Relationship Between Controlled Attenuation Parameter (CAP) and Magnetic Resonance Imaging-Derived Proton Density Fat Fraction (MRI-PDFF) in Subjects at High Risk for Nonalcoholic Fatty Liver Disease (NAFLD)

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BACKGROUND

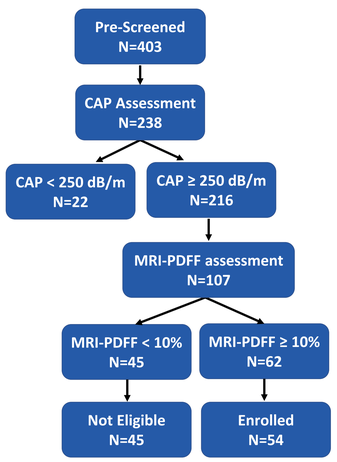
- The use of paired liver biopsies in early phase NAFLD/NASH trials is not pragmatic due to the short nature of these studies.
- MRI-PDFF is well correlated with histology-determined steatosis in patients with NAFLD and is often used as a surrogate non-invasive biomarker of hepatic steatosis in NAFLD/NASH clinical trials.
- There is, however, a need for an optimal screening strategy due to cost and timeline implications of subjects failing to meet MRI-PDFF inclusion criteria.
- The assessment of CAP is easy to perform and inexpensive relative to MRI-PDFF and is currently used as a screening tool to pre-identify subjects with NAFLD.

OBJECTIVE

The objective was to perform a post-hoc analysis of data from a phase 1 study and compare hepatic steatosis measurements obtained with CAP and MRI-PDFF in the same individual to evaluate the utility of CAP to pre-identify subjects likely to have fatty liver.

SUBJECTS AND METHODS

- Subjects with pre-diabetes or diabetes underwent CAP as a screening assessment for hepatic steatosis as part of a phase 1, multi-center NAFLD trial.
- Subjects with a CAP value of ~250 dB/m or greater and meeting all other study criteria were eligible for MRI-PDFF.
- CAP and MRI-PDFF were performed in the fasting state at different centers. MRI-PDFF was read centrally.
- Data from subjects (n=107) who received both CAP and MRI-PDFF assessments were included in the data analyses.
- Kruskal-Wallis analysis of variance and Dun's multiple comparison were used to assess group differences. Spearman correlations were used to examine associations and the Youden Index was used to determine optimal CAP cutoff. A *P*-value <0.05 was considered statistically significant.

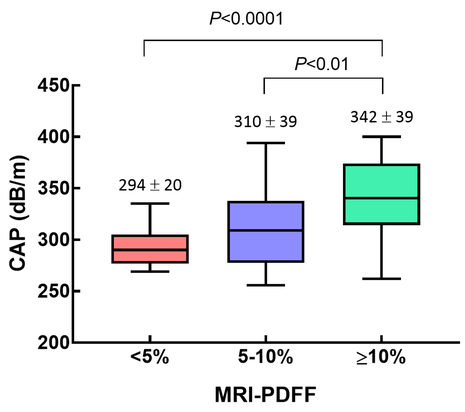


RESULTS

Table 1: Subject Characteristics

Parameter	All Subjects	MRI-PDFF <10%	MRI-PDFF ≥10%	*P*-Value PDFF <10% vs ≥10%
N	107	45	62	N/A
Age (years)	54 ± 8	55 ± 7	53 ± 9	0.25
Female/Male (%)	49/51	49/51	48/52	N/A
Weight (kg)	92 ± 14	92 ± 16	92 ± 13	0.90
BMI (kg/m^2)	33.0 ± 3.6	32.9 ± 3.8	33.1 ± 3.6	0.77
A1C (%)	7.2 ± 1.1	6.9 ± 0.9	7.5 ± 1.2	*<0.01*
Glucose (mg/dL)	139 ± 44	130 ± 37	145 ± 48	0.11
AST (U/L)	23.4 ± 9.5	21.5 ± 7.8	24.8 ± 10.4	0.09
ALT (U/L)	30.8 ± 20.0	25.9 ± 19.6	34.4 ± 19.6	*<0.01*
GGT (U/L)	43.0 ± 43.3	54.0 ± 59.6	34.9 ± 22.8	0.06
Total Cholesterol (mg/dL)	192.8 ± 44.3	180.4 ± 36.2	202.1 ± 47.7	*<0.05*
LDL-Cholesterol (mg/dL)	109.8 ± 35.7	102.0 ± 28.8	115.9 ± 39.5	0.07
HDL-Cholesterol (mg/dL)	47.5 ± 12.4	50.0 ± 14.8	45.7 ± 9.9	0.13
Triglycerides (mg/dL)	174.5 ± 81.4	142.4 ± 63.7	198.6 ± 85.4	*<0.001*
Platelet Count (10^9/L)	269.7 ± 66.6	276.6 ± 77.6	264.4 ± 57.1	0.51
MRI-PDFF (%)	13.1 ± 8.1	5.9 ± 2.2	18.3 ± 6.6	*<0.0001*
CAP (dB/m)	325.9 ± 41.5	303.5 ± 33.6	342.1 ± 39.3	*<0.0001*
M/XL probe (%)	57/43	50/50	62/34	N/A
AUROC (95%CI)			0.77 (0.59-0.86)	N/A
Cutoff (dB/m)			328	N/A
Sensitivity (%)			66	N/A
Specificity (%)			80	N/A

