Liver Fibrosis, Sleep Apnea and Cardiovascular Events in Stroke Patients

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We read with interest the recent publication of Baik et al. [1], studying the burden of nonalcoholic fatty liver disease (NAFLD) as a predictor of medium-term cardiovascular events in patients with ischemic stroke. As stated by the authors, concordant studies have confirmed in the general population the relationship between liver diseases and secondary occurrence of major cardiovascular events (including stroke) and mortality [2]. NAFLD and cardiovascular diseases share the same exposures and intermediary mechanisms, namely, smoking, decreased physical activity and obesity, systemic inflammation, and the different components of metabolic syndrome [3–6]. To establish a direct causal relationship between one of the 3 histological components of NAFLD (steatosis, inflammatory changes leading to nonalcoholic steatohepatitis, and fibrosis) and late cardiovascular events remains therefore challenging [2].

Recently, a clear association has been established between presence and severity of sleep apnea and liver damage [see for review: 7]. A reduction of hepatic steatosis by continuous positive airway pressure treatment, the gold standard treatment of obstructive sleep apnea is suggested by observational studies [8] but has not been firmly established by randomized controlled trials [9, 10]. Also, in a population

of chronic obstructive pulmonary disease patients, sleep apnea came out as a major predictor of liver damage [11]. In a longitudinal follow-up of chronic obstructive pulmonary disease patients [12], in line with the results of Baik et al. [1], and as previously shown by Angulo et al. [13], liver fibrosis patients exhibited more cardiovascular events and higher mortality than those with no fibrosis. We also found that steatosis and nonalcoholic steatohepatitis were not associated with increased cardiovascular events or mortality. These concordant results reinforce the idea that the 3 histological components of NAFLD have differential impact on patient's prognosis and that fibrosis is the most deleterious. Apart from lifestyle and diet modification, no treatment is currently validated. Early diagnosis of liver disease as well as identification of patients for actionable risk factors such as sleep apnea should be implemented in clinical routine.

A potential drawback of Baik et al. [1] cohort is that sleep apnea was not assessed as a confounding factor. In a recent meta-analysis [14], the prevalence of sleep-disordered breathing with apnea-hypopnea index >5/h was 73% at acute phase, 66% at subacute phase, and 71% at chronic phase. The overall prevalence of sleep-disordered breathing was 71% in stroke patients. This

comorbidity is known to be related to both NAFLD and incident cardiovascular events [15]. Another interesting point would be to know the proportion, expected high, of patients treated with statins before the onset of stroke and during follow-up. There has been evidence from studies involving patients with biopsy-proven NAFLD that statins improve several aspects of NAFLD histology [16, 17] in addition to a reduction in cardiovascular events when used in secondary prevention.

At the end the multimorbidity associating NAFLD, sleep apnea and stroke should be more recognized in the future and data provided by Baik et al. [1] contribute to this important awareness.

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The authors have no conflicts of interest to declare.

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