Research Article

Analysis of the Performance of Gadoxetic Acid Disodium MRI in Predicting Microvascular Invasion of Hepatocellular Carcinoma

Jiao Chen, Xianfang Ming, Zhen Wang, and Yu Ye

Department of Radiology, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, Edong Healthcare Group, Huangshi City 435000, China

Correspondence should be addressed to Zhen Wang; 20152210095@m.scnu.edu.cn and Yu Ye; 20152901020@m.scnu.edu.cn

Received 30 July 2022; Revised 6 September 2022; Accepted 14 September 2022; Published 28 September 2022

Copyright © 2022 Jiao Chen et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Objective. This study aimed to evaluate the predictive value of gadoxetic acid disodium magnetic resonance imaging (MRI) in the microvascular invasion (MVI) of hepatocellular carcinoma (HCC). Methods. 87 HCC patients (2019–01–2022–01) admitted to the hospital were selected for retrospective analysis, gadoxetic acid disodium MRI scan was performed before surgery, and the patients were divided into two groups according to whether the MVI occurred, including the invasion group (n = 47) and the non-invasion group (n = 40). The influencing factors of MVI in HCC patients were explored, independent risk factors were determined, and the correlation between independent risk factors and MVI in HCC patients was analyzed. Results. There were significant differences in tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) between the two groups (P < 0.05). Logistic regression analysis showed that unsmooth tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) were independent risk factors for MVI in HCC patients (P < 0.05). The results of Spearman correlation analysis showed that unsmooth tumor margin was negatively correlated with MVI in HCC patients (\(r = -0.66, P = 0.037\)). Moreover, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) were positively correlated with MVI in HCC patients (\(r_1 = 0.63, r_2 = 0.68, r_3 = 0.72, P_1 = 0.030, P_2 = 0.023, P_3 = 0.017\)). Conclusion. Unsmooth tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) are significantly correlated with MVI in patients with HCC, which can provide a reference for the formulation and implementation of clinical interventions.

1. Introduction

Hepatocellular carcinoma (HCC) is a common type of cancer and is usually treated by surgery, but the recurrence rate is about 70% five years after surgery, and the prognosis of patients is poor [1]. Relevant literature reports that microvascular invasion (MVI) can reflect the invasive ability of HCC and is a risk factor affecting postoperative recurrence and prognosis [2]. However, at present, MVI can only be determined based on the histopathological examination results and cannot be diagnosed until the specimen is obtained. With the advancement of imaging technology, magnetic resonance imaging (MRI) plays an essential role in the preoperative diagnosis of HCC. MRI can predict the MVI state according to the tumor’s morphological characteristics, such as tumor margin and size, and has the advantages of no ionizing radiation and high soft tissue contrast [3]. Gadoxetic acid disodium is a novel contrast agent for detecting focal liver lesions and has excellent potential in predicting MVI [4]. This study aimed to investigate the predictive value of gadoxetic acid disodium MRI in the MVI of HCC and to provide a reference for clinical treatment.

2. Materials and Methods

2.1. General Information. 87 HCC patients (2019–01–2022–01) admitted to the hospital were selected for retrospective analysis, gadoxetic acid disodium MRI scan was performed before surgery, and the patients were divided into two
groups according to whether the MVI occurred, including the invasion group (n = 47) and the non-invasion group (n = 40). There were ten females and 77 males (aged 30–84 years; average age of 59.10 ± 11.42 years; medical history: 71 cases of hepatitis B, 1 case of hepatitis C, and 43 cases of liver cirrhosis).

2.2. Inclusion and Exclusion Criteria

(1) Inclusion: consistent with the diagnostic criteria for HCC [5]; no macrovascular invasion, no tumor thrombus, and no distant metastasis of cancer cells; single lesion; maximum diameter of the tumor was 5 cm; no contraindications for MRI examination; and surgery was performed 2 weeks after MRI examination.

(2) Exclusion: combined with other malignant tumors; received treatment in the past, including interventional treatment, surgical treatment, and so on; and clinical data or imaging images were unclear.

