

## Abstract - Liver elasticity evolution in metabolic dysfunction-associated steatotic liver disease patients: a real-life prospective study

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### Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the first cause of chronic liver disease worldwide with a variable course over time. There is little prospective data on the long-term follow-up of these patients.

### Aim

The aim of our study is to evaluate the evolution of liver disease, in real life, using hepatic elastometry by identifying patients who will improve or progress over time.

### Methods

This is a prospective, single-centre study including patients with MASLD. Transient elastography was performed at baseline and checked after one (Y1) and three years (Y3). Patients were stratified into three groups based on the evolution of liver elasticity. Regression or progression of liver disease were defined as a decrease or increase in liver elasticity of  $> 1.5$  kPa compared with baseline value. Stable patients are those with elasticity changes  $\leq 1.5$  kPa.

### Results

229 patients were included (126 women and 103 men) with the following characteristics: mean age 52 years, mean body mass index  $33.9 \text{ kg/m}^2$ , significant proportion (98%) with an enlarged waist circumference ( $F \geq 80 \text{ cm}$ ;  $M \geq 94 \text{ cm}$ ) and a mean of 114 centimetres, 20 patients (9%) had an history of cardiovascular events, 86 patients (38%) were treated for type 2 diabetes. The baseline mean liver elasticity was  $10.5 \text{ kPa}$  ( $\pm 8.8$ ) and the mean controlled attenuation parameter (CAP) was  $331.1 \text{ dB/m}$  ( $\pm 43.5$ ). 100 patients (44%) were classified as F0-F1, 64 (28%) as F2, 43 (19%) as F3 and 22 (10%) as F4. Most received lifestyle advice by the hepatologist ( $n=157$ , 69%), others underwent bariatric surgery ( $n=30$ , 13%), were either included in an interventional clinical study in the context of MASLD or metabolic syndrome ( $n=21$ , 9%) or referred to the dietitian ( $n=18$ , 8%). 146 patients (64%) and 110 patients (48%) underwent follow-up elastography at one and three years respectively. Mean liver elasticity (Y0:  $10.5$ , Y1:  $7.8$ , Y3:  $7.9 \text{ kPa}$ ;  $p=0.0008$ ) and CAP (Y0:  $331.1$ , Y1:  $307.1$ , Y3:  $317.4 \text{ dB/m}$ ;  $p=0.0007$ ) decreased over time. At Y1, a minority of patients were progressors ( $n=26$ , 18%), 71 (49%) remained stable, and 49 (34%) exhibited improvement in liver elasticity. After three years (Y3), 21 (19%) experienced progression, 43 (39%) remained stable, and 46 (42%) demonstrated improvement. Interestingly, compared with progressors (P) or stable patients (S), improvers (I) at Y1 exhibit a more severe condition at baseline (Y0), characterized by higher BMI (I:  $34.6$ , S:  $31.7$ , P:  $32.5 \text{ kg/m}^2$ ;  $p=0.05$ ), waist circumference (I:  $116$ , S:  $108$ , P:  $110 \text{ cm}$ ;  $p=0.0048$ ), fasting glucose (I:  $125$ , S:  $105$ , P:  $110 \text{ mg/dL}$ ;  $p=0.0015$ ), low HDL (I:  $43$ , S:  $52$ , P:  $51 \text{ mg/dL}$ ;  $p=0.0157$ ), elasticity (I:  $12.2$ , S:  $6.6$ , P:  $7.5 \text{ kPa}$ ;  $p<0.0001$ ) and CAP values (I:  $343$ , S:  $322$ , P:  $328 \text{ dB/m}$ ;  $p=0.05$ ). The same is also true for Y3 vs. baseline (Y0) with additionally an elevated mean AST at Y0 (I:  $47$ , S:  $34$ , P:  $39 \text{ UI/L}$ ;  $p=0.0012$ ). The improvement in this group is associated at Y1 with a significant BMI reduction ( $-3.7 \text{ kg/m}^2$ ;  $-9\%$ ) compared with stable patients ( $-1.1 \text{ kg/m}^2$ ,  $-2.6\%$ ) and progressors ( $-0.1 \text{ kg/m}^2$ ,  $-0.4\%$ ) ( $p=0.0003$ ). At Y3, improvers had also a significant BMI decrease ( $-2.1 \text{ kg/m}^2$ ;  $-6\%$ ) compared with stable patients ( $-0.6 \text{ kg/m}^2$ ,  $-1.7\%$ ) and progressors ( $+0.6 \text{ kg/m}^2$ ,  $+1.7\%$ ) ( $p=0.0005$ ). All the patients who underwent bariatric surgery demonstrated disease regression at either one or three-year follow-up, however more than the half (Y1 vs. Y0: 60%, Y3 vs. Y1: 50%) of lost to follow-up patients was seen in this category. Among the events occurring during follow-up, 11 patients developed diabetes, 2 had hepatocellular carcinoma and 2 experienced a cardiovascular event.

### Conclusions

These are the first prospective data on the evolution of liver elasticity in MASLD patients. Standard hepatological management can have an impact on liver disease, interestingly, particularly in patients with severe initial MASLD. We confirm that a 6 to 9% of loss in BMI is associated with a regression in hepatic elasticity, consistent with regression of fibrosis. Patients who progress represent a fifth of population and are easily identified by the absence of weight loss over time. So, the focus should be on weight reduction.