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Value of Multi-slice Spiral CT Combined with Tumor Markers in Diagnosing Benignity and Malignancy of Hepatic Tumors

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ABSTRACT

Background: multi-slice spiral computed tomography (MSCT) combined with tumor marker detection can distinguish the nature of hepatic tumors. Meanwhile, diagnosing hepatic tumors is crucial for improving the survival rates (SR) of patients. ***Materials and Methods:*** data from 98 patients with hepatic tumors who underwent radiological examinations and treated in our hospital from December 2022 to December 2023 were collected. Pathological reports were arranged for patients, and based on the results, patients were categorized into benign tumor and malignant tumor groups (BT and MT groups). Clinical information such as pathological results, gender, and medical history was recorded and compared. After MSCT examination, the imaging features of patients were documented, and tumor markers in serum were detected. The accuracy of tumor markers alone and combined examination in determining the nature of hepatic tumors was compared. ***Results:*** the positivity rate (PR) of MSCT combined with tumor markers in the MT group (89.02%) was higher to that in the BT group (64.44%). The accuracy of the combined diagnosis in judging hepatic tumor nature was 64.57%, with a sensitivity of 89.02% and specificity of 35.56%. The area Under Curve (AUC) of the combined examination was 0.813, being higher than that of MSCT or tumor marker diagnosis alone. ***Conclusion:*** MSCT combined with tumor markers exhibited remarkable clinical value in determining benign and malignant hepatic tumors, with improved diagnostic accuracy and sensitivity, enabling its widespread application in early screening of hepatic tumors.

INTRODUCTION

The high incidence and increasing trend of hepatic tumors make it one of the most common malignancies worldwide, and due to its lack of early symptoms, patients can be diagnosed with distant metastases [1]. Therefore, accuracy in the diagnosis of hepatic tumors is extremely important. The high incidence of liver metastases is due in part to the structural and functional features of blood flow from the digestive system to the liver and the sinusoids, which are able to coordinate colonization that promotes metastases, and have a hepatic tumors-tolerant microenvironment that is capable of suppressing protective immune responses [2, 3]. The presence of pro-tumor macrophages and other myeloid cells in the microenvironment that promotes hepatic tumor metastasis can suppress immunogenesis [4, 5]. Therefore, the exact nature of hepatic tumors is extremely important, which has important clinical implications for determining effective treatment options, improving the survival rate (SR) of patients and improving their quality of life.

Imaging has been widely used in the diagnosis of cancer diseases, and some studies have found that early diagnosis of cancer can improve the health of patients, although there are no obvious clinical symptoms in the early stage of cancer, but the cancerous changes of the liver will gradually show some characteristic changes in imaging examinations [6, 7]. In clinic, it is mostly used for liver imaging, which is a non-invasive method to evaluate liver morphology, blood flow and the detection and characterization of liver tumors [8]. Studies have shown that multi-slice spiral computed tomography (MSCT) exhibits the characteristics of high sensitivity and high resolution, and has the advantage of being able to avoid the interference of obesity, respiration and other factors [9]. The MSCT scan results of patients with primary nodular hepatocellular carcinoma lesions were mainly hypodense, accompanied by a small amount of calcification, which was manifested as "rapid appearance and quick out" enhancement, and the enhancement was uneven, and the arterial phase scan showed patchy and nodular enhancement, and the venous phase and equilibrium phase showed continuous decrease in enhancement. On the other hand, MSCT scans of focal nodular hyperplasia of the liver are predominantly

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low-density, uneven in density, stellate, striated, or fissure-like, and most of the lesions have typical central scars [10, 11]. Some studies used CT to observe the liver status of patients, and the results showed that it was less sensitive to detect hepatocellular carcinoma in the diagnosis of patients with liver cirrhosis [12]. The similarity of these two imaging findings suggests that there are still some limitations to a single imaging technique, especially in differentiating benign and malignant tumors. Because the benign and malignant manifestations of hepatic tumors often intersect on CT images, benign lesions may also exhibit irregular margins, while some malignancies may exhibit relatively regular morphology [13-16]. This makes it relatively difficult to accurately judge the nature of the tumor at an early stage.