2.3. Scanning Method of Gadoxetic Acid Disodium MRI. The instrument was a magnetic resonance scanner (Philips, model: Achieva 3.0T), and abdominal 16-channel coil was used. First, a conventional plain scan was performed, and diffusion weighted imaging (DWI) sequence, $T_2$-weighted image ($T_2$WI) fat-suppressed sequence, and $T_1$-weighted image ($T_1$WI) double-echo sequence were used. DWI scanning parameters were as follows: echo time of 55 ms, repetition time of 3000–5000 ms, slice spacing of 1 mm, slice thickness of 5 mm, and matrix of 128 × 160. $T_2$WI scanning parameters were as follows: echo time of 70 ms, repetition time of 2000 ms, slice spacing of 1 mm, slice thickness of 5 mm, and matrix of 250 × 230. $T_1$WI scanning parameters were as follows: echo time of 2.3 ms, repetition time of 3 ms, slice thickness of 2.5 mm, and matrix of 250 × 230, and no spacing scan was performed. Then, enhanced scan was performed, $T_1$ high resolution isotropic volume excitation (THRIVE) sequence was used, and gadoxetic acid disodium (Bayer Schering Pharma AG, approval number: H20100664) was administered by intravenous bolus; the injection rate and dosage were 1.0–1.5 mL/s and 0.1 mL/kg. The arterial phase images were collected at 20 s after injection, the portal venous phase images were collected at 60 s after injection, and the transitional phase images were gathered at 180 s after injection. Enhanced scanning parameters were as follows: echo time of 1.5 ms, repetition time of 3 ms, slice thickness of 2.5 mm, and matrix of 250 × 230, and no spacing scan was performed.

2.4. MRI Imaging Indicators. All images acquired by the MRI scanner were uploaded to an image archiving and communication system, and imaging signs related to MVI were evaluated by two experienced radiologists. The symptoms to be observed are as follows: (1) Tumor diameter: take the maximum tumor diameter measured on the coronal and axial planes of hepatobiliary phase as the tumor diameter. (2) Whether there are nodular processes at the tumor margin and they are not smooth. (3) Whether there is a high signal area around the tumor, and it shows medium signal after entering the delayed phase and venous phase [6]. (4) Tumor signal intensity [7]. (5) Whether there is a low signal area around the tumor, and sheet, flame or wedge low signal areas appear around the tumor. (6) Whether there are irregular or regular high-intensity rings around the tumor. (7) Intratumoral fat content.

2.5. Statistical Methods. The data were processed by SPSS22.0, and the measured data were expressed by (±s), and t-test was performed. The counting data is expressed in n (%), and test is performed. Logistic multiple regression equation was used for multivariate analysis, and Spearman was used for correlation analysis. P < 0.05 was considered statistically significant.

3. Results

3.1. Univariate Analysis of MVI in HCC Patients. There was no significant difference in tumor diameter, tumor signal intensity, and intratumoral fat between the groups (P > 0.05). There were significant differences in tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) between the groups (P < 0.05), as shown in Table 1.

3.2. Multivariate Analysis of MVI in HCC Patients. The occurrence of MVI in HCC patients was regarded as the dependent variable (yes = 1, no = 0), and the factors with statistically significant differences in Table 1 were considered as independent variables. The assignments are shown in Table 2. Logistic regression analysis showed that unsmooth tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) were independent risk factors for MVI in HCC patients (P < 0.05), as shown in Table 3.

3.3. Correlation Analysis of MVI in HCC Patients. The results of Spearman correlation analysis showed that unsmooth tumor margin was negatively correlated with MVI in HCC patients ($r = −0.66$, $P = 0.037$). Moreover, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) were positively correlated with MVI in HCC patients ($r_1 = 0.63$, $r_2 = 0.68$, $r_3 = 0.72$, $P_1 = 0.030$, $P_2 = 0.023$, $P_3 = 0.017$).
4. Conclusion

MVI is an important prognostic factor in HCC patients. Studies have confirmed a close relationship between MVI, postoperative tumor progression, and early recurrence in HCC patients [8]. For HCC patients with other MVIs, the treatment plans are different. In addition, considering the error rate of needle biopsy and the lag of postoperative pathological examination results, preoperative non-invasive prediction of MVI has tremendous significance [9].

