



to CPAP was assessed. Patients were followed every 3 months for 1 year, then annually (median follow-up 72 months).

After adjustment for multiple covariants, severe OSA without CPAP was associated with higher cardiovascular mortality (HR 3.5; 95% CI, 1.2–10) compared with controls without OSA. Cardiovascular mortality did not differ in patients with adequate CPAP ( $\geq 4$  hours per day) compared with controls.<sup>3</sup>

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## What are common causes of elevated transaminases in asymptomatic patients?

### Evidence-Based Answer

Viral hepatitis, alcohol use, and hepatotoxic medications can cause elevated transaminase levels in asymptomatic patients (SOR: **B**, cross-sectional survey, cohort study, and case series). In individuals who have a negative ingestion history and negative viral serology, the most common etiology is nonalcoholic fatty liver disease (SOR: **C**, case series).

In the American National Health and Nutrition Examination Survey (NHANES) 1999–2002, a cross-sectional population study of noninstitutionalized patients older than 20 years, 9.8% of 6,823 nonpregnant patients had an elevated AST ( $>40$  IU/L) or ALT ( $>47$  IU/L).<sup>1</sup> Excessive alcohol consumption ( $>1$  alcoholic drink per day for women and  $>2$  for men) or hepatitis C accounted for only 1.7% of these elevations. Other viral hepatitis or medications were not discussed in this study.

A more recent study using NHANES data from 1988 through 2008 showed that the prevalence of major causes of chronic liver disease has remained stable, with the exception of nonalcoholic fatty liver disease (NAFLD), which has increased from 46% in 1998–1994 to 75% in 2005–2008.<sup>2</sup>

A Scottish population-based, retrospective cohort study followed nearly 96,000 primary care patients

older than 16 years who had any liver enzyme testing over a mean of 3.7 years.<sup>3</sup> Out of this group, 5,107 had abnormal transaminases (either ALT or AST elevated above the laboratory cutoff); 231 (4.5%) were diagnosed with a liver disease. In patients with elevations more than 2.5 times the upper limit of normal (ULN), 12% had a liver diagnosis. Some of the most common diagnoses were 76 alcohol-related liver disease, 61 current or recovered viral hepatitis, 42 cirrhosis, and 21 NAFLD. This epidemiological study did not provide details on workup or diagnosis for any of the patients. Not all diagnoses thought to be related to the transaminases were recorded.

A prospective case series examined 354 patients without serological, ultrasound, or historical explanations for persistently elevated transaminases ( $>2\times$  ULN) or gamma glutamyl transferases.<sup>4</sup> Steatohepatitis (34%), steatosis (32%), cryptogenic hepatitis (9%), drug-related damage (7.6%), and a normal liver (6%) accounted for 90% of the pathologic diagnoses on liver biopsy. Less common diagnoses ( $<2\%$ ) included autoimmune causes, sarcoidosis, primary biliary cirrhosis, and hemochromatosis.

An American prospective observational study examined 1,124 symptomatic and asymptomatic adults referred to a gastroenterology department for further workup of persistently elevated transaminases (50% above ULN on  $\geq 2$  occasions).<sup>5</sup> The cause was found in 1,043 patients through history or serology. The causes included infectious, metabolic, or autoimmune liver disease; excessive alcohol use; or hepatotoxic drug use. The prevalence of each was not specified in this study. Of the 60 asymptomatic adults who were not diagnosed with 1 of the above etiologies, the diagnosis after biopsy was steatosis (48%) and steatohepatitis (35%). Also, 6 people had a normal liver on biopsy, 3 had fibrosis, and 1 had cirrhosis.

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