Therefore, to have a more comprehensive understanding of the biological characteristics of tumors, MSCT was combined with tumor markers for diagnosis in this study, which can not only reflect the biological behavior of tumors, but also provide important early warning information in the early stage of patients without obvious clinical symptoms. Hepatic tumors are often accompanied by elevated levels of some tumor-specific markers alpha -fetoprotein (AFP) and carcinoembryonic antigen (CEA), which are widely used in cancer diagnosis and surveillance, and are commonly used to detect a variety of cancers such as the gastrointestinal tract [17]. Serum CEA levels are often elevated in hepatic tumors, particularly in patients with hepatocellular carcinoma (HCC) [18]. In contrast, AFP is commonly used to diagnose primary liver cancer, but its isolation has poor sensitivity and specificity [19]. Some studies have found that the combined determination of AFP and other tumor markers may improve the diagnostic efficiency [20].

In this work, MSCT and tumor markers were combined to explore the differences in imaging features and serum marker levels between patients with benign and malignant hepatic tumors. Tumor markers are serological biological indicators, which can indirectly reflect the growth and spread of tumors. The combination of MSCT and tumor markers can compensate for the shortcomings of imaging techniques and provide supplementary information on the biological characteristics of tumors. Therefore, the combination of MSCT and tumor markers is expected to provide a more comprehensive and accurate assessment for the early diagnosis of hepatic tumors, so as to provide more targeted support for the treatment and management of patients.

MATERIALS AND METHODS

Research subjects

127 patients with hepatic tumors examined in the Department of Radiology of our hospital from December 2022 to December 2023 were enrolled herein, and all patients underwent cancer surgery at our hospital. The patients enrolled had to satisfy all the following conditions: all patients were diagnosed with pathology and confirmed in our hospital; all had been treated with hepatic tumors prior to diagnosis; and they had no history of hematologic disorders. Patients with any of following conditions had to be excluded: patients with contraindications to CT examination; patients with the presence of other tumors; and those with severe renal disease.

This study has been approved by the Ethics Committee of our hospital [approval number: * * * (registration date and registration number)], and all the patients involved have signed informed consent forms.

Research methodology

(1) Clinical data: clinical data such as pathological diagnosis, gender, age, and disease history of patients were collected and recorded.

(2) MSCT examination method: the Siemens SOMATOM Definition AS Sliver 128-slice spiral CT machine(Siemens, Germany) was utilized for the examination. On the day preceding the examination, the patient was instructed to undergo fasting and refrain from drinking after 12 o'clock in the morning. During the examination, the patient was positioned supine on the platform, and the scanning parameters were configured as follows: voltage 120 kV, current 70 mA, layer spacing 5 mm, layer thickness 5 mm, pitch 1.25 mm, time interval 5s, matrix 512×512. A whole liver perfusion scan was initiated 10 seconds later. Breath-holding instructions were given to the patient during the examination, and the scanning speed was regulated to conduct 13 scans within 90 seconds. Subsequently, the scanned images were uploaded to a workstation for processing, and the region of interest (ROI) was established to enable the software to automatically generate a time-density curve. ROIs encompassed tissue exhibiting mass lesion enhancement, perilesional tissue, and normal liver tissue. Special attention was given to avoiding intrahepatic large vessels when placing oval or circular regions of interest to ensure precise data acquisition. The time-density curve reflected the intensification of different tissues or regions over time. Analysis of these curves allowed the extraction of perfusion parameters concerning the mass lesion, the tissue surrounding the lesion, and the normal liver tissue. These parameters were utilized to generate color images illustrating perfusion characteristics of different tissue regions. Figure 1 is a MSCT image of a patient's liver tissue.

(3) Detection of tumor markers: Atellica automatic biochemical immunoassay analyzer (Siemens AG, Germany) and CEA, AFP, NSE (neuron-specific enolase) and CA-125 (glycoprotein) kits (Siemens AG,

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Germany) provided by the company were used to detect tumor markers CEA, AFP, NSE and CA-125 in the blood of the subjects. The venous blood of patients in the morning was collected in a test tube, centrifuged at a low speed of 3500r/10min, and the serum was collected and stored at -20℃. Use the kit and instrument described above to detect tumor markers. CEA, AFP, CA-125 and NSE are detected by direct chemiluminescence method. Prepare the samples and liquid reagents used for detection according to the instructions, and then put them directly into the instrument for detection. The detection shall be carried out in strict accordance with the instructions.