As a medical imaging diagnostic technology, MRI has the advantages of multidirectional, multisequence, and no radiation. It can display the enhancement range, enhancement characteristics, blood supply, number of lesions, and bleeding of lesions, which provides valuable information for identifying HCC [10, 11]. In addition, MRI can reflect the hardness of HCC lesions and the spread of cancer cells, and MRI also has great value in the prediction of HCC MVI [12]. As a liver-specific contrast agent, gadoxetic acid disodium not only has the efficacy of a conventional contrast agent but also can be taken up by hepatocytes, highlighting the tumor boundary and reflecting the pathological changes of HCC [13]. Gadoxetic acid disodium MRI plays an active role in the evaluation of liver function and the diagnosis of liver lesions, but there are few studies on its value in predicting MVI in HCC [14]. Relevant studies have shown that tumor diameter bigger than 5 cm is an influencing factor for MVI. Therefore, this study included HCC patients with tumor diameter ≤ 5 cm to explore the risk factors for MVI in patients with smaller lesions [15]. In this study, logistic regression analysis was performed using the elements with statistical significance in the univariate analysis as independent variables, and the results showed that unsmooth tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral hyperintensity ring (arterial phase), and peritumoral enhancement (arterial phase) are significant influencing factors for MVI. The univariate analysis results are shown in Table 1, the binary logistic regression analysis results are shown in Table 2, and the multivariate analysis results are shown in Table 3.

| Variable | Assignments |
|----------|-------------|
| Dependent variable | Occurrence of MVI |
| Tumor margin | Yes = 1, no = 0 |
| Peritumoral enhancement (arterial phase) | Yes = 1, no = 0 |
| Peritumoral hyperintensity ring (arterial phase) | Yes = 1, no = 0 |
| Peritumoral low signal (hepatobiliary phase) | Yes = 1, no = 0 |

| Influencing factors | β | S.E. | Waldχ² | P | OR | Lower limit | Upper limit |
|---------------------|---|------|--------|---|----|-------------|-------------|
| Unsmooth tumor margin | 1.062 | 0.368 | 8.334 | < 0.001 | 2.893 | 1.018 | 8.223 |
| Peritumoral enhancement (arterial phase) | 1.029 | 0.343 | 9.002 | < 0.001 | 2.799 | 1.146 | 6.834 |
| Peritumoral hyperintensity ring (arterial phase) | 1.321 | 0.416 | 10.085 | < 0.001 | 3.748 | 1.532 | 9.167 |
| Peritumoral low signal (hepatobiliary phase) | 1.233 | 0.389 | 10.041 | < 0.001 | 3.430 | 1.271 | 9.258 |

Table 1: Univariate analysis of MVI in HCC patients.

Table 2: Assignment.

Table 3: Multivariate analysis of MVI in HCC patients.
enhancement (arterial phase), and peritumoral hyper-intensity ring (arterial phase) were independent risk factors for MVI in HCC patients ($P < 0.05$); therefore, it is necessary to pay attention to the above factors clinically. Dhiman [16] pointed out that peritumoral hyperintensity ring and peritumoral low signal are independent risk factors for MVI in HCC patients, similar to the results of this study.

