

# Nonalcoholic Fatty Liver Disease and Risk of Dementia

## A Population-Based Cohort Study

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Cite as: *Neurology*® 2022;99:e574–e582. doi:10.1212/WNL.0000000000200853

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### Study Question

Is nonalcoholic fatty liver disease (NAFLD) associated with an increased risk of dementia?

### What Is Known and What This Paper Adds

NAFLD is the hepatic manifestation of a metabolic disorder that is a known risk factor for dementia. While the metabolic disorder is not unique to NAFLD or dementia, it is unknown whether NAFLD contributes to dementia independent of these factors. Few studies have explored the joint effect of NAFLD and cardiovascular disease (CVD) on dementia risk despite the high prevalence of CVD in patients with NAFLD. We, in this study, addressed these questions using a population-based cohort study. This study provides Class II evidence that nonalcoholic fatty liver disease is associated with the development of vascular and nonvascular dementia.

### Methods

This nationwide population-based cohort includes data from all patients aged 65 years or older diagnosed with NAFLD between 1987 and 2016. Data were obtained from the Swedish National Patient Register. Each patient ( $n = 2,898$ ) was matched with on age, sex, and municipality with up to 10 controls without a diagnosis of NAFLD ( $n = 28,357$ ) randomly selected from the Total Population Register. NAFLD, CVD, and dementia were identified from population-based registers using the *International Classification of Diseases* 9th and 10th codes (median age 70 years and 55.1% females). Multiadjusted Cox regression models were applied to estimate the hazard ratio (HR) of dementia associated with NAFLD, and cumulative incidences were calculated accounting for competing risk of death. We also tested the interaction between NAFLD and CVD and assessed the magnitude of risk by creating indicator variables in the Cox regression models.

### Results and Study Limitations

There were 145 (5%) patients with NAFLD and 1,291 (4.6%) of the matched individuals who developed dementia during the study period. This translated to an adjusted HR of 1.3

**Table** Number of Events/Person-Year, Cumulative Incidence (%), and HRs With 95% CI From a Stratified Cox Regression for Dementia Associated With NAFLD in the Total Population, by Sex and Age Groups

Study population	No. of events/person-year (%)		
	Matched cohort	NAFLD	aHR (95% CI)
<b>Total population</b>	1,291/164,167 (4.6)	145/12,554 (5.0)	1.38 (1.10–1.72)
<b>Male</b>	512/69,705 (4.0)	59/5,069 (4.5)	1.40 (0.99–2.02)
<b>Female</b>	779/94,461 (5.0)	86/7,485 (5.4)	1.39 (1.03–1.84)
<b>Age group (65–74)</b>	569/125,257 (2.7)	75/9,699 (3.6)	1.41 (1.01–1.94)
<b>Age group (75–84)</b>	564/35,400 (8.6)	58/2,606 (8.3)	1.26 (0.92–1.75)
<b>Age group (≥85)</b>	158/3,509 (16.1)	12/258 (11.1)	1.08 (0.55–2.22)

Abbreviations: aHR = adjusted hazard ratio; NAFLD = nonalcoholic fatty liver disease.

The reference group is the matched cohort under each category. aHR adjusted for diabetes, obesity, dyslipidemia, hypertension, stroke, heart disease, and depression.

(95% CI 1.1–1.7) for all-cause dementia and 1.4 (95% CI 1.0–2.2) for vascular dementia, compared with that for the matched individuals. The 5-year cumulative incidence was 3.6% for patients with NAFLD and 2.0% for matched individuals. Comorbid NAFLD and CVD conferred a greater risk of dementia. The major limitation of the study was the unavailability of the primary care data, so the prevalence of NAFLD and the estimated risk might be underestimated. Our results can only be generalized to patients in secondary or tertiary settings. We cannot rule out the influence of residual confounding including education and socioeconomic status.

### Study Funding and Competing Interests

This study did not receive targeted funding. The authors report no competing interests. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

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*Neurology* 2022;99:e574-e582 Published Online before print July 13, 2022  
DOI 10.1212/WNL.0000000000200853

**This information is current as of July 13, 2022**

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