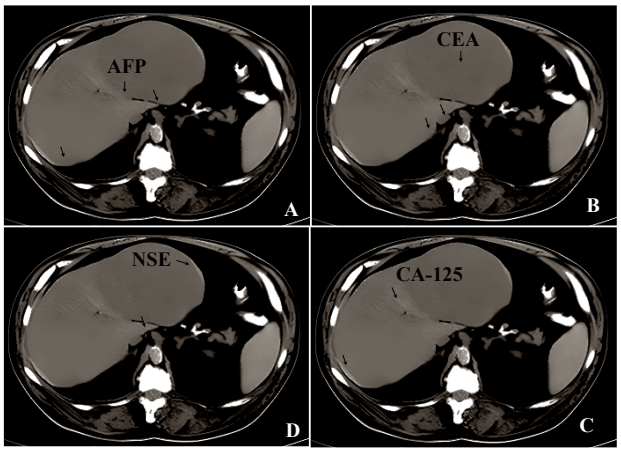

Figure 1. MSCT images of patients' liver tumors and tumor marker Region of interest(ROI) (**A** stands for AFP; **B** represents CEA; **C** stands for CA-125; **D** stands for NSE) The arrow in the figure points to the ROI area.

Observation indicators

The MSCT results were read by two professional physicians to observe the imaging perfusion parameters of hepatic tumors, including hepatic blood flow (HBF), hepatic blood volume (HBV), hepatic arterial perfusion volume (HAP), and hepatic arterial perfusion index (HPI).

Diagnostic criteria of tumor markers

The test result was determined as positive when the level of tumor markers was greater than the cut-off (i.e., CEA > 4.7 U/mL, AFP > 25 U/mL, NSE > 16.3 U/mL, and CA-125 > 35 U/mL). And any positive result indicated a positive diagnosis. All results below the cut-off value signified a negative diagnosis.

Methods for statistical analysis

SPSS26.0 data analysis software was leveraged to process the data herein. The continuous data were represented using mean ± standard deviation and compared with t-test. Count data were expressed as percentage (%) or number of cases (n) and compared with c^2 test. The accuracy, sensitivity, and specificity of MSCT, tumor markers, and PR diagnosed by MSCT and tumor markers in patients with hepatic tumors were calculated. The Receiver Operating Characteristic (ROC) was utilized to analyze the efficacy of the diagnostic method, and the area under the curve (AUC) was calculated. The significance level was set to $P<0.05$.

RESULTS

Patients grouping based on pathological diagnosis results

127 patients with hepatic tumors were enrolled in this research. According to the pathological diagnosis, 45 patients with benign tumors (BT group) and 82 patients with malignant tumors (MT group) were diagnosed. In the MT group, there were 52 cases of liver cancer, 21 cases of liver metastases, 4 cases of cholangiocarcinoma, 2 cases of hepatoblastoma, and 3 cases of hepatic angiosarcoma. In contrast, there were 21 cases of hepatic hemangioma, 16 cases of hepatic cyst, and 8 cases of hepatic adenoma in the BT group. Moreover, among the 82 malignant tumors, liver cancer (63.41%) was the most common, and among the 45 benign tumors, liver hemangioma (46.67%) was the most common. Figure 1 was given for details of above data.

Table 1. patients grouping based on pathological diagnosis results.

MT group	Number(n=82)	Percentage(%)
liver cancer	52	63.41
Liver metastases	21	25.61
Cholangiocarcinoma	4	4.88
Hepatoblastoma	2	2.44
Hepatovascular sarcoma	3	3.66
BT group	Number(n=45)	Percentage(%)
Hepatic angiomatosis	21	46.67
Hepatic cyst	16	35.56
Hepatoadenoma	8	17.78

General data of patients in different groups

The BT group encompassed 23 male patients and 22 female patients, and they were (50.46 ± 12.17) years old in average, with 1 patient experiencing with a family history of cancer and 1 patient suffering from a history of liver disease. In contrast, 42 male patients and 40 female patients were enrolled in the MT group, showing an average age of (59.63 ± 12.84) years old. Meanwhile, 34 patients with a family history of cancer and 81 patients with a history of liver disease. The age ($P=0.023$) and family history of tumor ($P=0.012$) exhibited remarkable significance ($P<0.05$) for patients in the BT group and MT group, while the gender and liver disease history were not greatly different ($P>0.05$). The details of above data were summarized and compared in figure 2.

MSCT perfusion parameters of patients

The MSCT perfusion parameters were compared between BT group patients and MT group patients, as depicted in figure 3. The HBF values of patients in the BT group and MT group groups were both increased obviously, while the HBV and HAP values of all

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patients were sharply decreased, all showing great differences in contrast to the value before they were intervened (P<0.05). However, no considerable difference was observed in HPI value for patients in the BT group and MT group (P>0.05).

