2016-A : AUTOMATED AI-BASED MORPHOMETRIC ANALYSIS OF FIBROSIS REVEALS SIGNIFICANT CHANGES IN T2DM VS NON-T2DM MASH PATIENTS WITH ADVANCED FIBROSIS

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BACKGROUND AND OBJECTIVES

Metabolic dysfunction associated steatohepatitis (MASH) is the most severe form of steatotic liver diseases. Type 2 diabetes mellitus (T2DM) is known as a major risk factor for fibrosis development, and some drugs currently under development in MASH address both health issues, with no drug approved so far. Knowing T2DM patients are at high-risk of severe fibrosis, we have compared fibrosis stages and characteristics of MASH patients according their T2DM status using MorphoQuant, a fully-automated user-independent morphometric software.

MATERIALS AND METHODS

One hundred and seven MASH patients (NAS ≥ 4, with at least one point per category), including 44 T2DM patients, were included in this analysis. Untreated patients were considered as T2DM patients (n = 6). Liver biopsies were scored by a blinded expert pathologist according to the NASH CRN. For MorphoQuant™ analysis, picrosirius red (PSR)-stained slides were used. Steatosis, vesicle size, total collagen, periductular, perisinusoidal, perivascular and septal collagens, as well as collagen fiber width and length were assessed. T2DM and non-T2DM patients were compared.

CONCLUSION

T2DM MASH patients displayed significantly different features from non-T2DM MASH patients. These differences could be only captured using morphometric digital analysis of MASH and fibrosis features. Particularly, fibrosis was more developed, with an increase in perivascular and septal fibrosis. Such findings are in alignment with longer history of liver injury and more advanced fibrosis in T2DM NASH patients and show the interest of using quantitative morphometric digital analysis for patient's risk stratification.

.01 PATIENTS' MASH AND FIBROSIS CHARACTERISTICS

	All Patients (n = 107) n (%)	
Type 2 Diabetis Mellitus	No	Yes
(T2DM)	63	44
Steatosis grade		
S1	1	3
S2	42	27
S3	20	14
Lobular inflammation grade		
I1	24	22
I2	36	18
I3	3	4
Ballooning grade		
B1	44	28
B2	19	16
Fibrosis stage		
F0	0	0
F1	28	11
F2	19	17
F3	16	16
F4	0	0

Table 1. Patients' MASH and fibrosis characteristics. NAS : NAFLD Activity Score. SAF: Steatosis Activity Score.

.02 COMPARISON OF MASH AND FIBROSIS FEATURES IN NON-T2DM VERSUS T2DM MASH PATIENTS USING MANUAL SCORING AND AI-MORPHOMETRIC ANALYSIS

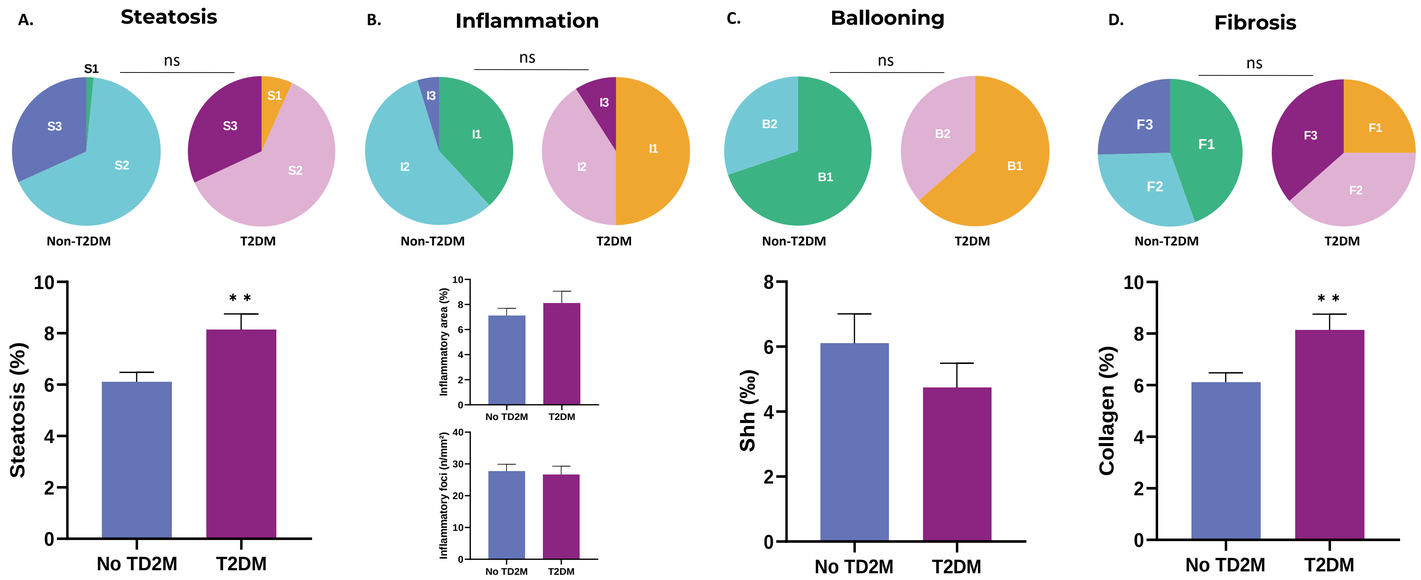

Figure 2. Comparison of steatosis, inflammation, ballooning and fibrosis in diabetic versus non-diabetic MASH patients, using the conventional method and MorphoQuant. A. NAS steatosis grade and steatosis area. **B.** NAS lobular inflammation grade, inflammatory area and inflammatory foci. **C.** NAS ballooning grade and Shh expression. **D.** SAF fibrosis stage and collagen content. Parametric t-test or non-parametric Mann-Whitney. ns : non significant; * p < 0.05 ;** p < 0.01.

