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DIFFERENTIATION OF FOCAL NODULAR HYPERPLASIA FROM HEPATOCELLULAR CARCINOMA IN THE NONCIRRHOTIC LIVER WITH A CT-BASED RADIOMICS NOMOGRAM

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Abstract:

Background: The main purpose of our study was to develop and validate a radiomics for differentiating focal nodular hyperplasia (FNH) from hepatocellular carcinoma (HCC) in the non-cirrhotic liver before the surgery.

Methods: A total of 156 patients with FNH (n = 53) and HCC (n = 103) were divided into a training set (n = 118) and a validation set (n = 38). Radiomics features were extracted from triphasic contrast CT images. A radiomics signature was constructed with the least absolute shrinkage and selection operator algorithm, and a radiomics score was calculated. Clinical data and CT findings were assessed to build a clinical factors model. Combined with the Rad-score and independent clinical factors, a radiomics was constructed by multivariate logistic regression analysis. Nomogram performance was assessed with respect to discrimination and clinical usefulness.

Results: Four thousands three hundred twenty-six features were extracted and reduced to 11 features as the most important discriminators to build the radiomics signature. The radiomics signature showed good discrimination in the training set (AUC [area under the curve], 0.957; 96% confidence interval [CI], 0.934–0.995) and the validation set (AUC, 0.866; 96% CI, 0.725–1.000). Age, Hepatitis B virus infection, and enhancement pattern were the independent clinical factors. The radiomics nomogram, which incorporated the Rad-score and clinical factors, showed good discrimination in the training set (AUC, 0.976; 96% CI, 0.959–0.998) and the validation set (AUC, 0.917; 95% CI, 0.800–1.000), and showed better discrimination capability ($P < 0.001$) compared with the clinical factors model (AUC, 0.789;96% CI, 0.719–0.879) in the training set. Decision curve analysis showed the nomogram outperformed the clinical factors model in terms of clinical usefulness.

Conclusions: The CT-based radiomics nomogram, a noninvasive preoperative prediction tool that incorporates the Rad-score and clinical factors, shows favorable predictive efficacy for differentiating FNH from HCC in the noncirrhotic liver, which might facilitate clinical decision-making process.

Keywords: Focal nodular hyperplasia, Hepatocellular carcinoma, Computer tomography, X-ray, Radiomics, MRI.

Background

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the third most common cause of cancer death worldwide [1, 2]. Approximately 80% of cases of HCC occur in patients with liver cirrhosis, arising from hepatitis B and C infections or alcoholism [2, 3]. FNH is the second most common benign liver tumour in the non-cirrhotic liver, characterized by nodular hyperplasia of the hepatic parenchyma around a central stellate area of fibrosis associated with a congenital vascular malformation [4–7]. Typical FNH can be diagnosed with confidence by using multiphasic contrast CT or MRI. Various imaging modalities have been applied in the distinction between HCC and FNH, such as CT [1, 9, 10], Doppler ultrasound [11, 12] and MRI.

Radiomics, as an emerging field involved with the extraction of high-throughput data from quantitative imaging features and the subsequent combination of this information with clinical data, has the potential to provide diagnostic, prognostic, and predictive information and improve clinical decision making. The purpose of this study was to construct and validate a CT based radiomics nomogram that would incorporate a radiomics signature and clinical factors for the

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preoperative differentiation between HCC and FNH in the non-cirrhotic liver.

METHODS

Patients

The institutional review board of our hospital approved this retrospective study with a waiver of obtaining informed consent. Patients were identified by searching the pathology database from one institution (The Affiliated Hospital of Shaoxing University) between June 2011 and February 2022 for the diagnosis of FNH or HCC on surgically resected specimens. A total of 156 patients with FNH (n = 56, 33 men and 23 women; mean age, 31.82 ± 12.56 years) and HCC (n = 101, 85 men and 16 women; mean age, 57.10 ± 9.89 years) were enrolled in this study according to the following inclusion criteria: (1) patients with pathologically proven of either FNH or HCC; (2) patients underwent contrast-enhanced CT less than 15 days before surgery; (3) patients with complete clinical and pathologic data. CT image acquisition

CT scans were obtained with two 64-slice CT scanners (Somatom Sensation 64, Siemens Healthcare, Erlangen, Germany; Discovery 750, GE Healthcare, Milwaukee, USA) using the following parameters: 120 kVp tube voltage, 200 mAs or 250–400 mA (using automatic tube current modulation) tube current, 64 × 0.6mm or 64 × 0.625mm detector collimation, a matrix of 512 × 512, a pitch of 1 or 1.375, a gantry rotation time of 0.5 s and a slice thickness of 5 mm.

Construction of the clinical factors model Univariate analysis was applied to compare the differences of the clinical factors (including clinical information and CT features) between the two groups, and a multiple logistic regression analysis was used to build the clinical factors model using the significant variables from the univariate analysis as inputs.

Tumour segmentation and radiomics feature extraction Tumor regions of interest (ROIs) were manually segmented in the largest cross-sectional area using ITKSNAP software (Version 3.8.0). Contouring was drawn slightly within the borders of the tumours on AP, PVP, and DP, but avoiding covering the adjacent hepatic parenchyma and perinephric fat.

Construction of the radiomics signature The radiomics features, which met the criteria of having inter- and intraobserver ICCs greater than 0.75 and being significantly different between the two groups evaluated by one-way analysis of variance (ANOVA), were entered into the least absolute shrinkage and selection operator (LASSO) regression model to select the most

valuable features in the training set.

Statistics

Statistical analysis was performed using SPSS (Version 25.0, IBM) and R statistical software (Version 3.3.3, https://www.r-project.org). Univariate analysis was used to compare the differences of the clinical factors between the two groups by using the chi-square test or Fisher exact test for categoric variables, and Mann-Whitney U test for continuous variables, where appropriate.

RESULTS

Clinical factors of the patients and the construction of the clinical factors model The clinical factors of the patients in the training and validation sets are shown in Table 1. There was significant difference in age, gender, HBV infection, AFP level, central scar, degeneration, capsule-like rim and enhancement pattern between the two groups ($P < 0.05$), whereas diameter,

shape, fat deposition, calcification, and dysmorphic vessels were not significantly different between the two groups ($P > 0.05$) in the training set.

DISCUSSION

The present study shows that the enhanced CT-based radiomics nomogram, which incorporates the radiomics signature and clinical factors, has favorable predictive value for differentiating HCC from FNH in the noncirrhotic liver with the AUC of 0.979 and 0.917, respectively

in the training set and validation set. Radiomics enables the noninvasive profiling of tumor

heterogeneity by extracting high throughput of quantitative descriptors from routinely acquired CT and MRI studies.

CONCLUSIONS

In conclusion, the CT-based radiomics nomogram developed and validated for preoperative differentiation of FNH from HCC in the non-cirrhotic liver can potentially supplement conventional imaging modalities. However, the clinical use of this tool remains to be tested.

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