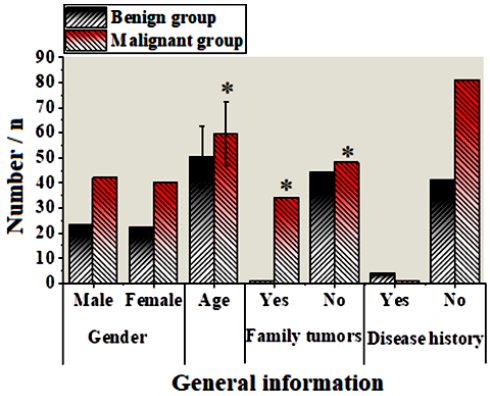

Figure 2. Brief introduction of patients in various groups. * Suggested a remarkable difference with P<0.05 to the BT group.

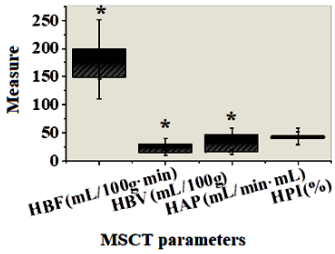

Figure 3. MSCT perfusion parameters of patients (the upper and lower limits of HBF were MT group and BT group, respectively; the upper and lower limits of HBV, HAP, and HPI were BT group and MT group, respectively).The y-axis represents the difference of MSCT observation indexes between the two groups, and the x-axis represents the MSCT observation indexes. The lower limit of HBF bar graph is benign group and the upper limit is malignant group; The lower limit of HBV, HAP and HPI bar charts is malignant group, and the upper limit is benign group. Note: * suggested a remarkable difference with P<0.05 to the BT group.

MSCT examination results of patients in different groups

The MSCT diagnostic results revealed that there were 18 patients experiencing with positive BT group diagnosis and 27 patients suffering from negative BT group diagnosis, with a PR of 40.00%. Furthermore, 55 patients were found to be with positive MT group diagnosis and 27 patients with negative MT group, yielding a PR of 67.07%. The c^2 test unveiled a remarkable significance with P<0.05. According to the calculations, the accuracy, sensitivity, and specificity of MSCT in the diagnosis of benign hepatic tumors were 66.93%, 67.07%, and 60.00%. The results above were supported by checking the data in figure 4.

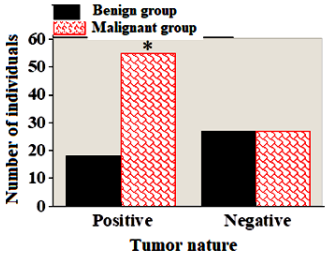

Figure 4. MSCT examinations of patients in the BT group and MT group. Note: * suggested a remarkable difference with P<0.05 to the BT group.

Changes in tumor markers levels

The levels of tumor markers CEA, AFP, NSE, and CA-125 in all patients from different groups were detected and comparatively analyzed, as demonstrated in Figure 5A. It was evident that the CEA levels for patients in the MT group groups were greatly downshifted in comparison to those in the BT group, showing a substantial difference with P<0.05. Patients in the MT group experienced elevated AFP, NSE, and CA-125 levels when compared to those in the BT group, exhibiting sharp differences (P<0.05). However, the level of CA-125 was negative in both groups (figure 5A).

For PR of CEA, it was 0% in BT group and 20.73% in MT group. A comparison on PR of CEA suggested that it was higher in the MT group, showing a great difference with P<0.05 to that in the BT group. The detected PR of AFP PR was 0% in the BT group and 25.61% in the MT group. It was evident that the PR of AFP in the MT group was sharply higher, exhibiting a great difference to that in the BT group (P<0.05). In addition, the PR of NSE was 0% and 30.40% in the BT group and MT group, respectively. It suggested that patients in the MT group presented sharply high PR of NSE in contrast to those in the BT group (P<0.05). The specific data were summarized in figure 5B to support above results.

