Predicting differentiation of hepatocellular carcinoma at pre-transplant MRI in patients undergoing orthotopic liver transplantation

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Purpose: The Edmondson-Steiner grade of hepatocellular carcinoma (HCC) is an important predictor of disease free survival and tumor recurrence in patients undergoing liver surgery. Preoperative diagnosis of HCC differentiation can help predict which patients are likely to achieve long term cure, thus possibly allowing appropriate patient selection for liver allocation. Hence, the goal of this study was to correlate pre-transplant MRI features with hepatocellular carcinoma (HCC) differentiation at histopathology in patients undergoing orthotopic liver transplantation (OLT).

Methods: In this HIPAA compliant retrospective single center study, all patients who underwent liver transplantation and had gadolinium enhanced MRI performed 90 days prior to OLT over a 10 year period were included. Our study cohort consisted of 60 patients (47 M, 13 F; mean age 58 years). Two observers in consensus blinded to patient's clinical or pathologic information analyzed the following imaging parameters: number and size of HCCs, T1 and T2 signal intensity, qualitative enhancement pattern, presence or absence of washout, and presence of capsule/pseudocapsule for each tumor. Diffusion weighted imaging (DWI) was available in 21 patients. DWI was performed using axial breath-hold or respiratory-triggered SS EPI sequence (TR/TE 1600-3400/67-82/slice thickness 8 mm/ matrix up to 192x192/ parallel imaging factor 2) with b value of 0 and either 400 or 500s/mm^2. ADC maps were automatically generated at the scanner by monoexponential fitting ln(SI) as a function of b value. A blinded observer without knowledge of histopathology placed a large ROI over the tumor and measured the ADC values. Pre and post contrast 3D GRE T1 fat saturated (VIBE) acqusitions (2 arterial, portal venous, and equilibrium phases of enhancement) were loaded to a standalone workstation DynaCAD (Invivo Corp, Orlando, FL). Quantitative enhancement kinetics were examined in 20 tumors by generating a color parametric map of relative changes in each pixel's signal intensity over time; an ROI was then placed over the lesion's highest relative enhancement; peak relative enhancement, time to peak (TTP), and rate of enhancement were recorded. Size and number of HCCs, and HCC differentiation were determined at histopathology. Fisher's exact test was used to assess the relationship of HCC differentiation with categorical imaging measures. HCC subtypes were compared with respect to quantitative measures using unpaired t-test.

Results: 104 HCCs were identified at both pathology and MR imaging. 15 HCCs were necrotic due to prior chemoembolization and HCC differentiation was not available in 2 cases at pathology. Hence 87 HCCs were characterized at histopathology and imaging. 38 HCCs (43.6%) were well differentiated, 34 (39.1%) moderately differentiated, and 15 (17.2%) poorly differentiated. T1 hypointensity was significantly associated with poorly differentiated HCC (p=0.0085). There was no significant association of HCC differentiation (p>0.16) with any other categorical imaging measures. There was no difference in ADC between well, moderate, and poorly differentiated HCC (p>0.5). There was no significant difference between pathologic grades of well and moderate HCC in regards to any of the quantitative measures. There was statistically significant higher rate of peak enhancement in poorly differentiated HCC compared to well (p=0.02) and moderately differentiated HCC (p=0.04).

Pathology	ADC (10^{-3} mm^2/s)	TTP (sec)	Rel. peak enhancement (%)	Rate of enhancement
Well differentiated (n=8)	1.4 ± 0.17	60 ± 18	266 ± 108	4.5 ± 1
Moderately differentiated (n=4)	1.3 ± 0.4	68 ± 9	232 ± 89	3.4 ± 0.9
Poorly differentiated (n=8)	1.4 ± 0.4	42 ± 18	278 ± 61	7.7 ± 3.5

Footnote: TTP was significantly lower in poorly differentiate HCC compared to well/moderate HCCs (p=0.01)

Conclusion: T1 signal intensity, TTP, and rate of enhancement were the only imaging features which differed significantly in poorly differentiated HCCs. There was however, some overlap in the rate of enhancement and TTP between different HCC histologic grades; this bears more critical evaluation with high temporal resolution perfusion imaging which may improve diagnostic accuracy in differentiating poorly differentiated HCCs from well and moderately differentiated tumors.

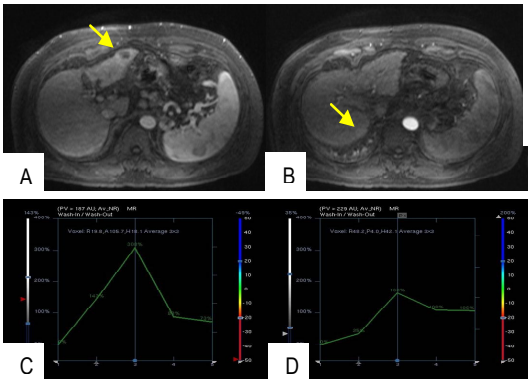

Figure: T1 post-contrast axial image and DynaCAD plot of enhancement in a poorly differentiated T1 hypointense tumor (A,C) shows higher rate of enhancement than the well-differentiated T1 hyperintense tumor (B,D).

References:
1. Kim BK, Han KH, Park YN, et al. J Surg Oncol 2008; 97:246-252
2. Wayne JD, Lauwers GY, Ikai I, et al. Ann Surg 2002; 235:722-730
3. Wiener JI, Schilling KJ, Adami C, et al. *AJR* 2005;184:878–886
4. Nasu K, Kuroki Y, Tsukamoto T, et al. AJR 2009; 193:438-444