A longitudinal assessment of cardiovascular risk for NASH/MASH patients enrolled in TARGET-NASH

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Introduction

- Primary cardiovascular (CV) risk can be estimated by risk scores like the Framingham and Pooled Cohort Equations (PCE)
- There is a lack of data assessing CV risk in patients with cirrhotic metabolic dysfunction-associated steatohepatitis (MASH) or non-cirrhotic MASH (previously NASH), and comparing the CV risk between these cohorts
- These risk equations do not factor in the severity of liver disease, let alone presence, which can significantly impact CV outcomes, morbidity, and mortality in patients with MASH
- Cardiovascular disease (CVD) is the most common cause of mortality among patients with MASH
- The American Heart Association has recognized metabolic dysfunction-associated steatotic liver disease (MASLD) as an independent risk factor for CVD

Methods

- The study population for this analysis includes adults in the United States (US) with MASH enrolled in the ongoing, longitudinal, observational TARGET-NASH study
- Index date was date of the first eligible MASH diagnosis
- Patients with any CV history at or prior to index were excluded to mitigate bias
- 10-year baseline CV risk was estimated using the Framingham and PCE risk models
- Risk was compared by cirrhosis and noncirrhotic MASH and among subgroups of patients with and without history of type 2 diabetes (T2DM) using the Kruskal-Wallis test
- Fine-Gray subdistribution hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between disease phenotype (cirrhotic or non-cirrhotic MASH) and likelihood of experiencing a CV event, adjusted for the traditional risk factors (age, sex, race/ethnicity, etc.) included in the Framingham and PCE models

Results

- Of the 6,568 patients included in TARGET-NASH, 2,512 patients aged 30-74 years at index with MASH met inclusion criteria, of which up to 836 had data for calculation of baseline CV risk (of which 119 were biopsy confirmed)
- The median predicted 10-year CV risk from the Framingham model was significantly greater for patients with cirrhotic MASH compared to those with non-cirrhotic MASH (16.6% vs. 12.3%, p<0.001) (Table 1)
- The difference was significant among subgroups of patients with T2DM (18.8% vs. 16.6%, p=0.04) and without T2DM (11.3% vs. 8.4%, p=0.03) (Table 1)
- Findings were consistent with results from the PCE
- Based on observed CV events, patients with cirrhotic MASH had a significantly greater likelihood of experiencing a CV event compared to those with non-cirrhotic MASH (HR 1.70, 95% CI 1.03-2.79) (Figure 1)

