

# Title: Clear cell hepatocellular carcinoma: Gadoteric acid-enhanced MR imaging features and prognosis

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# Background

- Clear cell hepatocellular carcinoma (CCHCC) is a relatively rare pathological subtype of HCC characterized by glycogen accumulation in cytoplasm with clear cell morphology. CCHCC is generally diagnosed when the proportion of clear cells is larger than 80% according to the 2019 5<sup>th</sup> edition of the WHO Classification of Digestive System Tumors.
- Imaging features of CCHCC have been reported in some papers which were mainly focusing on CT or MRI using extracellular gadolinium contrast agent.
- Gadoxetic acid-enhanced MR imaging features of CCHCC has not been elucidated to date.

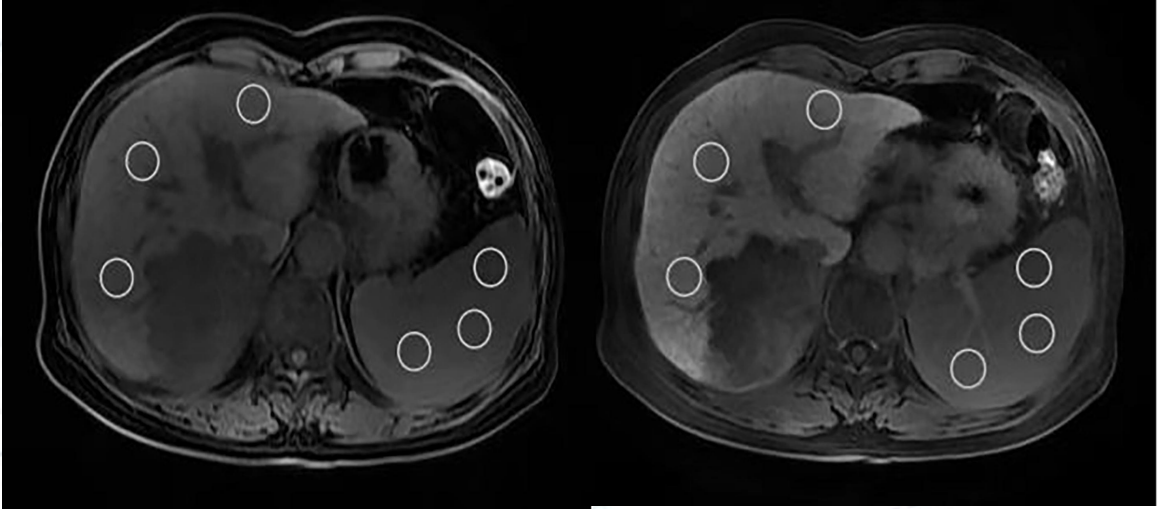
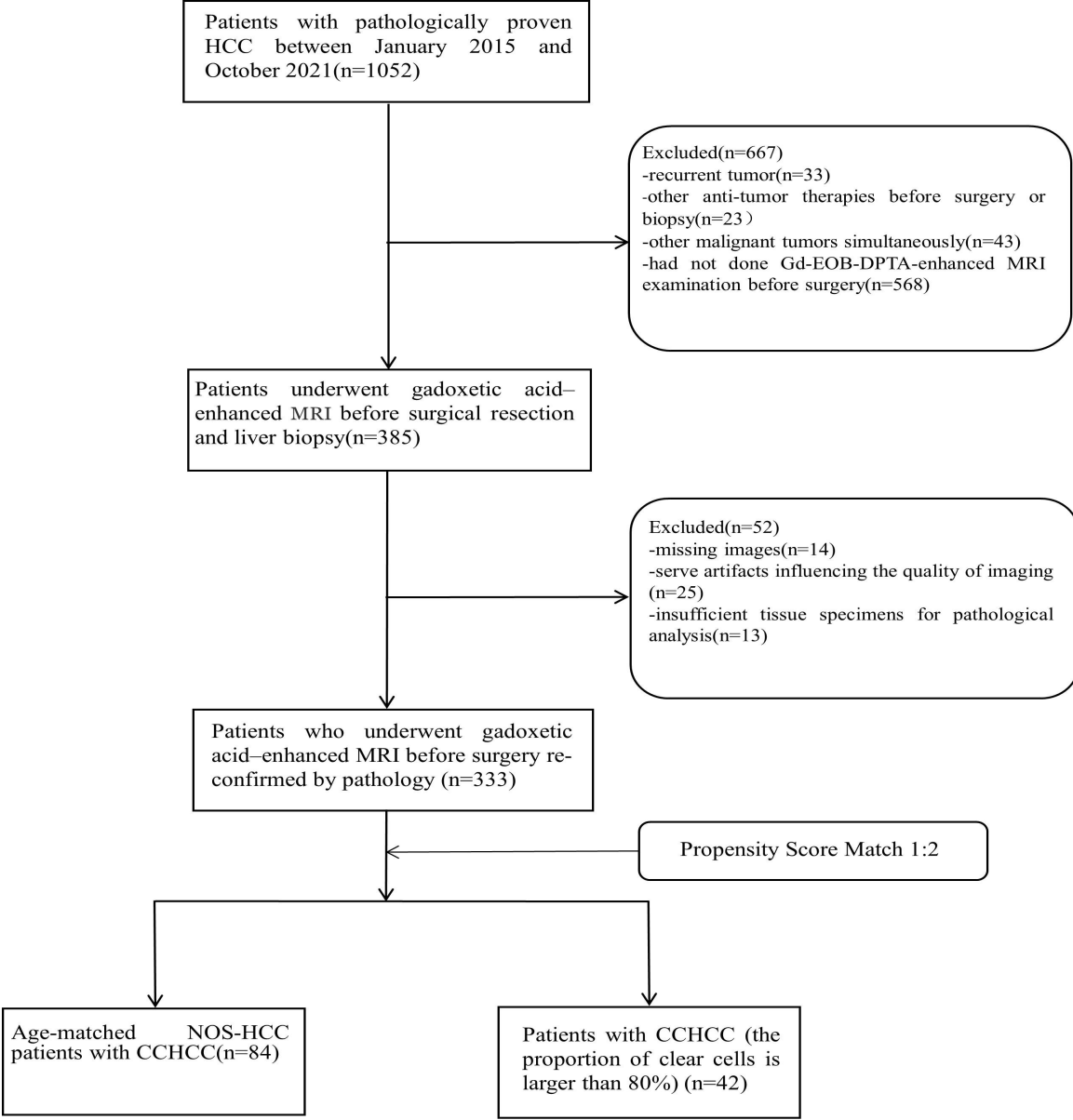
# Aim

