

of patients died within ten years of COPD diagnosis, 57.8% were men.

The mMRC dyspnoea score in the 12 months leading up to diagnosis was recorded in only 61.7% of participants but when it was, there was a strong correlation with the proportion of patients who died: 6.3% when the mMRC dyspnoea score was 0 or 1, 8.5% when the score was 2, and 12.5% when the score was 3 or 4.

In the 70% of patients for whom comorbidities were recorded, asthma, hypertension, and depression were the three most common.

The two risk factors which had the greatest effect on mortality were:

- **Heart failure**

HR 1.92 (95% CI: 1.87-1.96)

- **Current smoker**

HR 1.68 (95% CI: 1.66-1.71)

The other prognostic factors with large effect sizes that were also significant (>20% increased risk of mortality) were:

- **Ischaemic heart disease**

HR 1.49 (95% CI: 1.45-1.54)

- **Former smoker**

HR 1.49 (95% CI: 1.46-1.51)

- **Male gender**

HR 1.26 (95% CI: 1.25-1.27)

- **mMRC dyspnoea score ≥ 3**

HR 1.33 (95% CI: 1.28-1.39)

- **Breathlessness**

HR 1.25 (95% CI: 1.24-1.26)

- **Physical activity limitation**

HR 1.37 (95% CI: 1.33-1.42)

Hypertension, anxiety, a history of pulmonary TB, and depression had more modest effects on mortality.

Although a large and robust study the authors acknowledge that smoking data is often prone to error. They also acknowledge that as primary care data alone were used, hospitalisations may have been missed.

The study authors state: 'While the model developed achieved strong internal validation performance, it is now important to externally validate this model before deploying it in clinical practice.'

The study emphasises that COPD patients with heart failure should be a priority for optimisation of control of both conditions. It offers further evidence for the importance of smoking cessation management in COPD patients and also identifies other adverse prognostic factors that may require action.

DR PETER SAUL

Shah SA, Nwaru BI, Skeikh A et al. Development and validation of a multivariable mortality risk prediction model for COPD in primary care. *NPJ Prim Care Respir Med* 2022;32:21

Gastrointestinal disease

NAFLD associated with raised risk of heart failure

Non-alcoholic fatty liver disease (NAFLD) is associated with a 1.5 times higher risk of new-onset heart failure, independent of the presence of diabetes, hypertension and other common cardiovascular risk factors, a large meta-analysis has found.

The authors searched Scopus, Web of Science and PubMed, from database inception to March 2022, to identify observational cohort studies that assessed the association of NAFLD with risk of new onset heart failure.

Inclusion criteria were the identification of NAFLD through serum biomarkers or scores, ICD codes, imaging techniques or liver histology together with evidence of a primary outcome of new onset heart failure, as assessed mainly by ICD codes.

Eleven studies were identified which provided aggregate data on 11,242,231 individuals (50% women), mean age 55 years, from a range of countries including the UK. A total of 2,944,058 (26.2%) had NAFLD at baseline.

There were 97,716 cases of incident heart failure over a median follow-up of ten years.

The presence of NAFLD was associated with a moderately higher risk of new onset heart failure (11 studies); pooled random-effects hazard ratio (HR) 1.50 (95% CI: 1.34-1.67, $P < 0.0001$; $I^2 = 94.8\%$). This risk was independent of age, gender, ethnicity, adiposity, diabetes, hypertension and other common cardiovascular risk factors. Further analysis did not show

any evidence of significant publication bias.

The risk for new-onset heart failure appeared to be further increased with more advanced liver disease, especially with higher levels of liver fibrosis, as assessed by non-invasive fibrosis biomarkers or histology (two studies); pooled random-effects HR 1.76 (95% CI: 0.75-4.36; $I^2 = 96.9\%$).

It is becoming increasingly clear that NAFLD is part of a multisystem disease with adverse effects not only on the liver but also on extrahepatic organs, including the heart and vasculature. Recent studies have reported an association between NAFLD and the risk of new-onset heart failure. However, the size of the risk, and whether this risk changes with the severity of liver disease, has been uncertain.

Though the study does not prove causality, the significant association between NAFLD and new-onset heart failure supports other findings of increased rates of cardiovascular disease in those with NAFLD, and strengthens guidance that patients found to have NAFLD should be considered for cardiovascular risk assessment in addition to liver investigation and monitoring.¹

The study authors conclude: 'We believe that the results of our meta-analysis further highlight the need for a patient-centred, multidisciplinary and holistic approach to manage both liver disease and cardiovascular risk in people with NAFLD.'

'Future high-quality prospective and mechanistic studies are certainly needed to better elucidate the existing but complex link between NAFLD and risk of new-onset heart failure,' they add.

DR JEZ THOMPSON

Mantovani A, Petracca G, Csermely A et al. Non-alcoholic fatty liver disease and risk of new-onset heart failure: an updated meta-analysis of about 11 million individuals. *Gut* Published Online First 25 July 2022

REFERENCE

1 Kasper P, Martin A, Lang S et al. NAFLD and cardiovascular diseases: a clinical review. *Clin Res Cardiol* 2021;110:921-37

See also Managing cardiovascular risk key in non-alcoholic fatty liver disease, p11

»