diagnostic methods are important for the early diagnosis and treatment of high-risk patients.

Alpha-fetoprotein (AFP) is a serum glycoprotein produced by the embryonic yolk sac, and the fetal liver and is the most widely used biomarker to detect hepatocellular carcinoma (HCC) worldwide (3). It is also often used as an independent factor in predicting the overall survival of patients because of its high sensitivity, high specificity, and high accuracy in the patient's body. Pregnant women have higher blood AFP levels (4), whereas elevated serum AFP levels may be associated with a higher risk of tumors of gonadal origin, such as liver-like adenocarcinoma and HCC, and non-malignant chronic liver disease, including acute or chronic viral hepatitis (5,6). Of HCC patients, 40% had normal AFP levels at initial diagnosis. AFP serum levels were reduced in 30% patients, despite AFP specificity. Therefore, clinical examinations, such as ultrasound (US)-guided percutaneous transhepatic and radiological imaging, should be combined with AFP levels for HCC diagnosis.

US-guided puncture is a minimally invasive method for the diagnosis of HCC. Cytological and histological samples can be obtained by US or computed tomography (CT) guidance (7). Despite recent advances in imaging technology, the diagnostic value of US-guided percutaneous transhepatic puncture is still applied to optimal sensitivity and specificity, as well as future guidance, determination of chemotherapy regimens, and other treatments. A false-positive diagnosis may still exist, even if AFP of 200 ng/mL is used as the diagnostic criterion, based on American Association for the Study of Liver Diseases guidelines, which may lead to unnecessary treatment and pain. A false-negative diagnosis caused by a false explanation of low serum AFP cannot be ignored. Therefore, in the present study, we aimed to reassess the importance and determined the overall accuracy of serum AFP ≤200 ng/mL in a patient population as a diagnostic value in future clinical practice by percutaneous transhepatic puncture guided by US. We present the following article in accordance with the STARD reporting checklist (available at https://dx.doi.org/10.21037/tcr-21-701).

Methods

General information

A total of 300 patients with PLC, who were treated in Central South University Xiangya School of Medicine Affiliated Haikou Hospital from January 2016 to December 2020, were analyzed retrospectively. Inclusion criteria were as follows: (I) PLC diagnosed by CT, magnetic resonance imaging (MRI), and histopathological biopsy; (II) AFP content ≤200 ng/mL; and (III) patients who had undergone US-guided percutaneous transhepatic puncture. Exclusion criteria were as follows: (I) pregnant or lactating; (II) mental illness; (III) coagulation dysfunction; (IV) serious liver and kidney function disorders; and (V) lost to follow up. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Central South University Xiangya School of Medicine Affiliated Haikou Hospital (No.: 2014HN096) and informed consent was taken from all the patients.

Observation indicators

Observation indicators were as follows: (I) comparison of patients' general clinical data; (II) analysis of diagnostic results in patients with liver cancer with different AFP expression levels; and (III) effect of US-guided percutaneous transhepatic puncture on diagnostic results for different tumor sizes.

Statistical analysis

Data were statistically analyzed by GraphPad Prism 8.0 (GraphPad Software Inc., San Diego, CA, USA) to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy (compared with the final diagnosis after follow up). Measurement data were represented as means ± standard deviations and analyzed by *t*-test. Counting data were expressed as percentages and analyzed by χ^2-test. $P<0.05$ was considered statistically significant.

Table 1 Comparison of patients' general clinical data

Variable	Cases (n)	%
Sex		
Male	205	68
Female	95	32
Alpha-fetoprotein expression level (ng/mL)		
<50	80	27
50–100	75	25
100–150	73	24
150–200	72	24
Tumor size (mm)		
<20	34	11
20–50	27	9
50–80	51	17
80–100	99	33
>100	89	30
Cirrhosis		
Yes	169	56
No	131	44

