POOR GADOXETATE DISODIUM HEPATOBILIARY ENHANCEMENT IN MRI OF PATIENTS WITH CIRRHOSIS: FACTORS FOR PREDICTION

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Target Audience: Radiologists who use Gadoxetate disodium (Gd-EOB-DTPA, Eovist, Primovist; Bayer) for evaluating patients with liver disease.

Purpose: To identify factors that predict poor gadoxetate-enhancement in cirrhotic patients.

Methods: This HIPAA-compliant retrospective study was approved by our Institutional Review Board. 91 cirrhotic patients who underwent gadoxetate-enhanced MRI examinations were selected. Three blinded readers independently assessed degree of liver enhancement by measuring regions of interest of liver relative to spleen (LS), portal vein (LPV) and paraspinal muscle (LM) on the 20-minute hepatobiliary phase sequence. Presence or absence of bile duct enhancement (BDE) was also determined. Independent variables included liver length and degree of ascites measured by three separate blinded readers, as well as laboratory indicators of liver and renal function. A Pearson product-moment correlation matrix of all variables was calculated. Logistic and multiple regression analyses were conducted. DBili (n=69) and ferritin (n=30) were excluded from the regression analyses because of large numbers of missing values; for other variables with a smaller number of missing values, the missing value was replaced with the variable mean.

Table 1: Correlation Matrix

Variable	BDE	LM	LPV	LS
ALP	-0.16	-0.07	0.04	-0.06
ALT	0.05	-0.14	-0.18	-0.24*
AST	-0.63	-0.27*	0.34*	-0.34*
Albumin	0.44*	0.51*	0.49*	0.58*
Ascites	-0.46*	-0.39*	-0.19	-0.42*
BUN	-0.01	-0.01	-0.06	-0.04
Creatinine	-0.05	-0.15	-0.03	-0.13
DBili	-0.32*, n=69	-0.22, n=69	-0.27*, n=69	-0.26*, n=69
Ferritin	-0.30, n=30	-0.27, n=30	-0.21, n=30	-0.21, n=30
INR	-0.49*, n=82	-0.31*, n=82	-0.38*, n=82	-0.40*, n=82
Liver Length	0.18	-0.08	0.01	0.02
MELD score	-0.56*, n=82	-0.40*, n=82	-0.46*, n=82	-0.48*, n=82
PT	-0.50*, n=82	-0.31*, n=82	-0.39*, n=82	-0.41*, n=82
Platelets	0.22*, n=89	0.27*, n=89	0.30*, n=89	0.38*, n=89
TBili	-0.34*	-0.21*	-0.28*	-0.28*
GFR	0.07	0.19	0.13	0.20

*Correlation is significant at the 0.05 level, n=91 unless otherwise noted

Results: Intercorrelation between the four dependent variables was high (r=0.42-0.75, p <0.0001). Of 64 correlations between independent and dependent variables, 34 were significant to the 0.05 level and 18 were significant to the 0.0007 level (Table 1). The highest correlations were noted between albumin and all the dependent variables (r=0.45-0.58); ascites and BDE (r=0.46); INR and BDE (r=0.49); MELD score and BDE, LPV and LS (r=0.46-0.56); and PT and BDE (r=0.50), p<0.0001 for all. ALP, liver length and renal parameters did not show strong correlations with other independent variables (r<0.33 for all). These variables and ferritin did not correlate with any of the dependent variables.

In the multiple regression models (Table 2), albumin accounted for most of the variance of the dependent variable (partial R-square of 0.24, 0.26 and 0.34 for LPV, LM and LS, respectively). Other variables (MELD score, AST, ALP, liver length, GFR, INR, ascites and creatinine) accounted for less of the variance (partial R-square of 0.02-0.04). Two variables, MELD score and ascites, correlated with BDE in the logistic regression model. MELD score accounted for most of the variance (area under the curve =0.79 for MELD score alone versus 0.83 for both variables).

Discussion: Our study evaluates potential predictors of poor hepatobiliary enhancement by gadoxetate, an MRI contrast agent with both extracellular and hepatobiliary-specific properties. Gadoxetate has increased sensitivity and accuracy in detecting hepatocellular carcinoma in cirrhosis compared to CT and MRI with extracellular agents.[1,2] Some cirrhotic patients demonstrate poor hepatic enhancement, poor biliary excretion and prolonged blood pool enhancement with gadoxetate, limiting utility in this subset of patients (Figure 1). Prospective identification of these patients would be helpful. The few studies on this subject report inconsistent observations about potential predictors, including MELD score, TBili, Child-Pugh class, DBili and indocyanine green clearance test. A DBili greater than 2.18 mg/dL was shown to predict poor enhancement.[3]

Table 2: Summary of Stepwise Selection for Liver-Spleen Ratio

Variable Entered	Partial R-Square	Model R-Square
Albumin	0.34	0.34
GFR	0.03	0.36
AST	0.04	0.40
INR	0.02	0.42
Liver Length	0.02	0.45
Ascites	0.02	0.46
Creatinine	0.02	0.48

Our results show significant correlation between several independent and dependent variables, particularly albumin and MELD score, suggesting that they may be potential predictors of poor hepatobiliary enhancement. While the multiple and logistic regression models identified a single variable responsible for most of the variance, several additional variables showed independent correlation. It is not surprising that albumin and MELD score are potential predictors. Albumin, produced by the liver, is a marker of synthetic liver function. MELD score reflects overall severity of chronic liver disease calculated using TBili, INR and creatinine.

Conclusion: Prior to this study, there have been few conflicting reports as to potential predictors of poor gadoxetate hepatobiliary enhancement. Our findings suggest that albumin and MELD score should be considered. Future directions include creating and testing a model to predict poor enhancement that can be used in daily clinical practice.

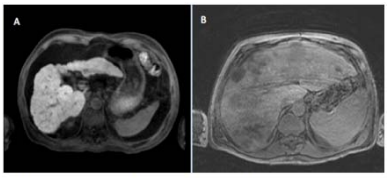

Figure 1: Examples of adequate (A) and poor (B) gadoxetate enhancement.

Abbreviations

ALP *alkaline phosphatase*; ALT *alanine aminotransferase*; AST *aspartate aminotransferase*; BDE *bile duct enhancement*; BUN *blood urea nitrogen*; DBili *direct bilirubin*; GFR *glomerular filtration rate*; INR *international normalized ratio*; LM *liver-muscle ratio*; LPV *liver-portal vein ratio*; LS *liver-spleen ratio*; MELD *model for end-stage liver disease*; PT *prothrombin time*; TBili *total bilirubin*

References:
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