Characterising Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis Patients in Secondary Care in England

Arcturis

Filipa Tunaru[1], Danielle Robinson[1], Shammi Luhar[1], Grace Hatton[1], Ines de Santiago[2], Lewis Carpenter[1]

[1] Arcturis Data, Building One, Oxford Technology Park, Technology Drive, Kidlington, OX5 1GN UK
[2] e-therapeutics plc, 4 Kingdom St, Greater London W2 6BD
Filipa.Tunaru@arcturisdata.co.uk

Introduction

- Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are increasingly common conditions, with an estimated prevalence in the UK of 20-30% and 2-12% respectively. [1,2]
- However, challenges around diagnosis, such as non-specific symptoms and need for biopsy diagnosis, mean that many early-stage patients are missed.
- Real world evidence (RWE) can help to fill the knowledge gap around the characteristics and outcomes of NAFLD/NASH patients to support the identification of novel risk factors and treatment targets. [2]

Objectives

1. To characterise NAFLD/NASH patients receiving routine care in hospitals in England.
2. To assess the incidence of outcomes (overall survival (OS), liver failure, hepatocellular carcinoma (HCC), major adverse cardiovascular events (MACE) in the years following NAFLD/NASH diagnosis.
3. To estimate key clinical endpoints (OS, liver failure, HCC and MACE).

Methods

Patient Identification

Patients with NAFLD/NASH identified in the Arcturis Real World Data Network research database (**Figure 1**) using de-identified electronic hospital records from January 2015 to March 2024.

Patients entered on first recorded NAFLD/NASH diagnosis (ICD-10: K74.6, K75.8, K76.0) and were excluded if they have any record of alcoholic liver disease (ICD-10: K70.x)

Descriptive Analysis

Baseline characteristics, including demographics, comorbidities, laboratory results, recent medications and procedures of the cohort were summarised.

Crude overall, 1-year and 5-year incidence rates of key clinical outcomes were calculated per 10,000 person years.

Time to each key clinical endpoint* was described with Kaplan Meier curves.

*A proxy for cardiovascular death was used whereby patients with a key cardiovascular diagnosis in the 60 days prior to death were considered as cardiovascular deaths.
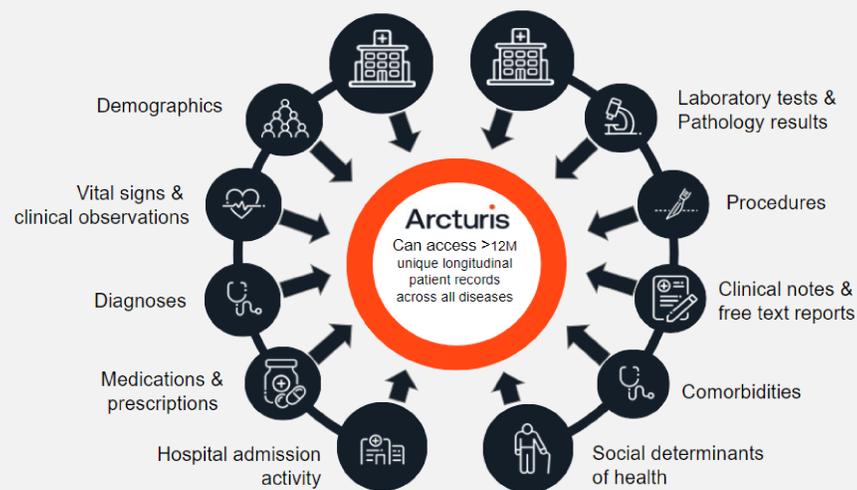

Figure 1: Data captured in The Arcturis Real World Data Network.

Results – Patient Characteristics

- The cohort of 22,444 patients diagnosed with NAFLD/NASH were on average aged 57.85 (standard deviation =16.54) at diagnosis.
- Sex was approximately evenly distributed (11,121 [49.6%] female).
- Most patients (71.0%) were white and of the patients who had deprivation recorded (39.5%) the majority lived in less deprived postcodes (72.1% in the 50% least deprived postcodes).
- The mean BMI was 30.79 (SD=7.57).
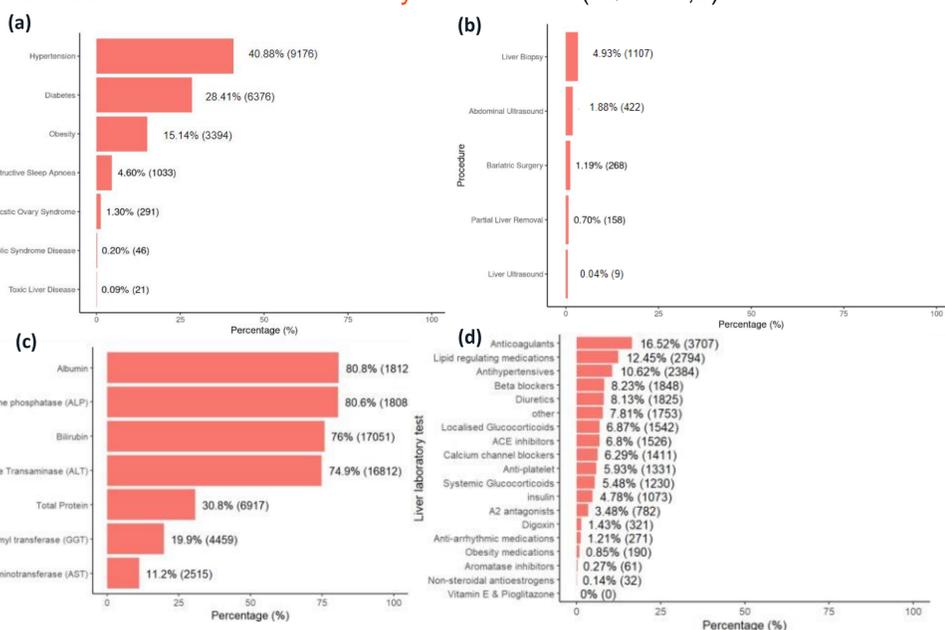- The median Charlson Comorbidity Index was 2 (IQR = 1,3).

