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### Letter to the Editor

#### Shift work and subclinical atherosclerosis: Recommendations for fatty liver disease detection

To the Editor,

We have read with great interest the article by Puttonen et al. about the association between shift work and subclinical atherosclerosis in young people [1]. The authors reported that shift workers showed a higher carotid intima-media thickness (IMT) and a 2.2-fold increased risk of carotid plaques than those observed in day workers. Unfortunately, shift work schedule has been associated with several deleterious effects on the cardiovascular and metabolic systems. For instance, shift work was associated with a significant high risk of death due to ischemic heart disease [2,3]. In fact, results from large prospective studies showed that shift work is associated with myocardial infarction [4]. A recently published study showed that shift work is a risk factor for myocardial infarction even at younger ages [5]. Otherwise, we observed that shift workers exhibit most of the risk factors of the cardiometabolic syndrome, including elevated body mass index, waist-hip ratio, diastolic blood pressure, fasting insulin, HOMA index and triglycerides [6]. In addition, our results emphasize the presence of low-grade inflammation in shift workers, which may be a contributing factor to the health problems that characterize the shift work. Taken together, all these data are of remarkable importance as shift work contributes to the morbimortality of cardiovascular diseases in young exposed people as emphasized by Puttonen et al. [1]. It must also be noted that shift workers represent approximately 20% of the workforce worldwide.

Based on the above-mentioned comments, we believe that a final observation should be added. In the last couple of years, several epidemiological studies showed that nonalcoholic fatty liver disease (NAFLD), a highly prevalent disease characterized by excess fat accumulation in the liver, is associated with an increased risk for cardiovascular disease [7]. Moreover, NAFLD is now considered the hepatic manifestation of the cardiometabolic syndrome [8]. In a recent systematic review of the literature that included 3497 individuals, we observed that patients with hepatic steatosis have an increase of 13% of carotid IMT in comparison with individuals without fatty liver [9]. Hence, in the light of all these observations about the high risk for cardiovascular disease that individuals exposed to a working schedule of shift work have, and considering that shift workers exhibit most of the features of the cardiometabolic syndrome, it is reasonable to postulate that shift workers have also a high prevalence of NAFLD. Therefore, it appears mandatory to assess the overall cardiovascular risk of rotating shift workers, including the systematic detection of fatty liver disease. Until now, there are no accurate noninvasive methods for the diagnosis of NAFLD; liver biopsy is still regarded as the gold standard in determining not only the presence of fatty liver, but also in distinguishing the clinical forms of NAFLD. Nevertheless, the presence of fat accumulation in the liver can be detected by various imaging modalities that range

from a cheap and readily available imaging method, such as liver ultrasound, to the use of a semi-quantitative estimation of liver fat by magnetic resonance imaging (MRI), which is the most expensive modality. In special settings, such as the workplace of shift workers, and for initial screening purposes, a liver ultrasound examination may be useful for confirming the clinical suspicion of fatty liver disease.

In addition, the screening strategy may also include a systematic measurement of circulating concentrations of the liver transaminases, alanine aminotransferase (ALT) and aspartate aminotransferase (AST). These two liver enzymes, besides being surrogate markers of NAFLD, were previously shown to have a high predictive value for coronary events, independent of the traditional risk factors and features of the metabolic syndrome [10]. Moreover, some other simple anthropometrical and biochemical measurements, such as BMI, waist circumference and HOMA index may be added. We have previously shown how they can be incorporated in a composite index that has a highly predictive score for differentiating the clinical forms of NAFLD: simple steatosis and non-alcoholic steatohepatitis [11].

Proper screening for cardiovascular risk and fatty liver disease will be critical in primary prevention and in the treatment of existing but undiagnosed cardiovascular and liver disease in young individuals. Accordingly, NAFLD may contribute to the systemic inflammation and insulin resistance, which are critical events in the pathophysiology of the cardiometabolic syndrome. In such cases, type II angiotensin receptor blockers are promising therapeutics agents [12].

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