1. MRE has excellent diagnostic performance for the diagnosis of significant, advanced fibrosis and cirrhosis in patients with NAFLD.

2. We established cut-offs of 2.65kPa, 3.14kPa, 3.53kPa and 4.45kPa for any(≥F1), significant(≥F2), advanced(≥F3) fibrosis and cirrhosis, respectively.

3. Severe activity NASH and raised GGT level may affect diagnostic accuracy of MRE in staging early liver fibrosis.

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Establishing the Cut-offs and Confounding factors of Magnetic Resonance Elastography for staging NAFLD-fibrosis: an IPD meta-analysis

J.Liang[1.2.3], J.Ampuero[1.2], K.Imajo[4], M.Noureddin[5], J.Behari[6], DH.Lee[7], RL. Ehman[8], F.Rorsman[9], J.Vessby[9], JR. Lacalle[10], F.Mozes[11], M.Pavlides[11.12], Q.M. Anstee[13.14], S.A. Harrison[11], J.Castell [15], R.Loomba[16.17], M.Romero-Gómez[1.2]

1. Digestive Diseases Unit and ciberehd, Virgen del Rocío University Hospital, Seville, Spain.
2. Institute of Biomedicine of Seville (HUVR/CSIC/US), Seville, Spain, University of Seville, Seville, Spain.
3. Department of Diagnostic Radiology, People's hospital of Zhengzhou, Zhengzhou, China
4. Department of Gastroenterology, Yokohama City University Graduate School of Medicine, Yokohama, Japan
5. Fatty Liver Program, Division of Digestive and Liver Diseases, Comprehensive Transplant Program, Cedars-Sinai Medical Center, Los Angeles, CA, USA
6. Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Center for Liver Diseases, University of Pittsburgh Medical Center, Pittsburgh, PA
7. Departments of Internal Medicine, Gachon University Gil Medical Center, Gachon University College of Medicine, Incheon, South Korea
8. Department of Diagnostic Radiology, Mayo Clinic College of Medicine, Rochester, USA
9. Department of Medical Sciences, Section of Gastroenterology and Hepatology, Uppsala university. Uppsala, Sweden
10. Biostatistics Unit, Department of Preventive Medicine and Public Health, University of Seville, Seville, Spain.
11. Oxford Centre for Clinical Magnetic Resonance Research, Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, UK
12. Translational Gastroenterology Unit, University of Oxford, UK.
13. Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK
14. Newcastle NIHR Biomedical Research Centre, Newcastle upon Tyne Hospitals, NHS Trust, Newcastle upon Tyne, UK.
15. Department of Radiology, Virgen del Rocío University Hospital, Seville, Spain.
16. Division of Epidemiology, Department of Family Medicine and Public Health, University of California San Diego, La Jolla, CA, United States
17. NAFLD Research Center, Division of Gastroenterology and Hepatology, Department of Medicine, University of California San Diego, La Jolla, CA, United States

1 Introduction

Even though MRE has shown the highest diagnostic accuracy for staging liver fibrosis, a discrepancy between fibrosis based on histology and MRE-related liver stiffness measurement (LSM) sometimes occurs. In addition, there is not a generally accepted cut-off value for diagnosing the different stages of fibrosis.

2 Aim

We conducted an individual patient data (IPD) meta-analysis to summarise diagnostic accuracy of Magnetic Resonance Elastography (MRE) in staging liver fibrosis and to assess potential confounding factors.

3 Method

A systematic review of the literature identified studies reporting MRE data in biopsy proven NAFLD patients, and data were obtained from the corresponding authors. Pooled diagnostic cutoff value for the various fibrosis stages were determined in a two-stage meta-analysis as the primary outcome. Multilevel modelling methods were used to analyses potential confounding factors influencing diagnostic accuracy of MRE in staging liver fibrosis.