Results

Comparison of patients' general clinical data

The data analysis showed that 32% of the patients with AFP liver cancer were women. Different AFP expression levels were also found among patients. Patients with AFP levels 50 ng/mL accounted for less than 50% of all patients, those with AFP levels 50–100 ng/mL accounted for 25% of all patients, those with AFP levels 100–150 ng/mL accounted for 25% of all patients, and those with AFP levels 150–200 accounted for 24% of all patients. Cancer patients with tumors <20 mm accounted for 11% of total patients, those with tumors 20–50 mm accounted for 9% of the total, those with tumors 50–80 mm accounted for 17% of the total, those with tumors 80–100 mm accounted for 33% of the total, and those with tumors >100 mm accounted for 30% of the total. In total, 56% of patients had cirrhosis. The statistical analysis data are shown in *Table 1*.

Diagnostic analysis results of HCC patients with different AFP expression levels

A total of 88 patients had an AFP level of 0–50 ng/mL, 75 patients had an AFP level of 51–100 ng/mL, 57 had an AFP level of 101–150 ng/mL, and 83 patients had an AFP of 151–200 ng/mL. The sensitivity of detection was ≥90%, specificity was 100%, PPV was 100%, and NPV was ≥90% (*Table 2*).

Effect of US-guided percutaneous transhepatic puncture on diagnostic results for different tumor sizes

Thirty-four patients had a tumor size <20 mm. The sensitivity of US-guided percutaneous transhepatic puncture was 93.33%, 100% specificity, 100% PPV, and 64.35% NPV. A total of 266 patients had a tumor size >20 mm. The sensitivity of US-guided percutaneous transhepatic puncture was 97.65%, 100% specificity, 100% PPV, and 55.42% NPV (*Table 3*).

Analysis of complications and adverse reactions caused by US-guided percutaneous transhepatic puncture

US-guided percutaneous transhepatic diagnosis accounted for 5% of complications in patients with AFP liver cancer and 7% of gastrointestinal bleeding. Nausea and vomiting accounted for 15%, diarrhea 10%, and bone marrow suppression 8% (*Table 4*).

Discussion

The accuracy of cancer diagnosis is important, as the treatment will vary based on the type of cancer. The incorrect diagnosis may result in a wrong or delayed treatment harm to the patient. Over the past several decades, there has been controversy concerning the role of US-guided percutaneous transhepatic puncture in the detection of HCC. Advances in dynamic imaging techniques have improved the accuracy of HCC diagnosis in most nodules, and most of these dynamic imaging techniques are based on angiogenesis and metastasis (8). CT and MRI have high sensitivity (55–91%) and specificity in diagnosing HCC (77–96%) (9). However, there are some limitations in assessing HCC occurrence when only

Table 2 Diagnostic results of liver cancer patients with different expression levels of alpha-fetoprotein

Indicators	0–200 ng/mL	0–50 ng/mL	51–100 ng/mL	101–150 ng/mL	151–200 ng/mL
No. of patients	300	88	75	57	83
Malignant/benign tumors	287/16	82/6	70/5	55/2	80/3
Actual value	300	88	75	57	83
Error value	16	6	5	2	3
False report	0	0	0	0	0
False negative	287	82	70	55	80
Sensitivity (%)	95.66	93.18	93.33	96.49	96.38
Specificity (%)	100	100	100	100	100
PPV (%)	100	100	100	100	100
NPV (%)	94.58	91.28	93.54	94.58	95.58

NPV, negative predictive value; PPV, positive predictive value.

Table 3 Impact of ultrasound-guided percutaneous transhepatic puncture on the diagnostic results of different tumor sizes

Indicators	<20 mm	>20 mm
No. cases	34	266
Malignant/benign tumors	30/4	256/10
Sensitivity (%)	93.33	97.65
Specificity (%)	100	100
PPV (%)	100	100
NPV (%)	64.35	55.42

NPV, negative predictive value; PPV, positive predictive value.

