Type 2 Diabetes and Obesity are The Main Metabolic Risk Factors for The Development of Cirrhosis in People With Metabolic Dysfunction-Associated Steatohepatitis (MASH)

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INTRODUCTION

- Type 2 diabetes (T2D) is believed to promote progression of MASH to cirrhosis, but limited prospective data are available.
- There is an ongoing debate about whether type 2 diabetes (T2D) is independently related to a higher risk of progression to cirrhosis in metabolic dysfunction-associated steatohepatitis (MASH).
- The role of T2D as an independent cardiometabolic risk factor of fibrosis progression in MASH are currently lacking.

AIM

- Determine the prevalence of MASLD and "at-risk" MASH in adults with and without T2D from primary care and endocrinology clinics.

METHODS

- TARGET-NASH is a real-world longitudinal observational cohort of people with MASLD from hepatology and endocrinology clinics in the US. Diagnosis of T2D was derived from medical history, medication use, or HbA1c ≥6.5%. Data were derived from the U.S. TARGET-NASH study
- Longitudinal observational cohort study including people with MASLD managed in Hepatology and Endocrinology Practices in the USA.
- Diagnosis of T2D was derived from medical history, medication use or HbA1c ≥6.5 %
- Index: earliest evidence of MASH during a 3-year retrospective period
- People without MASH or with decompensated cirrhosis at baseline were excluded.
- Hazard ratios (HR) were derived from multivariable modeling.

RESULTS

Table 1. People with T2D are at an elevated risk of advanced fibrosis at index as determined by NITs

	No-T2D (n=1204)	T2D (n=1211)	p-value
Age (years)	53.2 ± 13.6	57.2 ± 11.7	<0.001
Females (%)	53.6	63.8	<0.001
BMI (kg/m^2)	32.0 ± 7.1	35.4 ± 7.8	<0.001
HbA_{1c} (%)	5.6 ± 0.4	7.3 ± 1.5	<0.001
Disease severity at index (%)			<0.001
Compensated MASH cirrhosis	19.9	35.3	
Non-cirrhotic MASH	80.1	64.7	
Mean Fib-4	1.9 ± 2.2	2.4 ± 2.7	<0.001
Fib-4 category			<0.001
Low fibrosis risk (%)	59.4	45.9	
Intermediate fibrosis risk (%)	23.6	27.2	
High risk (%)	17.0	26.9	
Mean CAP (dB/m)	305 ± 52	314 ± 59	0.10
Mean LSM (kPa)	11.1 ± 8.0	14.6 ± 9.8	<0.001

Values are expressed as Mean ± SD

Figure 1. T2D is associated with a higher prevalence of advanced fibrosis at index as determined by liver biopsy

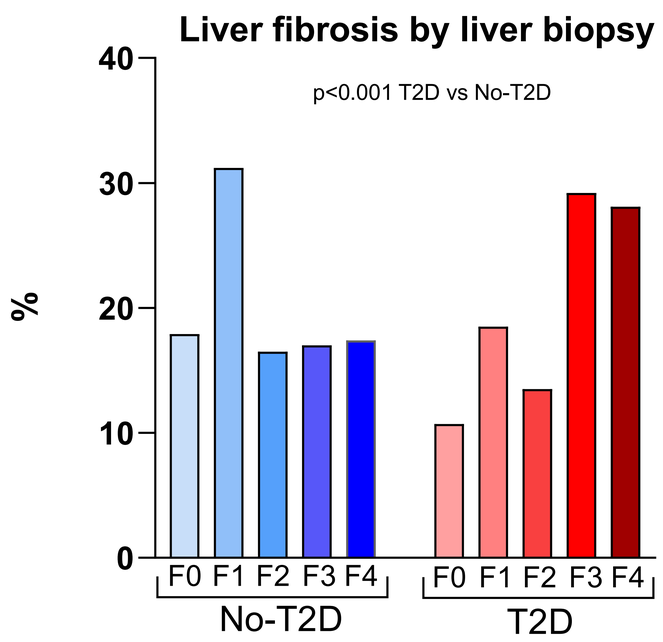
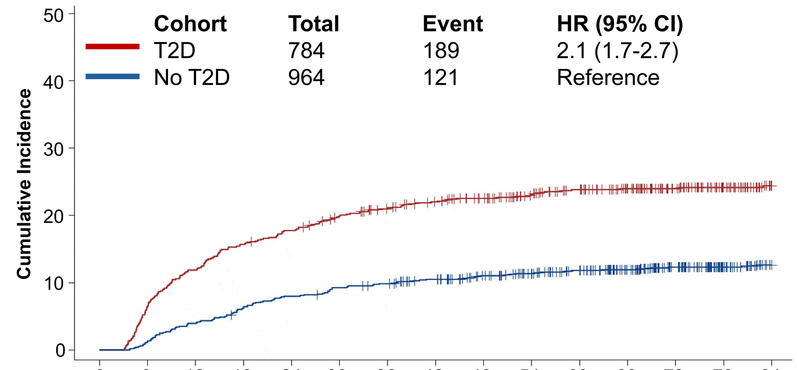


Figure 2. People with T2D and non-cirrhotic MASH have higher progression rates to cirrhosis than those without T2D



Patients-at-Risk

T2D	784	733	688	654	624	596	568	524	509	466	421	367	306	250	188
No-T2D	964	951	922	893	865	842	811	769	718	678	613	551	471	388	320

- People with non-cirrhotic MASH and T2D had a 2.1 (CI 1.6-2.6; p<0.001) higher hazard ratio (HR) for progression to compensated cirrhotic MASH compared to those without T2D (No-T2D) after adjustment for age and sex and also in the subgroups of different fibrosis risk at baseline (high FIB-4: 1.9 [CI 1.1-3.1]; low FIB-4: HR 2.1 [CI 1.4-3.1]; p<0.001).
- In multivariable analysis (including age, sex, diabetes status and FIB-4 stage) obesity was also a major risk factor for the progression from MASH to cirrhosis in people with type 2 diabetes (HR: 1.35 [1.01, 1.81]; p = 0.046).
- Risk of progression from compensated to decompensated cirrhosis was independent of the presence of T2D at index in all individuals (1.2 [CI 0.9-1.5]) and across fibrosis risk groups (high fibrosis risk: 1.2 [CI 0.8-1.7]; low fibrosis risk: 0.9 [CI 0.2-4.7]).

CONCLUSIONS

- Among people with MASH, the presence of T2D is associated with a higher risk of progression from MASH to cirrhosis. This underlines the importance of early case-finding of MASH in people with T2D to reduce the growing individual and societal burden of MASLD-related severe liver disease.

REFERENCES

- Barritt et al. (2017). Design and rationale for a real-world observational cohort of patients with nonalcoholic fatty liver disease: The TARGET-NASH study. Contemp Clin Trials, 61, 33-38

Acknowledgment

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