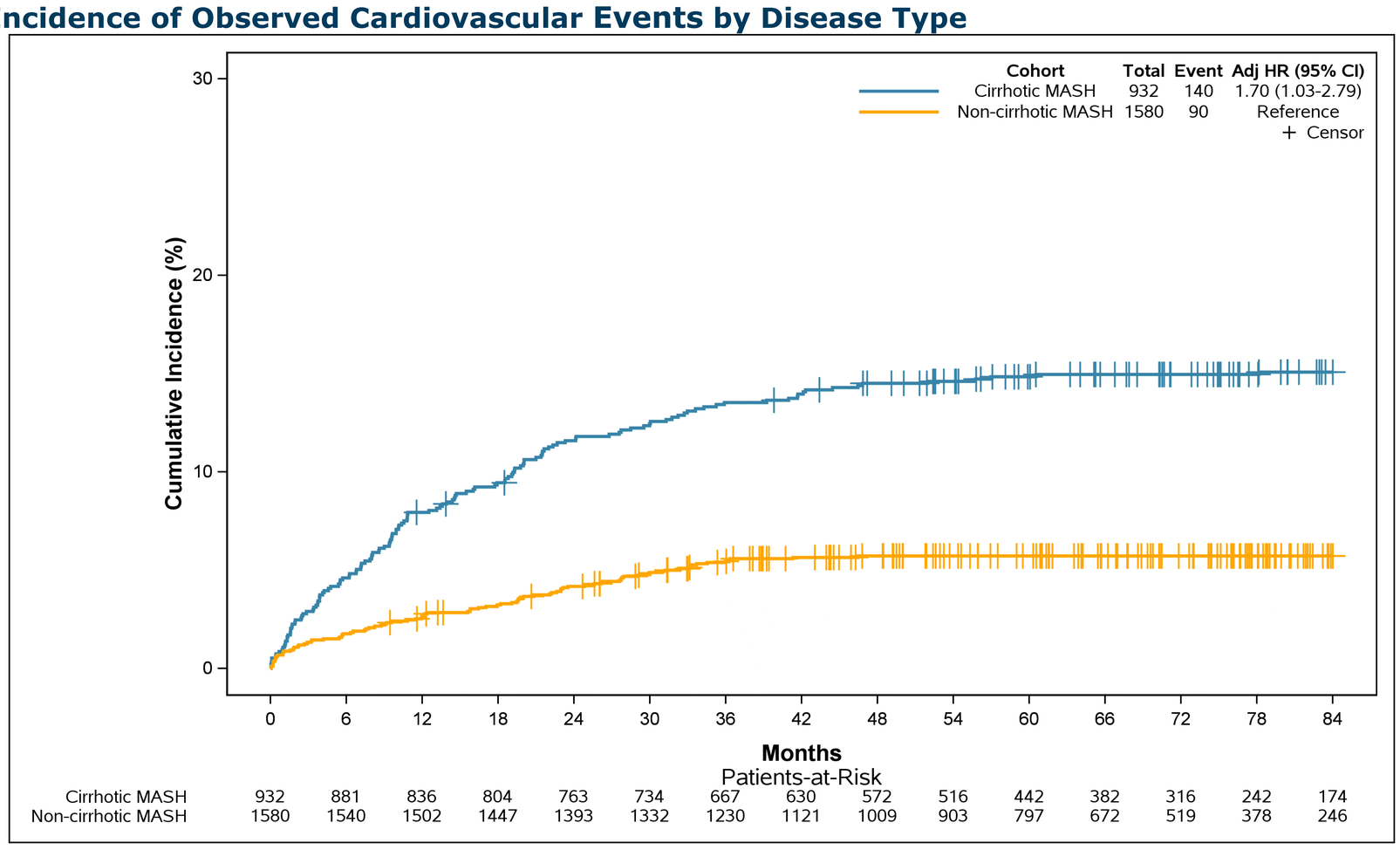
Table 1: Framingham predicted CV risk by disease type and diabetes status

	Non-cirrhotic MASH (n=622)	Cirrhotic MASH (n=214)	P-value
Age at index (years) Median (n) Q1-Q3 (IQR)	54.0 (622) 44.0-61.0 (17.0)	60.0 (214) 52.0-65.0 (13.0)	<0.001
Sex, n (%) Female	361 (58.0)	124 (57.9)	0.98
T2DM, n (%) Yes	340 (54.7)	154 (72.0)	<0.001
Framingham 10-year CV risk %, all patients Median (n) Q1-Q3 (IQR)	12.3 (622) 7.1-20.7 (13.5)	16.6 (214) 10.6-28.1 (17.5)	<0.001
Framingham 10-year CV risk %, Patients with T2DM Median (n) Q1-Q3 (IQR)	16.6 (340) 10.7-25.7 (15.0)	18.8 (154) 12.0-30.6 (18.6)	0.04
Framingham 10-year CV risk %, Patients without T2DM Median (n) Q1-Q3 (IQR)	8.4 (282) 5.1-13.4 (8.4)	11.3 (60) 5.6-18.0 (12.4)	0.03

Conclusions

Patients with cirrhotic MASH were found to be at an increased predicted and observed risk of CV events compared to patients with non-cirrhotic MASH, even after adjusting for traditional CV risk factors for observed risk of CV, which supports the notion that the severity of liver disease impacts the level of CV risk. Understanding this differential risk is an important consideration that will be instrumental in chronic care management. Treatments that could delay progression to cirrhosis may potentially reduce health events like CV outcomes, morbidity and mortality in patients with MASH.

Figure 1. Incidence of Observed Cardiovascular Events by Disease Type



Note: Hazard ratio is adjusted for age, sex, race/ethnicity, total cholesterol, HDL, hypertension treatment, systolic blood pressure, smoking status, and type 2 diabetes

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