Primary care recorded NAFLD and the risk of incident MI and stroke: Findings from analyses of 18 million patients in the UK, the Netherlands, Spain, and Italy

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Background

Many consider non-alcoholic fatty liver disease (NAFLD) to be a high cardiovascular (CVD) risk state, but current data stem largely from cohort studies variably adjusted for usual CVD risk factors.

Objectives

We aimed to investigate the association between NAFLD diagnosis recorded in four European primary care databases and the risk of acute myocardial infarction (AMI) and stroke.

Methods

Data were extracted upon ethical approval from The Health Improvement Network (UK), Health Search Database (Italy), Information System for Research in Primary Care (Spain), and Integrated Primary Care Information (Netherlands). Patients with a recorded diagnosis of NAFLD (including non-alcoholic steatohepatitis) were identified after harmonizing clinical codes across databases. Each NAFLD patient was matched by age, gender, practice site, and visit recorded at +/− 6 months of date of diagnosis, to up to 100 patients without NAFLD. Patients with a history of AMI or stroke, with <1 year of enrolment and <6 months follow-up post index date were excluded. Events of interest were

fatal or non-fatal AMI and ischaemic or unspecified stroke. Hazard ratios were estimated using Cox models and were pooled across databases by random-effect meta-analyses.

Results

121 159 patients with an incident NAFLD diagnosis were identified out of 17.7 million patients. Average follow-up from index date varied between 2.1 and 5.5 years between the databases. The HRs for incident AMI adjusting for age and smoking status ranged from 1.03 (95% confidence interval: 0.90; 1.18) to 1.31 (1.16; 1.49) and pooled estimate was 1.17 (95% CI 1.05; 1.30; I^2: 66%, p value heterogeneity: 0.032). This pooled HR became non-significant with progressive adjustments for type 2 diabetes, systolic blood pressure, total cholesterol, statin use, and hypertension (1.01; 0.91-1.12; I^2:48.4%, p_{het}: 0.121). Pooled HR for incident stroke events adjusting for age and smoking status was 1.18 (1.11; 1.24, I^2: 29.3%, p_{het}: 0.24), which also became non-significant at 1.04 (0.99; 1.09, I^2 = 0.0%, p_{het}: 0.92) after adjustment for risk factors. Further sensitivity analyses, excluding NASH patients, showed comparable results.

Conclusions

Our study indicates that patients identified in routine care with NAFLD may not automatically be considered as having higher CVD risk as a result of their NAFLD diagnosis; rather, CVD risk assessment in these patients can be conducted in the same way as the general population.