The reasons are as follows. (1) Unsmooth tumor margin: the tumor margin is divided into unsmooth and smooth. This study showed that the tumor margin was negatively correlated with MVI in HCC patients, and this is because after the MVI occurred, the tumor edge tissue was invaded, resulting in a non-smooth edge [17]. (2) Peritumoral enhancement (arterial phase): when the portal vein around the lesion was invaded, tumor thrombus was formed, resulting in loss or reduction of portal blood flow and a compensatory increase in arterial perfusion. Based on this mechanism, studies have confirmed that portal vein-arterial shunt is essential for predicting MVI. Peritumoral signal enhancement in the arterial phase was positively correlated with MVI [18]. (3) High strength ring around tumor: invasive growth of the tumor leads to edema around the tumor or increased blood supply, so there is a high signal ring around the tumor, and the risk of MVI is increased [19]. (4) Peritumoral low signal (hepatobiliary phase): this study showed a positive correlation between the low signal around the hepatobiliary tumor and MVI. The MVI around the tumor in the hepatobiliary phase can change the hemodynamics in this area and also damage the function of liver cells, making it difficult for liver tissue to take in gadoxetic acid disodium, and the signal is reduced due to the decrease of contrast agent absorbed by the surrounding liver parenchyma [20].

To sum up, unsmooth tumor margin, peritumoral low signal (hepatobiliary phase), peritumoral enhancement (arterial phase), and peritumoral hyperintensity ring (arterial phase) are significantly correlated with MVI in patients with HCC, which can provide a reference for diagnosis and treatment, help physicians formulate a comprehensive treatment plan, help reduce the risk of postoperative metastasis and recurrence, and improve the prognosis of patients. However, this study had some shortcomings. (1) The sample size was small, and more cases need to be included for verification in the future. (2) Imaging image judgment was subjective, and a chief physician can be invited to make a decision when radiologists cannot reach an agreement. (3) The predictive value of gadoxetic acid disodium MRI in the grading of HCC MVI has not been explored, and further research on this aspect is needed in the future.

**Data Availability**

The data used to support the findings of this study are available from the corresponding author upon request.

**Disclosure**

Jiao Chen and Xianfang Ming are the co-first authors.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**Authors’ Contributions**

Jiao Chen and Xianfang Ming authors contributed equally to this work and should be considered co-first authors.

**Acknowledgments**

This study was funded by the Huangshi Medical and Health Science and Technology Project (2019A04).

**References**

[1] J. Zhu, Y. Ding, S. Wang, Q. Shi, and D. Wang, “The effect of ulinastatin therapy in the perioperative period on the percentage of Th22 cells in peripheral blood and plasma interleukin-22 in patients with hepatocellular carcinoma after hepatectomy,” *J Pract Hepatol*, vol. 22, no. 5, pp. 720–723, 2019.

[2] X. Sun, Y. Zheng, and S. Yuan, “The relationship between multi-slice spiral CT manifestations and liver cancer microvascular invasion,” *Chin J CT MRI*, vol. 19, no. 12, pp. 96–98, 2021.

[3] L. Jiao, C. Duan, H. Yu, J. Wang, M. Li, and A. Li, “The value of dadoxetic acid disodium enhanced MRI for quantitative and qualitative evaluation of microvascular invasion in liver cancer,” *Radiologic Practice*, vol. 36, no. 8, pp. 1026–1031, 2021.

[4] X. Li, P. Cai, L. Cheng, P. Liu, J. Wang, and X. Lin, “The clinical value of dadoxetic acid disodium enhanced magnetic resonance imaging in the preoperative diagnosis of thick beam-mass hepatocellular carcinoma,” *Chin J Digestive Surg*, vol. 20, no. 11, pp. 1218–1226, 2021.

[5] W. Lin, Z. Chen, B. Liu, and F. Li, “National multicenter prospective liver cancer very early warning screening Project (PreCar) expert group. Expert consensus on early screening strategies for liver cancer in China,” *Chinese Hepatology*, vol. 26, no. 8, pp. 825–831, 2021.

[6] G. Hu, Q. Zhang, M. Ning, J. Guo, J. Wang, and J. Huang, “Research progress of preoperative MRI predicting microvascular invasion of hepatocellular carcinoma,” *Chin J Magn Reson Imaging*, vol. 13, no. 2, pp. 159–162, 2022.