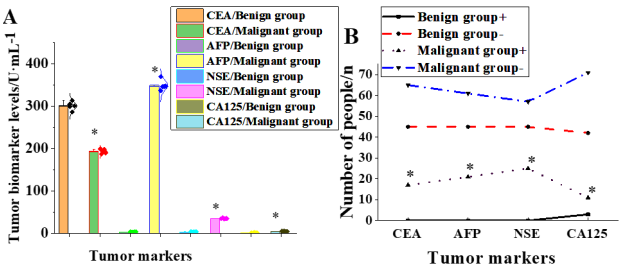

Figure 5. Changes in tumor markers levels. (**A:** tumor markers levels, **B:** the number of patients with tumor properties; +: positive, -: negative). Note: * suggested a remarkable difference with P<0.05 to the BT group.

Diagnosis efficacy of MSCT combined with tumor markers

The PR of benign and malignant hepatic tumors diagnosed by MSCT combined with tumor markers was 64.44% in the BT group and 89.02% in the MT group, as illustrated in figure 6. The comparative results signified that the PR of MSCT combined with tumor markers in the MT group patients was much higher and exhibited a visible difference with that in the BT group (P<0.05). Further calculated revealed an accuracy of 64.57%, a sensitivity of 89.02%, and a specificity of 35.56% for MSCT combined with tumor markers in diagnosis of benign and malignant hepatic tumors.

ROC curves of MSCT and tumor markers in diagnosing hepatic tumors

As demonstrated in figure 7, the AUC of MSCT was 0.659 for hepatic tumors, 0.692 for tumor markers,

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and 0.813 for MSCT combined with tumor markers in diagnosing the nature of hepatic tumors. It suggested that the MSCT combined with tumor markers exhibited the highest accuracy in diagnosing the nature of hepatic tumors.

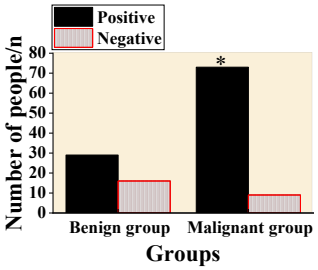

Figure 6. PR of MSCT combined with tumor markers in different groups. Note: * suggested a remarkable difference with P<0.05 to the BT group.

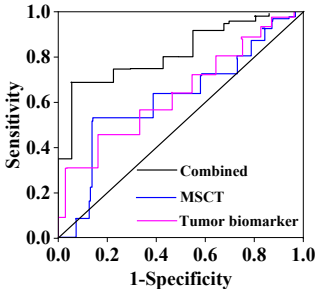

Figure 7. ROC curves for different methods in judging the nature of hepatic tumors.

DISCUSSIONS

The pathological types of hepatic tumors include both benign and malignant tumors. Among the 127 patients with hepatic tumors enrolled, the pathological results revealed 82 cases of malignant tumors and 45 cases of benign tumors. Malignant tumor types included hepatocellular carcinoma, hepatic metastasis, bile duct tumor, hepatoblastoma, and hepatic vascular tumor. On the other hand, benign tumor types included hepatic vascular tumor, hepatic vascular malformation, hepatic cyst, and hepatic adenoma. This work encompassed various types of hepatic tumors, providing a foundation for subsequent comparisons and analyses. In tumor screening, chest CT has been widely employed, and with the increasing incidence of tumors in recent years, there is a growing emphasis on chest CT screening [21]. utilized a CT-based radiomics model to predict the degree of microvascular infiltration in hepatocellular carcinoma, constructing a model based on the optimal AUC radiomics model and clinical imaging features, with AUC serving as an indicator of hepatocellular carcinoma severity [23]. applied CT radiomics to predict the massive lump subtype of hepatocellular carcinoma. However, diagnostic CT imaging for the nature of hepatic tumors has some limitations. Therefore, in this study, MSCT was combined with tumor markers for the diagnosis of the nature of hepatic tumors.