.03 STEATOSIS AND COLLAGEN QUANTIFICATION ACCORDING TO FIBROSIS STAGE

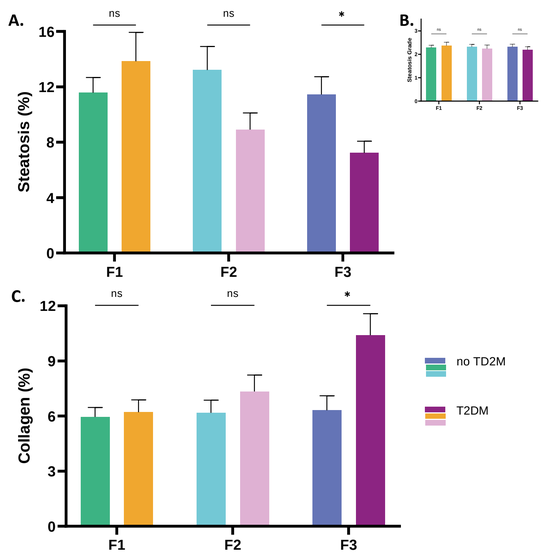

Figure 3. Assessment of steatosis and fibrosis according to SAF fibrosis stage using MorphoQuant. A. Steatosis according to SAF fibrosis stage. **B.** Steatosis grade according to SAF fibrosis stage. **C.** Collagen content according to SAF fibrosis stage.

.04 AI-MORPHOMETRIC ANALYSIS OF RELATED-FIBROSIS ENDPOINTS REVEALS DIFFERENT FIBROSIS DISTRIBUTION IN F3 T2DM MASH PATIENTS

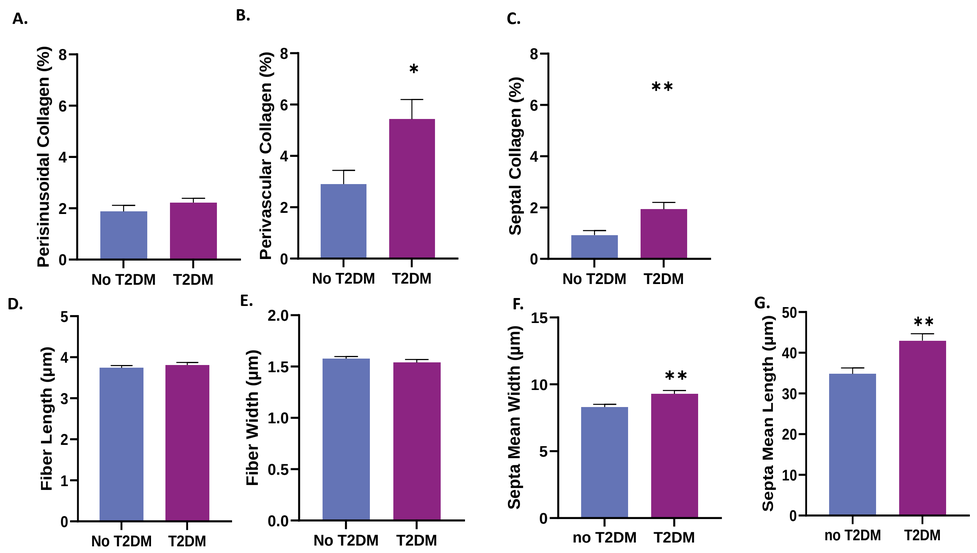

Figure 4. Assessment of fibrosis distribution and related endpoints in F3 T2DM versus non-T2DM NASH patients using MorphoQuant. A. Perisinusoidal collagen. **B.** Perivascular collagen. **C.** Septal collagen **D**. Fiber length. **E.** Fiber width. **F.** Septa Length. **G.** Septa width. Parametric t-test or non-parametric Mann-Whitney. ns : non significant; * p < 0.05 ;** p < 0.01.

AT A GLANCE

- Type 2 diabetes mellitus is a major risk factor of advanced fibrosis in MASH patients.
- Morphometric quantitative analysis of MASH and fibrosis may provide more granularity compared to visual assessment.
- We compared non diabetic and diabetic MASH patients for steatosis, inflammation, ballooning and fibrosis using both visual scoring and digital analysis.
- Overall, the quantitative analysis shows a significant decrease of steatosis and an increase of perivascular and septal fibrosis, in T2DM MASH population whereas none was seen with the scores.
- This work highlights the granularity provided by quantitative digital analysis and the potential interest to investigate fibrosis dimensions to stratify patients.