



Liver Enzyme Cut Offs in Patients with Advanced Nonalcoholic Fatty Liver Disease (NAFLD): A Multi-Center Study

European Association for the Study of the Liver

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1 INTRODUCTION

- Primary care physicians rely on liver enzymes to assess severity of nonalcoholic fatty liver disease (NAFLD).
- However the reliability of abnormal enzymes for determining this is uncertain.
- The prevalence of normal and abnormal liver enzymes and their cut offs with advanced NAFLD are not well determined.

2 AIM

- To assess the prevalence of abnormal alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in patients with advanced NAFLD

3 METHOD

- A multi-center study of NAFLD patients from Texas and California who underwent MRE were recruited from May 2016 to June 2018.
- The percentage of abnormal ALT, AST and ALP was calculated based on lab references and AASLD recommended references (normal ALT and AST ≤ 35 U/L for males and ≤ 25 U/L for females).
- Categorized into 3 groups:
 - Patients with MR elastography (MRE) ≥ 2.5 ka (possibly correlated with NASH)
 - MRE ≥ 3.62 kPa (advanced fibrosis) and
 - MRE ≥ 4.7 kPa (correlated with cirrhosis)
- Fisher's exact test was used for testing association strength.
- AUC for ALT and AST was used to detect advanced fibrosis.

4 RESULTS

Table 1. Patients' Characteristics

Variable	N = 245
Gender (Female)	131.0 (53.5%)
Age	56.0 (46-65)
Ethnicity	
Non-hispanic	164.0 (66.9%)
Hispanic	75.0 (30.6%)
Decline/Missing	6.0 (2.5%)
Race	
White	208.0 (84.9%)
Black	8.0 (3.3%)
Asian	12.0 (4.9%)
Other	16.0 (6.5%)
Declined/Unknown	1.0 (0.4%)
Type 2 DM	114.0 (47.0%)
HTN	118.0 (48.0%)
Hyperlipidemia	143.0 (59.8%)
Cirrhosis	30.0 (12.3%)
BMI Median (IQR) kg/m ²	32.0 (28.1-35.7)
HbA1C Median (IQR) %	6.0 (5.6-6.9)
ALT Median (IQR) U/L	43.0 (26.0-67.0)
AST Median (IQR) U/L	32.0 (23.0-49.0)
Alk.Phos Median (IQR) U/L	78.0 (62.0-98.0)
Albumin Median (IQR) g/dl	4.4 (4.2-4.6)
Bilirubin Median (IQR) mg/dl	0.6 (0.4-0.7)
Platelets (PLT) Median (IQR) (1000/mm ³)	229.5 (184.8-283.0)

Table 3. AUC of ALT based on local lab references

ALT (Local Lab)	AUC	Sensitivity	Specificity	Accuracy
MRE ≥ 2.5 kPa	0.5791	51%	57%	54%
MRE ≥ 3.62 kPa	0.5468	60%	56%	58%
MRE ≥ 4.7 kPa	0.5257	60%	55%	57%

Table 5. AUC of AST based on local lab references

AST (Local Lab)	AUC	Sensitivity	Specificity	Accuracy
MRE ≥ 2.5 kPa	0.5681	49%	77%	63%
MRE ≥ 3.62 kPa	0.6885	57%	68%	63%
MRE ≥ 4.7 kPa	0.7118	47%	64%	55%

Table 2. Associations between liver enzymes and 3 groups of patients

	Lab references			AASLD		
	MRE ≥ 2.5	MRE < 2.5	P vale	MRE ≥ 2.5	MRE < 2.5	P vale
	(%)	(%)		(%)	(%)	
Abn ALT	51	43	0.32	74	64	0.16
N ALT	49	57		26	36	
Abn AST	49	23	0.0001	64	47	0.016
N AST	51	77		36	53	
Abn ALP	19	6	0.009	N/A		
N ALP	81	94				
	MRE ≥ 3.62	MRE < 3.62		MRE ≥ 3.62	MRE < 3.62	
Abn ALT	60	44	0.0247	76	68	0.27
N ALT	40	56		24	32	
Abn AST	57	32	0.0006	69	53	0.03
N AST	43	68		31	47	
Abn ALP	22	11	0.05	N/A		
N ALP	78	89				
	MRE ≥ 4.7	MRE < 4.7		MRE ≥ 4.7	MRE < 4.7	
Abn ALT	60	45	0.05	73	69	0.64
N ALT	40	55		27	31	
Abn AST	47	36	0.15	60	56	0.66
N AST	53	64		40	44	
Abn ALP	23	12	0.06	N/A		
N ALP	77	88				

Table 4. AUC of ALT based on AASLD references

ALT (AASLD)	AUC	Sensitivity	Specificity	ACCURACY
MRE ≥ 2.5 kPa	0.59	74%	36%	55%
MRE ≥ 3.62 kPa	0.5803	76%	32%	54%
MRE ≥ 4.7 kPa	0.5646	73%	31%	52%

Table 6. AUC of AST based on AASLD references

AST (AASLD)	AUC	Sensitivity	Specificity	ACCURACY
MRE ≥ 2.5 kPa	0.659	64%	53%	59%
MRE ≥ 3.62 kPa	0.7162	69%	47%	58%
MRE ≥ 4.7 kPa	0.6762	60%	44%	52%

5 CONCLUSIONS

- A significant number of patients with normal liver enzymes based on local lab references had NASH (~50%) and/or advanced fibrosis (~40%)
- The AASLD cut offs performed slightly better.
- AST is better than ALT to detect advanced fibrosis.
- Lower cut offs reference ranges need to be used in NAFLD/NASH.

6 REFERENCES

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