

# Baffled by NAFLD? (The natural history of nonalcoholic fatty liver disease)

A MacGilchrist

Consultant Hepatologist, Royal Infirmary of Edinburgh, Edinburgh, Scotland

**TITLE** The natural history of nonalcoholic fatty liver disease: a population-based cohort study

**AUTHORS** Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P.

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**LIST OF ABBREVIATIONS** Nonalcoholic fatty liver disease (NAFLD)

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**Correspondence to A MacGilchrist, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA**

**tel.** +44 (0)131 242 1623

**fax.** +44 (0)131 242 1638

**e-mail**

**Alastair.MacGilchrist@luht.scot.nhs.uk**

## SUMMARY

This study examines the natural history of NAFLD in the setting of a community (as opposed to a specialist referral centre). The aim was to determine survival and liver-related morbidity among community-based NAFLD patients.

Four hundred and twenty patients diagnosed with NAFLD in Olmsted County, Minnesota, between 1980 and 2000 were identified using the resources of the Rochester Epidemiology Project. Medical records were reviewed to confirm diagnosis and determine outcomes up to 2003. Overall survival was compared with the general Minnesota population of the same age and sex.

Mean age at diagnosis was 49 years with an equal gender distribution and mean follow-up was 7.6 years (3192 person-years follow-up). Overall, 53 of 420 (12.6%) patients died. Survival was lower than the expected survival for the general population (standardized mortality ratio, 1.34; 95% CI, 1.003–1.76;  $P = .03$ ). Higher mortality was associated with age (hazard ratio per decade, 2.2; 95% CI, 1.7–2.7), impaired fasting glucose (hazard ratio, 2.6; 95% CI, 1.3–5.2), and cirrhosis (hazard ratio, 3.1, 95% CI, 1.2–7.8). Liver disease was the third leading cause of death (as compared with the thirteenth leading cause of death in the general Minnesota population), occurring in 7 (1.7%) subjects. 21 (5%) patients were diagnosed with cirrhosis, and 13 (3.1%) developed liver-related complications.

The authors concluded that mortality among community-diagnosed NAFLD patients is higher than the general population and is associated with older age, impaired

fasting glucose, and cirrhosis. Liver-related death is a leading cause of mortality, although the absolute risk is low.

## OPINION

NAFLD is the unwieldy acronym for nonalcoholic fatty liver disease, which is causing concern amongst hepatologists. It is the third wave of the rising tide of liver disease burden, after alcoholic liver disease and chronic viral hepatitis. Our wards are full of patients with liver failure due to alcohol; the treatment of hepatitis C consumes our specialist nursing and pharmacy resources; and the most common referrals to our clinics are patients with abnormal liver function tests, most of whom have NAFLD. Since NAFLD forms part of the metabolic syndrome, the epidemic of obesity and of diabetes mellitus looms large on our horizon.

Pure steatosis, i.e. fatty liver without inflammation or fibrosis, has been regarded as benign. Consequently, abnormal liver function tests are often disregarded in diabetic or obese patients, an approach justified by the apparent absence of cirrhosis as a significant cause of death in these patients. However, we now realise that most 'cryptogenic' cirrhosis is in fact end-stage NAFLD. These patients are at high risk of liver failure and hepatocellular carcinoma, adding to the demand for liver transplantation, which already outstrips the supply. To clarify this conundrum, we need reliable information on the natural history of NAFLD. This paper provides an important contribution, particularly because it is community-based.

With a well defined population, carefully established criteria for NAFLD and complete follow-up over seven

years, the results are reliable and the conclusions important. Patients with NAFLD have a higher than expected mortality, and cirrhosis is their third most common cause of death, after ischaemic heart disease and malignancy. The non-cirrhotic patients do run a benign course, albeit over a relatively short period, and the actual

number of deaths is reassuringly low. However if the results are viewed in the context of obesity affecting 30% of the population, they still add up to a lot of liver-related deaths. NAFLD is going to become a term familiar not just to hepatologists, but to all clinicians.

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