Fibrosis stage explains most variance in LSM-VCTE. LSM-VCTE was more dependent on fibrosis stage in older patients.

Determinants of liver stiffness measurements in patients with NAFLD – an individual patient data meta-analysis

F. E. Mózes[1], E. A. Selvaraj[1], A. N. A. Jayaswal[1], J. Boursier, C. Fournier, E. Bugianesi, R. Younes, S. Petta, S. Mahadeva, W.-K. Chan, P. J. Eddowes, P. N. Newsome, G. Hirschfield, V. W.-S. Wong, V. de Lédinghen, J. F. Cobbold[1], W. Kim, M. S. Lee, C. Cassinotto, G. Ooi, A. Nakajima, M. Yoneda, M.-H. Zheng, A. Geier, T. Tuthill, M. J. Brosnan, Q. M. Anstee, S. A. Harrison, P. M. Bossuyt[2], Michael Pavlides[1]

[1]OCMR, RDM Cardiovascular Medicine, University of Oxford
[2] Department of Epidemiology and Data Science, Amsterdam UMC, University of Amsterdam

1 Introduction

- Liver stiffness measurements performed with vibration-controlled transient elastography (LSM-VCTE) are used in the clinical assessment of patients with non-alcoholic fatty liver disease (NAFLD)[1]
- Fibrosis is the main determinant of LSM, but the contribution from other determinants and how they vary in patient subgroups is less well studied

2 Aim

- To describe the dependence of LSM on histological, demographic and laboratory parameters

3 Method

- Conducted an individual patient data meta-analysis (IPDMA) based on studies reporting paired LSM-VCTE and biopsy carried out within 6 months
- Parameters with correlation r > 0.15 with LSM-VCTE were selected as possible determinants of LSM-VCTE in the entire patient group
- Linear regression models were built by adding one predictor at a time to a base model including the log-transformed LSM and fibrosis stages as indicator variables. Partial R^2 values were compared to evaluate the contribution of each variable in explaining the variability of log-transformed LSM-VCTE
- Separate analysis evaluated the interaction between age and fibrosis stage.
- Analyses were carried out in R (R Foundation for Statistical Computing, Vienna, Austria)

4 Results

Parameter (n=2768)		Value
Demographics	Females (%)	44
	BMI > 30 kg/m^2 (%)	38
	Diabetes (%)	41
	Age (years)*	51
	BMI (kg/m^2)*	30
Liver function tests	ALT (IU/L)*	55
	AST (IU/L)*	39
	Platelets (×10^9/l) +	231
	Albumin (g/l) +	43
	GGT (IU/L)*	107

Table 1 Demographic and serum test characteristics of patients included in the IPDMA. *Median with IQR; +Mean with SD

Parameter	Correlation with LSM-VCTE
Fibrosis stage (0-4)	0.597
Age (years)	0.224
BMI (kg/m^2)	0.157
Platelet count (×10^9)	-0.234
AST (IU/L)	0.200
GGT (IU/L)	0.209
Presence of type 2 diabetes (Y/N)	0.273
Ballooning grade (0-2)	0.296
Lobular inflammation grade (0-3)	0.258

Table 2 Correlation coefficients of demographic and serum tests with LSM-VCTE greater then 0.15

Model predictors	Partial R^2
Age (years)	0.0018
BMI (kg/m2)	0.0514
Platelet count (×10^9)	0.0068
AST (IU/L)	0.0221
GGT (IU/L)	0.0232
Presence of type 2 diabetes (Y/N)	0.0183
Ballooning grade (0-2)	0.0119
Lobular inflammation grade (0-3)	0.0132

Table 3 Partial coefficients of determination (R^2) of predictors of LSM-VCTE. Fibrosis stage explained 41% of the variance of LSM-VCTE.
An interaction term between fibrosis stage and age explained log-transformed LSM better than the main effect of fibrosis stage alone (F-statistic = 3.171, p = 0.007)

5 Conclusions

- Fibrosis stage is the main determinant of LSM-VCTE, followed by AST, GGT and BMI explaining most of the remaining variance
- LSM-VCTE was less dependent on fibrosis stage in younger patients

6 Acknowledgements

The LITMUS project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No. 777377. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

This communication reflects the view of the author(s) and neither IMI nor the European Union or EFPIA are liable for any use that may be made of the information contained herein.

7 References

1. Dorairaj V, Sulaiman SA, Abu N, Abdul Murad NA. Nonalcoholic Fatty Liver Disease (NAFLD): Pathogenesis and Noninvasive Diagnosis. Biomedicines. 2021;10(1):15. Published 2021 Dec 22.