Liver, a Window to the Heart in Type 2 Diabetes

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Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of disease, characterized histologically by excessive accumulation of hepatic fat in the absence of significant alcohol consumption; with or without inflammation, varying fibrosis, and cirrhosis. The clinical significance of NAFLD is not so much because of its common occurrence in the general population, but because of its stated potential, in the presence of inflammation and fibrosis, to progress to cirrhosis and hepatocellular carcinoma.

NAFLD has been proposed as one of the components of the metabolic syndrome. It has been found to be associated with obesity, type 2 (non-insulin-dependent) diabetes mellitus, and hyperlipidemia. Studies have shown the central role of obesity and insulin resistance in NAFLD. However, regardless of body-mass index, the presence of type 2 diabetes mellitus significantly increases the risk and severity of NAFLD.

Patients with NAFLD tend to have higher calcium scores on CT coronary angiography and higher prevalence of coronary artery disease on angiography. The higher prevalence of calcified and noncalcified plaques, nonobstructive coronary lesions and coronary stenosis in patients with NAFLD occurs even in the absence of the metabolic syndrome. In a recent meta-analysis NAFLD was shown to be associated with increased cardiovascular risk and it was concluded that a multidisciplinary approach is needed for these patients to control the related risk factors and monitor for cardiovascular and liver complications. After all, the leading cause of death in patients with NAFLD is coronary events.

NAFLD is associated with cardiovascular disease independent of classical risk factors, glycemic control, medications, and metabolic syndrome features in patients with diabetes mellitus in the Western population. This excess risk of cardiovascular disease may be due to increased production of glucose, VLDL, C-reactive protein and coagulation factors by the fatty liver.

In this issue of the Journal, Agarwal et al. have estimated the prevalence of NAFLD on ultrasonography in patients with type 2 diabetes and correlated it with coronary artery disease and coronary risk factors. They found that diabetic patients with NAFLD have higher prevalence of coronary artery disease, hypertension, obesity, central obesity, poor glycemic control, dyslipidemia and carotid intimal thickness. This correlation of NAFLD with coronary artery disease was present also on multivariate analysis.

The study highlights the increasingly recognized association of NAFLD and coronary artery disease in the diabetic population. Is NAFLD a late development in the unfolding metabolic syndrome, and hence the association with more sinister parameters? Does NAFLD actually cause or increase the incidence of some of the coronary risk factors or is it merely a surrogate marker? The study suggests that NAFLD on ultrasonography may be a surrogate marker for coronary artery disease in type 2 diabetes. However, it was not designed to predict the development of coronary artery disease. It would be interesting to study the coronary vessels, maybe on CT coronary angiography, in these patients.

We need long-term follow-up studies from India on patients with NAFLD to assess the development of coronary artery disease over a period of time. This will help us understand the temporal evolution of NAFLD, metabolic syndrome and coronary artery disease in our population. We also need to study in more detail the role played by NAFLD in the pathogenesis of coronary artery disease. Important it is, especially from a hepatologist’s viewpoint, also to know whether these associations are uniform across the spectrum of NAFLD, or whether only steatohepatitis with or without fibrosis carries the burden presently attributed to the all-inclusive entity of NAFLD.

References