- To investigate gadoxetic acid-enhanced MR imaging findings and prognosis of clear cell hepatocellular carcinoma(CCHCC) comparing with non-otherwise specified hepatocellular carcinoma(NOS-HCC).

# Methods

- Forty-two patients with CCHCC and 84 age-matched patients with NOS-HCC were retrospectively enrolled. The clinical, pathological and MR imaging features were investigated in CCHCC and compared with NOS-HCC. Disease-free survival (DFS) and overall survival (OS) were determined by Kaplan-Meier analysis. Univariate and multivariate analyses were performed to examine factors that affected prognosis.

# The flow chart of patient inclusion and exclusion



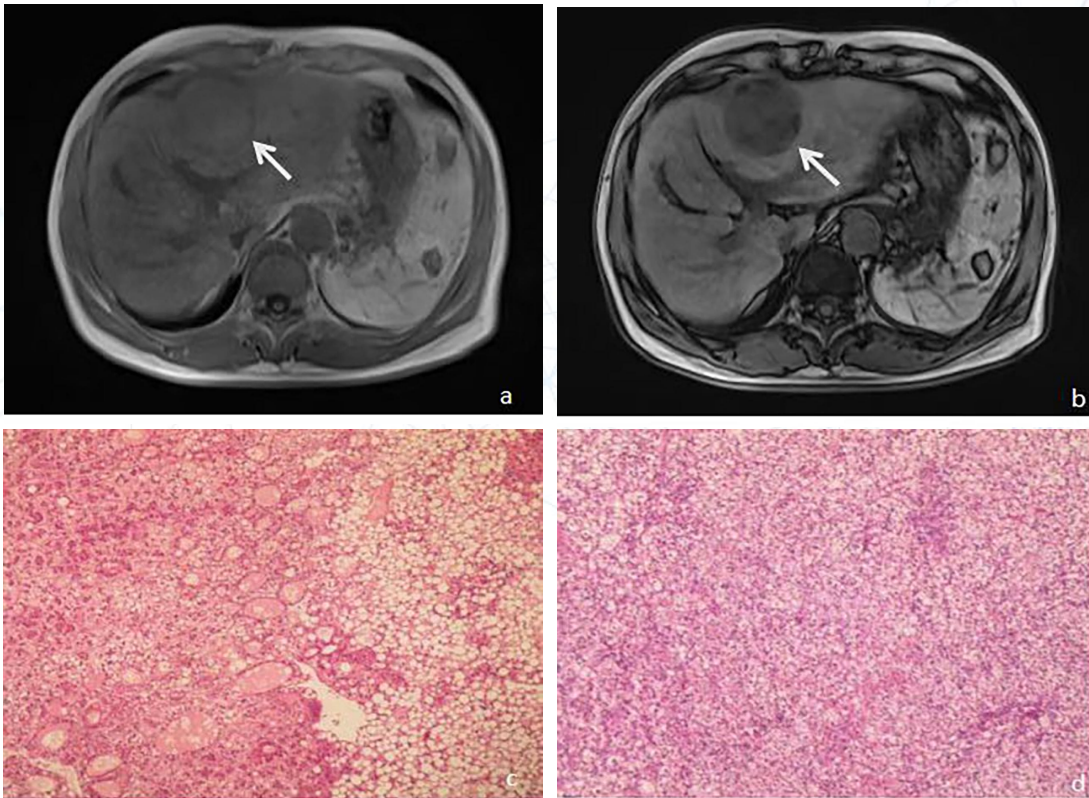
T1WI

HBP

The schematic diagram of liver and spleen ROI placement. The three ROIs were placed on the adjacent liver and spleen parenchyma at the same level of pre-contrast (a) and post-contrast (b) images on hepatobiliary phase (HBP) 20 min, respectively. Then the average values were calculated respectively as the final measurement values.

# Result 1

- CCHCC showed fat content more frequently ( $P < 0.001$ ) and relatively higher Edmondson tumor grade ( $P = 0.001$ ) compared with NOS-HCC.



Images in a 62-year-old man with 5cm clear cell hepatocellular carcinoma (CCHCC) referred for liver MRI. a Axial in-phase T1-weighted MR gradient-echo image shows an isointense lesion in segment S2/S3 (arrow). b Out-of-phase image demonstrates signal loss of this area (arrow), indicating a fatty component. c Microscopically, the mass shows fatty degeneration. (HE,  $\times 100$ ) d Photomicrograph (original magnification,  $\times 100$ ; hematoxylin-eosin stain) shows typical CCHCC appearance mainly composed of clear cells ( $>80\%$ ).

