SAN FRANCISCO – Among patients with type 1 diabetes, the ratio of total cholesterol to high-density lipoprotein cholesterol may be a better marker of cardiovascular disease, compared with elevated low-density lipoprotein cholesterol, observational data from a Swedish registry suggest.

"High LDL cholesterol is considered an important risk factor in the general population and in type 2 diabetes," Dr. Christel Hero said at the annual scientific sessions of the American Diabetes Association. "Subgroup and meta-analyses show a reduced risk for CVD with statin treatment in type 1 diabetes, but there is a lack of larger studies in type 1 diabetes concerning treatment of hyperlipidemia."

The aim of the current study was to assess LDL and total cholesterol to HDL cholesterol ratios as predictors of CVD in type 1 diabetes, and to evaluate the risk for CVD at different levels of LDL. To accomplish this, the researchers used different Swedish registries to link patients with type 1 diabetes, including the Swedish National Diabetes Registry, which contains data on more than 96% of individuals with the disease in that country. They also used the hospital discharge register, "from which we can get information about all hospital stays, including medical interventions and discharge diagnosis," said Dr. Hero of Sahlgrenska University Hospital in Gothenburg, Sweden. Reports of death were obtained from Sweden’s cause of death register.

Dr. Christel Hero

The study population included 30,778 patients with type 1 diabetes who were between the ages of 18 and 79 years. Baseline data were collected during 2003-2006 and the patients were followed until 2011, or until the first event, which resulted in a mean follow-up of 7 years. Outcome events were fatal or nonfatal CVD, which encompassed acute myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass graft surgery, stroke, and peripheral vascular disease.

The patients were divided into two groups: those on lipid medication (8,172) and those not taking lipid medication (22,608). The researchers formed two subgroups: one from the patients on lipid medication with a history of CVD at baseline (1,973) and one from the overall study population that comprised patients 40 years of age or older who had one CVD risk factor at baseline (9,324).

The researchers used Cox regression analyses with LDL and total cholesterol to HDL ratio as predictors of outcomes, adjusted for CVD risk factors including diabetes duration, body mass index, systolic blood pressure, smoking, and use of antihypertensive and lipid medication.

At baseline, the mean age of patients was 46 years and their mean duration of diabetes was 20 years. Compared with the patients not taking lipid medication, those taking lipid medication were older (56 vs. 43 years, respectively), had longer diabetes duration (26 vs. 19 years), were more commonly treated with hypertensive medication (70% vs. 25%), and had a lower mean estimated glomerular filtration rate (75 vs. 87 mL/min per 1.73 m²), as well as a higher risk of CVD (24% vs. 4%).
Baseline lipid values were similar between the two main groups: a mean LDL of 106 mg/dL and a mean ratio of cholesterol to HDL of 3.2 units.

Dr. Hero reported that there were 13.8 CVD events per 1,000 person-years among patients taking lipid-lowering medications, compared with 51.7 events per 1,000 years among those who were not taking lipid medications. The researchers also found that 67.9% of patients with a history of CVD had a CVD event over 7 years of follow-up.

The adjusted hazard ratios per 1 mmol/L increase in LDL for CVD was 1.02 in those taking lipid medications and 1.08 in those who were not. Both hazard ratios were nonsignificant. A similar association was observed in patients aged 40 years and older who had one CVD risk factor at baseline. In this subgroup "there is a slight but weak significance for the LDL as a predictor of cardiovascular disease, but when looking at the octiles [of LDL] you can see no significance at all," Dr. Hero noted.

The adjusted hazard ratios per 1 mmol/L increase in the cholesterol to HDL ratio were 1.06 in those taking lipid medications and 1.08 in those who were not, both statistically significant differences. "There is a strong correlation between CVD and the cholesterol to HDL ratio as a continuous variable; also, when we look at the ratio divided into octiles, we can see an obvious correlation with a linear trend," Dr. Hero said. "The higher the ratio, the stronger the correlation. The same is true for the patients 40 years and older with one CVD risk factor. There is a strong correlation for the ratio as a continuous variable and also a linear trend for the octiles of the ratio."

The findings suggest "there is no support for an LDL treatment target of 100 mg/dL," Dr. Hero concluded. "The ratio of cholesterol to HDL is a significant predictor of CVD in patients without lipid-lowering medication. The ratio of cholesterol to HDL seems to be a more reliable marker for CVD risk when considering primary prevention."

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