Table 4 Complications and adverse reactions caused by ultrasound-guided percutaneous transhepatic puncture diagnosis

Clinical symptoms	Cases (n)	%
Implantation transfer	15	5
Gastrointestinal bleeding	20	7
Nausea and vomiting	45	15
Diarrhea	30	10
Bone marrow suppression	25	8

using angiogenesis and metastasis. For example, enhanced patterns of small HCC depend on tumor sizes and cell differentiation, and tumors <2 cm may exhibit atypical enhancement. Subvascular tumors are likely to be ignored in that HCC diagnosis is based on vascular type; 52% of early arteriole enhancement lesions decrease over time and are considered false lesions (10). In the present study, 34 patients with tumors <20 mm in size underwent US-guided percutaneous transhepatic puncture. The sensitivity of the treatment was 93.33%, 100% specificity, 100% PPV, and 64.35% NPV. The sensitivity of US-guided percutaneous transhepatic puncture was 97.65%, 100% specificity, 100% PPV, and 55.42% NPV in 266 patients with tumor size >20 mm. There was no significant difference between tumors <2 mm and those ≥2 mm in the subgroups based on sensitivity, specificity, PPV, and NPV, which indicates the advantage of US-guided percutaneous transhepatic puncture for the diagnosis of small hepatic lesions.

US-guided percutaneous transhepatic puncture is the most commonly used confirmatory diagnostic method for HCC (11). Although this is a minimally invasive diagnostic approach, it still has serious side-effects and may aggravate patients' pain (12). Because AFP and US-guided percutaneous transhepatic puncture are common diagnostic methods for a confirmed diagnosis of PLC, it is important to assess the effectiveness and relevance of these two diagnostic methods to avoid unnecessary surgery and patient pain. Unfortunately, the value of US-guided percutaneous liver puncture in patients with serum AFP ≤200 ng/mL is rarely studied (13). The results of the present study indicated that 88 patients had 0–50 ng/mL AFP levels, 75 had 51–100 ng/mL AFP levels, 57 had 101–150 ng/mL AFP levels, and 83 had 151–200 ng/mL AFP

levels. Detection of sensitivity was 90%, 100% specificity, 100% PPV, and ≥90% NPV, indicating that changes in AFP content do not affect the accuracy of US-guided percutaneous transhepatic diagnosis.

Pathological diagnosis can provide a variety of benefits for patients looking for appropriate treatment options for suspicious malignant tumors. US-guided percutaneous transhepatic puncture can provide pathological samples for early diagnosis and data for medical research. In addition, for patients with suspected small liver cancer, especially with atypical imaging lesions, once liver nodules are found in patients, US-guided percutaneous transhepatic puncture can alleviate patients' anxiety. Early detection of liver nodules can decrease the cost of long-term imaging surveillance and enable early treatment options.

In previous report (14), biliary peritonitis was found to be a serious complication of US-guided transhepatic puncture. It is noteworthy that bile peritonitis was not detected in any patient in the present study, which could possibly be due to the inevitable avoidance of aspiration in cases of bile duct punctures. According to the data reported from recent study, US-guided percutaneous transhepatic diagnosis accounted for 5% of complications in patients with AFP liver cancer, 7% of gastrointestinal bleeding, 15% of nausea and vomiting, 10% of diarrhea, and 8% of bone marrow suppressions. Moreover, bleeding is usually associated with severe cirrhosis or large superficial tumors not covered by normal hepatic parenchyma, rather than coagulation curves and platelet counts (15). When the tumor is covered with sufficient liver parenchyma, it can still be punctured, regardless of tumor size, and there is no excessive risk of bleeding (16). For tumors that have relatively large or small coverage of normal liver tissue, bleeding after percutaneous liver puncture under US guidance should be carefully monitored. The risk of bleeding in each patient should be observed before therapy. If the risk of bleeding is high, imaging should be undertaken for diagnosis to avoid bleeding after US-guided percutaneous liver puncture.

In conclusion, US-guided percutaneous transhepatic puncture has a good clinical diagnostic value in patients with low-level AFP liver cancer because of its high sensitivity, high specificity, high accuracy, and relatively safe and low incidence of complications.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://dx.doi.org/10.21037/tcr-21-701

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Central South University Xiangya School of Medicine Affiliated Haikou Hospital (No.: 2014HN096) and informed consent was taken from all the patients.

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