In recent years, the incidence and mortality rates of hepatic tumors in males have been higher than in females [23]. In this work, a comparison of gender differences between two patient groups revealed a nearly equal male-to-female ratio for those with benign and malignant tumors, possibly due to the relatively small sample size in this study. However, significant differences were observed in terms of age and family medical history, with patients in the malignant tumor group having significantly higher ages and tumor family histories than those in the benign group, showing statistical significance. This suggests that age and family history may be related to the occurrence of malignant hepatic tumors. Consistent with the findings of Yang *et al.* [24], patients with a family history of hereditary liver diseases are more prone to malignant hepatic tumors. Studies indicate a positive correlation between age and tumor development [25], with the overall survival rates for liver transplant tumors being 90% at 1 month, 70% at 1 year, and 45.4% at 5 years [26]. Therefore, annual health check-ups for middle-aged individuals are essential to screen for cancer risk factors, undergo radiomics examinations, and detect and treat diseases early. Shimizu *et al.* [27] found in their study on dental implantation that compared to traditional CT, MSCT has better accuracy. Additionally, in the report by Li *et al.* [28], MSCT was utilized to examine the vascular infiltration degree of hepatocellular carcinoma. Herein, MSCT was employed to examine liver images, and the comparative results of MSCT perfusion parameters exhibited a remarkable increase in HBF in the MT group, while HBV and HAP were sharply decreased compared to the BT group. This indicates more significant blood flow changes in malignant tumors, and these parameters help distinguish the nature of hepatic tumors. Furthermore, PR in the MT group was much higher, with an accuracy of MSCT in diagnosing benign hepatic tumors of 66.93%, a sensitivity of 67.07%, and a specificity of 60.00%. This suggests that MSCT has a certain level of accuracy in the diagnosis of hepatic tumors, and MSCT is more sensitive in detecting malignant tumors. Shuqi *et al.* [29] found that CT morphological features and CT texture parameters had statistically significant differences between benign and malignant lesions, consistent with the results of this work.

Due to the overlap of MSCT radiomics in benign and malignant tumors, which will affect the accuracy of diagnosis, the levels of tumor markers CEA, AFP, NSE, and CA-125 were detected in this work. The outcomes revealed that the CEA, AFP, NSE, and CA-125 levels were greatly elevated in patients in the MT group, and levels of the former three were positive. However, they were relatively downshifted in the BT group, with negative AFP, NSE, and CA-125 levels. This suggests that these tumor markers may be helpful in the identification of malignant hepatic tumors [30, 31]. The positive rate of MSCT combined with tumor markers in the diagnosis of liver tumor was calculated. In this study, it was found that the positive rate of MSCT combined with tumor markers

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in the malignant group increased significantly, and the correct rate, sensitivity and specificity of combined diagnosis of liver tumor were 64.57%, 89.02% and 35.56%. In some studies, ROC curve was used to evaluate the diagnostic value of multi-slice spiral CT combined with alpha-fetoprotein level in the treatment of small hepatocellular carcinoma in patients with liver cirrhosis. It was found that its AUC, sensitivity and specificity were 95%, 94% and 83% respectively [32]. It shows that CT combined with AFP can obviously improve the diagnostic efficiency of hepatocellular carcinoma. The AUC and specificity of this study are significantly lower than that of this study, which may be due to the fact that only 35 patients with hepatocellular carcinoma were included in this study, and there were fewer cases, which affected the results. Additionally, ROC curves were made to evaluate the accuracy of diagnosing hepatic tumors by MSCT and tumor markers levels. It became evident that the combined diagnosis had the highest accuracy, with an AUC of 0.813. This signifies that the combination of MSCT and tumor markers can be more effective in determining the degree of malignancy of hepatic tumors. In van Kessel *et al.*' s study, the accuracy of MSCT in rectal liver metastasis was 77% [33]. There are also studies that use contrast-enhanced MSCT to diagnose stem cells with an accuracy of 82% [34]. All the above studies show that the accuracy of MSCT diagnosis alone decreases, while the accuracy of diagnosis can be improved by combining other methods.

CONCLUSION

In summary, the examination of liver imaging using MSCT technology found that there were more significant blood flow changes in the MT group, and these parameters helped to distinguish the nature of hepatic tumors. Combined with the detection of CEA, AFP, NSE, and CA-125 levels, the degree of malignancy of hepatic tumors can be more effectively determined. Findings in this work signified that MSCT combined with tumor markers exhibited a high accuracy rate and remarkably improved PR in diagnosing hepatic tumors, emphasizing the importance of combining multiple methods for comprehensive assessment. However, the sample was not broad enough, which may affect the comprehensiveness of the results.

***Ethical approval and consent to participate*:** This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were outlined in the study protocols approved by the ***and was conducted in agreement with principles of Helsinki declarations and local ethical standards. Patients of study participants provided written informed consent.

***Consent of publication*:** Not applicable.

***Availability of data and materials*:** The datasets used and/or analysed during the current study are available from the corresponding authors on reasonable request.

***Conflict of interest*:** The authors declare no competing interests.

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***Author Contributions*:** Drafting/revision of the manuscript for content and including medical writing for content and article frame design: XM, LY, and XL. All authors contributed to the article and approved the submitted version.

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