Figure 1: CAP scores stratified by MRI-PDFF



Total number of subjects with MRI-PDFF of <5%, 5-10% and ≥10% were 17, 28 and 62 respectively

RESULTS CONTINUED

Figure 2: Correlation between CAP and MRI-PDFF

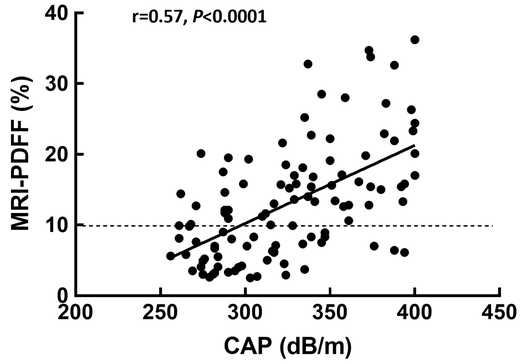


Table 2: Correlations between hepatic steatosis and subject characteristics

		MRI-PDFF (%)	CAP (dB/m)
CAP (dB/m)	Spearman correlation	**0.57**	-
	P-value	***<0.0001***	-
	N	**107**	-
MRI-PDFF (%)	Spearman correlation	-	**0.57**
	P-value	-	***<0.0001***
	N	-	**107**
Age (years)	Spearman correlation	-0.17	**-0.24**
	P-value	NS	***<0.05***
	N	106	**106**
Weight (kg)	Spearman correlation	0.03	**0.20**
	P-value	NS	***<0.05***
	N	106	**106**
BMI (kg/m^2)	Spearman correlation	0.03	**0.30**
	P-value	NS	***<0.01***
	N	102	**102**
HbA1c (%)	Spearman correlation	**0.26**	0.13
	P-value	***<0.01***	NS
	N	**105**	105
Fasting Glucose (mg/dL)	Spearman correlation	0.15	0.07
	P-value	NS	NS
	N	105	105
Triglycerides (mg/dL)	Spearman correlation	**0.31**	0.07
	P-value	***<0.01***	NS
	N	**105**	105
Total Cholesterol (mg/dL)	Spearman correlation	0.16	-0.04
	P-value	NS	NS
	N	105	105
LDL-cholesterol (mg/dL)	Spearman correlation	0.13	-0.03
	P-value	NS	NS
	N	103	103

RESULTS CONTINUED

Table 2 continued: Correlations between hepatic steatosis and subject characteristics

		MRI-PDFF (%)	CAP (dB/m)
HDL-cholesterol (mg/dL)	Spearman correlation	**-0.21**	-0.13
	P-value	***<0.05***	NS
	N	**105**	105
VLDL-cholesterol (mg/dL)	Spearman correlation	**0.28**	0.07
	P-value	***<0.01***	NS
	N	**103**	103
AST (U/L)	Spearman correlation	**0.32**	**0.22**
	P-value	***<0.001***	***<0.05***
	N	**105**	**105**
ALT (U/L)	Spearman correlation	**0.49**	**0.32**
	P-value	***<0.0001***	***<0.01***
	N	**105**	**105**
GGT (U/L)	Spearman correlation	-0.17	-0.09
	P-value	NS	NS
	N	106	106
Platelets	Spearman correlation	-0.02	-0.01
	P-value	NS	NS
	N	105	105

CONCLUSIONS

- CAP correlated modestly but significantly with MRI-PDFF in subjects at risk for NAFLD (r=0.57, P<0.0001)
- The use of CAP as a screening tool for hepatic steatosis potentially reduced MRI-PDFF screen fails by 50%.
- Subjects with MRI-PDFF ≥10% had increased HbA1c, ALT, total cholesterol and triglyceride concentrations compared to those with MRI-PDFF <10%.
- HbA1c, triglycerides, HDL-cholesterol, VLDL-cholesterol and liver enzymes also correlated significantly with hepatic steatosis.
- CAP scores significantly increased with increasing MRI-PDFF.
- A CAP score of 328 dB/m was identified as the optimal cut-off for identifying subjects with MRI-PDFF ≥10%.

DISCUSSION

The use of CAP proved to be a useful screening tool for identifying subjects with hepatic steatosis (MRI-PDFF ≥10%). The modest agreement between CAP and MRI-PDFF, however, warrants further evaluation of factors affecting the quality and potential discordance of these measurements

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