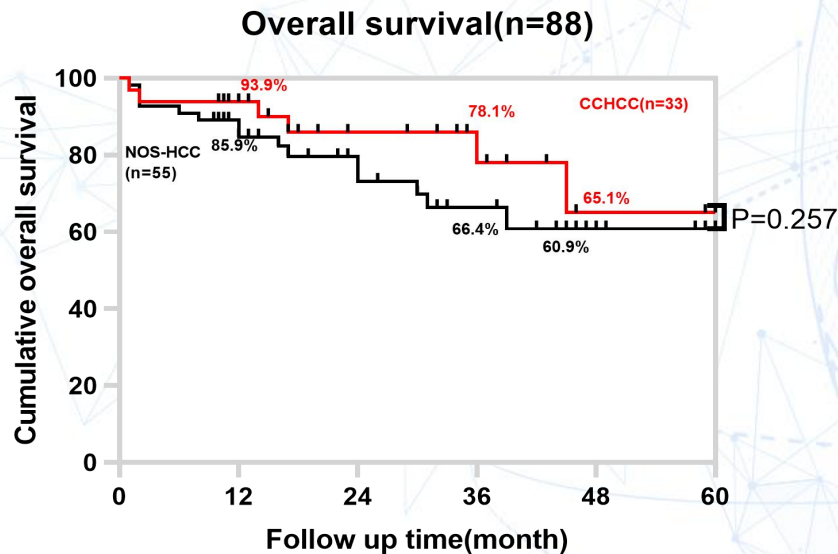
# Result2

- The lesion-to-muscle signal intensity ratio(LMR) and lesion-to-liver ratio(LLR) of CCHCC on pre-contrast T1WI( $P=0.001, P=0.003$ ) and hepatobiliary phase(HBP)( $P=0.007, P=0.048$ ) were significantly higher than those of NOS-HCC, while lesion-to-spleen ratio(LSR) of CC HCC on pre-contrast ( $P=0.339$ ) and HBP( $P=0.366$ ) did not show statistically significance albeit higher than those of NOS-HCC.

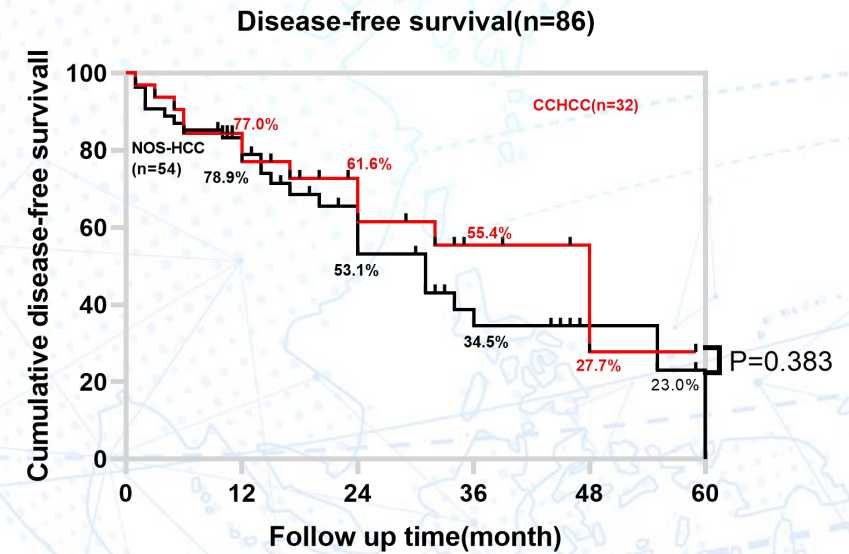
Pre-T1WI	CCHCC	NOS-HCC	P
LLR	0.86±0.17	0.77±0.14	0.003
LMR	1.21±0.34	1.02±0.29	0.001
LSR	0.95±0.32	0.89±0.24	0.339
HBP	CCHCC	NOS-HCC	P
LLR	0.69±0.22	0.62±0.22	0.048
LMR	1.45±0.37	1.27±0.41	0.007
LSR	0.97±0.40	0.92±0.37	0.366

# Result3

- The 1- and 3-year overall survival (OS) and disease-free survival (DFS) for patients with CCHCC were 93.9%, 78.1%, 77.0% and 65.4% respectively. Log-rank analysis revealed no statistical discrepancy in clinical outcome between CCHCC and NOS-HCC. Multivariate Cox analysis confirmed that tumor diameter (hazard ratio=0.086; 95% CI:0.008,0.947;  $P=0.045$ ) and enhancing capsule (hazard ratio=0.089; 95% CI:0.01,0.795;  $P=0.030$ ) were independent prognostic factors for DFS and OS of CCHCC patients, which were different from NOS-HCC.



CCHCC	33	27	/	11	/	1
NOS-HCC	55	41	25	/	6	1



CCHCC	32	23	13	/	2	/
NOS-HCC	54	38	21	9	4	1

# Conclusion

- Fat content and adjusted lesion signal intensity on pre-contrast T1WI and HB P could be used to differentiate CCHCC from NOS-HCC. CCHCC had similar prognosis with NOS-HCC and tumor size and enhancing capsule were independent predictive factor for survival of CCHCC patients.