Figure 2: NASH/NAFLD associated comorbidities (a), procedures (b), liver laboratory tests (c) and medications (d) in the year prior to NASH/NAFLD diagnosis.

In the year prior to NAFLD/NASH diagnosis:

- Hypertension was the most common NASH-specific comorbidity (40.88%),Fig. 2A.
- Only 4.93% of patients had a liver biopsy (Fig. 2B).
- The use of recommended liver laboratory tests was high, however tests to identify levels of liver fibrosis, ELF and FIB-4, were rare, 24 (0.1%) and 64 (0.3%) patients respectively (Fig. 2C).

Results – Clinical Endpoints Analysis

Incidence

Table 1. Incidence Rates of Clinical Endpoints of Interest At 1 Year, 5 Years and Across All Available Follow-up after NAFLD/NASH diagnosis.

Outcome	Window	Incidence Rate per 10,000 person years (95% confidence interval)
All-cause death	1-year	1373.9 (1315.6, 1432.3)
	5-year	798.1 (771.8, 82.4)
	Overall	763.0 (739.3, 787.8)
Liver Failure	1-year	208.1 (185.2, 231.1)
	5-year	97.9 (88.6, 107.2)
	Overall	90.7 (82.2, 99.2)
HCC	1-year	93.9 (78.5, 109.3)
	5-year	44.9 (38.6, 51.2)
	Overall	42.1 (36.4, 47.9)
MACE	1-year	789.8 (745.3, 834.3)
	5-year	417.9 (398.6, 437.1)
	Overall	437.2 (418.5, 455.8)

- A total of 49,440.0 person years were observed.
- Across endpoints, incidence is highest in the first year following NAFLD/NASH diagnosis.
- Median survival was not reached for any of the endpoints.
- In all endpoints, the sharpest drop in survival probability occurred in the first months following NAFLD/NASH diagnosis, indicating that a proportion of NAFLD/NASH patients are diagnosed at a late stage and are at higher risk of liver failure, HCC, MACE or death.
- Otherwise, the survival probability remains relatively high and stable across multiple years for all endpoints.
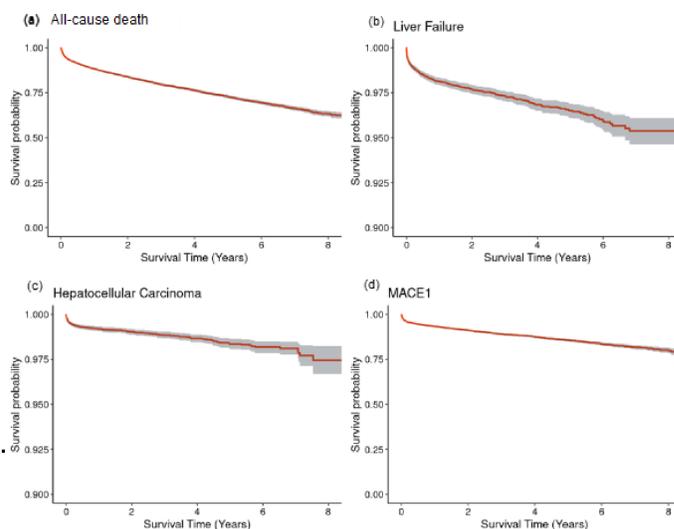
Survival

Figure 2. 8 Year Survival of Newly Diagnosed NAFLD/NASH patients until All-cause Death (a), Liver Failure (b), HCC (c) and MACE (d).

Conclusions

- We have identified and characterised **22,444 NAFLD/NASH patients**.
- Few patients diagnosed with NAFLD/NASH have liver procedures in the year prior to diagnosis.
- The incidence of death, liver failure, HCC and MACE are **highest in the year following diagnosis.**
- Across all endpoints, the sharpest drop in survival probability occurs in the months immediately following NAFLD/NASH diagnosis.
- These findings highlight the value of earlier diagnosis in NAFLD/NASH. Further studies could focus on the identification of predictors of diagnosis.

Acknowledgements

References

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[3] Schad, F. & Thronicke, A. Real-World Evidence—Current Developments and Perspectives. International Journal of Environmental Research and Public Health 19, 10159 (2022).