

were prescribed a VKA and 18,513 (47%) a DOAC at baseline.

Demographic and lifestyle factors were similar in those prescribed DOACs and VKAs and there was no difference in the history of stroke, a major risk factor for dementia, between the different treatment groups.

A total of 1,258 patients (3.2%) had a diagnosis of dementia recorded by their GP with an incidence of 16.5 per 1,000 person-years. Overall, 1,488 patients (4.0%) received a diagnosis of mild cognitive impairment, with an incidence rate of 20.05 per 1,000 person-years.

In the whole cohort, compared with VKA therapy DOAC treatment for AF was associated with:

- 16% reduction in dementia diagnosis; adjusted hazard ratio (HR) 0.84 (95% CI: 0.73-0.98)
- 26% reduction in mild cognitive impairment; adjusted HR 0.74 (95% CI: 0.65-0.84)

Dementia risk is almost double in patients with AF. This could be due to silent cerebral infarcts, microemboli or systemic inflammation. Certainly, cerebral hypoperfusion is linked to neurodegeneration.

Oral anticoagulant treatment is recommended to reduce the risk of stroke in high-risk individuals with AF and could potentially protect patients from the excess dementia risk associated with this arrhythmia.

The authors conclude: 'We observed that individuals taking DOACs for AF were less likely to be diagnosed with dementia and mild cognitive impairment than those taking VKAs, after adjusting for potential confounding factors.'

'While further evidence, including from randomised controlled trials, would strengthen this finding, it may be relevant to consider cognitive risk profile when prescribing oral anticoagulants for AF among older individuals.'

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Cadogan SL, Powell E, Wing K et al. Anticoagulant prescribing for atrial fibrillation and risk of incident dementia. *Heart* 2021;107:1898-1904

Gastrointestinal disease

NAFLD increases risk of all-cause mortality

In patients with non-alcoholic fatty liver disease (NAFLD), fibrosis stages F3 and F4 are associated with an increased risk of liver-related health problems and death from all causes, a large prospective study from the USA has found.

The authors followed 1,773 patients (64% women), mean age 52 years, with NAFLD for a median of four years. Participants were enrolled from multiple centres between 2009 and 2019.

Alcohol-related liver disease was excluded using the Alcohol Use Disorders Identification Test (AUDIT), and patients with liver disease from other causes, or with a history of liver transplant or hepatocellular cancer were also excluded.

All patients had undergone liver biopsy, and the stage of fibrosis for each participant was assigned by a specialist committee. More than half (55%) had definite nonalcoholic steatohepatitis (NASH), 20% had borderline NASH and 25% fatty liver without NASH.

The main outcomes included death from any cause, hepatic decompensation (clinically apparent ascites, overt encephalopathy, or variceal haemorrhage), the development of hepatocellular cancer, non-hepatic cancer, cardiovascular events, cerebrovascular events and new onset of coexisting conditions including type 2 diabetes, hypertension and chronic kidney disease.

All-cause mortality was higher in the study population than the expected background age-related rates:

- 0.57 vs 0.4 deaths per 100 person-years

All-cause mortality rates increased with increasing fibrosis:

- 0.32 deaths per 100 person-years for fibrosis stages F0 to F2 (no, mild or moderate fibrosis)
- 0.89 deaths per 100 person-years for fibrosis stage F3
- 1.76 deaths per 100 patient-years for fibrosis stage F4 (cirrhosis)

Likewise, the incidence of liver-related health problems increased with the degree of fibrosis.

Variceal haemorrhage rates:

- 0.00 per 100 person-years for F0 to F2
- 0.06 per 100 person-years for F3
- 0.70 per 100 patient-years for F4

Encephalopathy rates:

- 0.02 per 100 person-years for F0 to F2
- 0.75 per 100 person-years for F3
- 2.39 per 100 patient-years for F4

Patients with F4 fibrosis were more likely to have diabetes and a reduction of > 40% in eGFR during the study period compared with those with F0-F2 fibrosis. The incidence of cardiac events and non-hepatic cancers was similar across patients with all fibrosis stages.

When adjusted for age, gender, race, diabetes status, NASH or NAFLD and fibrosis stage at baseline, the occurrence of any hepatic decompensation event during the study period was associated with increased all-cause mortality; adjusted hazard ratio 6.8 (95% CI: 2.2-21.3).

The study authors conclude: 'This study showed an association between fibrosis stages F3 and F4 and hepatic decompensation and death in patients with NAFLD.'

'These data may be helpful in the assessment of prognoses and in the use of treatments for NASH.'

The development of NAFLD is strongly linked to obesity and type 2 diabetes, and its clinical and histopathological spectrum ranges from uncomplicated fatty liver to NASH which can progress to cirrhosis.

As a GP, lifestyle change and weight loss will remain the mainstay of treatment, as not only can they promote resolution of NAFLD, but they can also help reduce the risk of related conditions including diabetes and cardiovascular disease.

DR JEZ THOMPSON

Sanyal A, Van Natta JL, Clark J et al for the NASH Clinical Research Network (CRN). Prospective study of outcomes in adults with nonalcoholic fatty liver disease. *N Engl J Med* 2021;385:1559-69 >>