4 Results

Eight independent cohorts comprising 821 patients were included in the meta-analysis. Cut-offs were defined to explore concordance between MRE and histopathology: ≥F2: 3.14 kPa (AUROC: 0·93; 95%CI: 0·90–0·95); ≥F3: 3.53kPa (AUROC: 0·93; 95%CI: 0·91–0·95); F4: 4.45 kPa (AUROC: 0·94; 95%CI: 0·92–0·97)(Figure 1). In GLMM analysis, histological steatohepatitis with higher inflammatory activity [OR (95% CI) = 3.229 (1.433-7.278), P=0.005] and gamma-glutamyl transferase (GGT) concentration [OR (95% CI) = 1.004(1.001-1.007), P=0.012] were significant confounders in generating overestimated staging between MRE and histology, these two variables can inflate liver stiffness measurement by MRE in early liver fibrosis stage (F0-1). Steatosis, as measured by MRI-PDFF, and body mass index (BMI) were not confounders(Table 1).

Figure 1. a b c d. Pooled cut-offs for the diagnosis of each fibrosis stage in patients with NAFLD

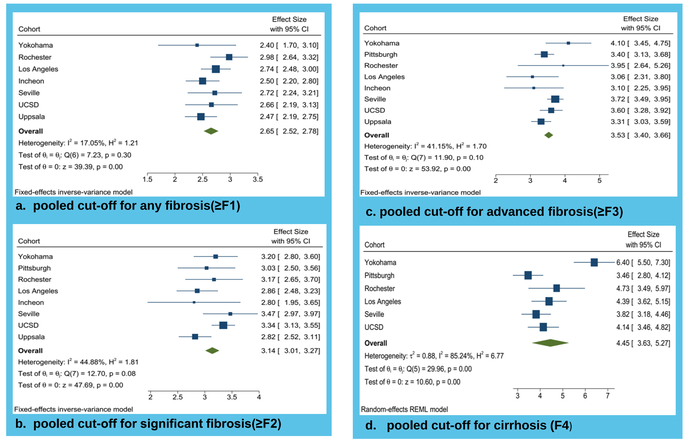

Table 1. GLMM (generalized linear mixed model) explore variables associated with prediction failure (overestimation and underestimation)

	Concordance vs Overestimation				Concordance vs Underestimation			
Variables	**Odds Ratio**	**95%CI**	**Z-value**	**P-value**	**Odds Ratio**	**95%CI**	**Z-value**	**P-value**
BMI	1.055	0.992-1.122	1.71	0.087	0.999	0.945-1.057	-0.03	0.979
Age	1.016	0.989-1.044	1.15	0.251	0.901	0.967-1.016	-0.71	0.479
T2DM (yes/no)	1.511	0.803-2.840	1.28	0.200	0.857	0.444-1.655	-0.46	0.646
ALT	0.994	0.984-1.004	-1.14	0.253	1.001	0.992-1.009	0.14	0.891
AST	1.008	0.997-1.019	1.37	0.172	0.998	0.985-1.011	-0.32	0.752
GGT	1.004	1.001-1.007	2.51	0.012	1.001	0.997-1.005	0.25	0.800
platelet	0.999	0.995-1.004	-0.33	0.745	0.999	0.994-1.003	-0.59	0.556
Steatosis stage								
S1 vs S0	0.926	0.094-9.114	-0.07	0.948				
S2 vs S0	0.480	0.043-5.383	-0.60	0.551	S2vs S1:0.644	0.261-1.586	-0.96	0.338
S3 vs S0	0.497	0.039-6.398	-0.54	0.592	S3vs S1:0.596	0.176-2.022	-0.83	0.407
NASH(no/MMA /SA)								
MMA-NASH vs no	1.618	0.573-4.565	0.91	0.363	2.530	0.977-6.555	1.91	0.056
SA-NASH vs no	3.229	1.433-7.278	2.83	0.005	2.329	0.958-5.659	1.87	0.062
MRI-PDFF	1.029	0.985-1.076	1.28	0.200	0.996	0.948-1.047	-0.14	0.888

MMA= Mild-moderate activity; SA=Severe activity;

5 Conclusions

MRE has excellent diagnostic performance for the diagnosis of significant, advanced fibrosis and cirrhosis in patients with NAFLD. Severe activity and raised GGT level may affect diagnostic accuracy of MRE in staging early liver fibrosis, but anthropometric measures such as BMI, steatosis degree do not.

6 Acknowledgements

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7 References

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8 Contact information

Manuel Romero-Gomez, MD, PhD
E-mail: mromerogomez@us.es

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