[7] C. Qu, Li Kun, P. Cai, J. Huang, L. Miao, and M. Cao, “Prediction of microvascular invasion in hepatocellular carcinoma with a feature model based on MRI radiomics,” *Chinese Journal of Bases and Clinics in General Surgery*, vol. 28, no. 2, pp. 175–180, 2021.

[8] X. Zhu, X. Zhang, Ru Zhao, L. Li, and S. Zheng, “Diagnostic value of enhanced MRI and diffusion-weighted imaging for microvascular invasion of small hepatocellular carcinoma,” *Shandong Medical Journal*, vol. 61, no. 31, pp. 65–67, 2021.

[9] L. Jiang, H. Chen, G. Wang, W. Zhang, and D. Li, “Evaluation of risk factors for microvascular invasion of small hepatocellular carcinoma by CT or MRI manifestations,” *J Clin Radiol*, vol. 38, no. 5, pp. 844–847, 2019.

[10] X. Li, X. Yi, Z. Liu, D. Zhu, and X. Li, “Diagnostic value of diffusion-weighted magnetic resonance imaging for microvascular invasion in hepatocellular carcinoma,” *Oncology Progress*, vol. 18, no. 18, pp. 1866–1869, 2020.
[11] H. Wang, M. Zeng, S. Rao, D. Dou, and P. Yang, “The value of conventional MRI image radiomics in evaluating microvascular invasion in hepatocellular carcinoma,” Chinese Journal of Radiology, vol. 53, no. 4, pp. 292–298, 2019.

[12] Y. Lu, W. Zhang, P. Wang, F. Li, and Y. Zhang, “Predictive value of preoperative magnetic resonance imaging analysis for microvascular invasion in solitary hepatocellular carcinoma,” Guangxi Med J, vol. 41, no. 13, pp. 1605–1608, 2019.

[13] X. Xu, S. Sun, Q. Liu, J. Guo, and H. Fan, “Application of different MRI contrast agents in predicting microvascular invasion of hepatocellular carcinoma,” Journal of Nanjing Medical University, vol. 42, no. 1, pp. 96–102, 2022.

[14] Y. Tian, Y. Hu, Q. Peng, Y. Li, J. Chen, and B. Lv, “The value of dadoxetic acid disodium enhanced MRI nomogram model in predicting microvascular invasion of small hepatocellular carcinoma,” Chin J Magn Reson Imaging, vol. 12, no. 10, pp. 57–60, 2021.

[15] S. Dai, J. Liu, E. Xiao, S. Dai, W. Zeng, and S. Miao, “The predictive value of preoperative CT or MRI features for microvascular invasion in hepatocellular carcinoma,” Chin J Mod Oper Surg, vol. 24, no. 3, pp. 177–182, 2020.

[16] G. Dhiman, V. Vinoth Kumar, A. Kaur, and A. Sharma, “Don: deep learning and optimization-based framework for detection of novel coronavirus disease using x-ray images,” Interdisciplinary Sciences: Computational Life Sciences, vol. 13, no. 2, pp. 260–272, 2021.

[17] J. Jayakumar, B. NagarajNagaraj, S. ChackoChacko, and P. Ajay, “Conceptual implementation of artificial intelligent based E-mobility controller in smart city environment,” Wireless Communications and Mobile Computing, vol. 2021, pp. 1–8, Article ID 532516, 2021.

[18] X. Liu, Y.-X. Su, S.-L. Dong, W.-Y. Deng, and B.-T. Zhao, “Experimental study on the selective catalytic reduction of NO with C3H6 over Co/Fe/Al2O3/cordierite catalysts,” Ranliao Xuebao/Journal of Fuel Chemistry and Technology, vol. 46, no. 6, pp. 743–753, 2018.

[19] R. Huang and X. Yang, “Analysis and research hotspots of ceramic materials in textile application,” Journal of Ceramic Processing Research, vol. 23, no. 3, pp. 312–319, 2022.

[20] Z. Guo and Z. Xiao, “Research on online calibration of lidar and camera for intelligent connected vehicles based on depth-edge matching,” Nonlinear Engineering, vol. 10, no. 1, pp. 469–476, 2021.