Pancreatitis Rates Higher in Adults With Diabetes

A U.K. database study of more than 75,000 diabetes patients found a highly significant increase.

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

STOCKHOLM – Both the prevalence and the incidence of pancreatitis were significantly greater among adults with diabetes than in those without, in an analysis of a U.K. database comprising more than 2 million general practice adult patients.

Rates of pancreatitis have been rising in recent years, along with increases in obesity and related conditions, including gallstones and hyperlipidemia. Previous studies have identified a link between type 2 diabetes, antihyperglycemic medications, and pancreatitis, but these have mainly used small population sizes and have not stratified by age and sex, Dr. Hamidreza Mani, an endocrinologist at the University of Leicester (England), said at the meeting.

Dr. Mani and his associates used the U.K. General Practice Research Database, one of the largest patient databases in the world, comprising 2.34 million adults. Of those, 75,322 were identified with a history of type 2 diabetes. Among those, 574 (0.76%) also had a history of pancreatitis, compared with just 0.17% of the 2.2 million without diabetes.

This gave a crude hazard ratio of 4.5 for those with diabetes, compared with those without diabetes. After adjustment for age and sex, the odds ratio for a history of pancreatitis in those with diabetes, compared with those without, was 3.1, which was highly statistically significant, he said.

In all, 74,748 diabetes patients who were not found to have prevalent pancreatitis were followed forward for a mean of 3.1 years beyond a specified index date. Controls were followed for a mean of 3.2 years. There were 134 incident cases of diabetes among the diabetic group and 1,975 among the controls, giving crude incidence rates of 58 and 27 per 100,000 population, respectively. After adjustment again for age and sex, the relative risk of acute pancreatitis that was associated with diabetes was 1.47.

Striking age and sex differences were found. By sex overall, the incidence of pancreatitis among women with diabetes, compared with those without, was 1.95, whereas that rate for men was 2.23.

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Among women with diabetes aged 18-39 years, the incidence of pancreatitis was nearly sixfold, compared with those without diabetes, whereas the rate among women with diabetes aged 50-59 years was actually a bit less than among those without (hazard ratio, 0.86).

Among the men, the greatest incidence occurred in the 50- to 59-year age range, with a hazard ratio of 2.9, compared with men without diabetes. In diabetic men older than 80 years of age, the incidence of pancreatitis dropped to just half that of nondiabetic men (HR, 0.53).

The reason for the sex difference is unclear. Hormonal and other physiologic differences may account for some of it, but not for the sixfold increase among young women, he commented.

The overall pancreatitis incidence of 27.4 per 100,000 among patients with diabetes in this database is far greater than the 10 per 100,000 U.K. incidence that was reported in 1998, Dr. Mani noted. ■

Disclosures: *Dr. Mani stated that he had no disclosures.*

Cystatin C May Be Biomarker for Diabetic Nephropathy

BY BRUCE JANCIN

EXPERT OPINION FROM A CONFERENCE ON MANAGEMENT OF DIABETES IN YOUTH

KEYSTONE, COLO. — Serum cystatin C isn't ready for prime-time use in clinical practice as an alternative to urinary albumin excretion and serum creatinine in screening for diabetic nephropathy, but the unfolding research on this novel biomarker is definitely worth keeping an eye on.

"From a pediatric diabetes perspective, were we to have more data on cystatin C, it would sure be appealing to be able to collect it from a blood sample and not have to try to get overnight urines or even spot urines. This is a biomarker that may pan out as something useful in the future," Dr. David M. Maahs said at the conference, sponsored by the Children's Diabetes Foundation at Denver.

A growing body of evidence suggests serum cystatin C provides a more accurate estimate of glomerular filtration rate (GFR) than do predictive equations based upon serum creatinine, such as the widely used Cockroft-Gault or Modification of Diet in Renal Disease equations.

"Cystatin C has been described as like an HbA_{1c} for renal function," observed Dr. Maahs of the Barbara Davis Center for Childhood Diabetes and the University of Colorado, Denver.

Cystatin C also appears to be superior to serum creatinine as a predictor of the risk of death and cardiovascular events in the elderly in general (N. Engl. J. Med. 2005;352:2049-60). Furthermore, in an analysis restricted to 691 elderly diabetic participants in the Cardiovascular Health Study, cystatin C–based estimated GFR predicted mortality more strongly than did serum creatinine–based estimated GFR (Diabetes Care 2009;32:1833-8).

Cystatin C, which is 'like an HbA_{1c} for renal function,' also appears to be superior to serum creatinine as a predictor of the risk of death and cardiovascular events in the elderly in general.

Moreover, in a study of 509 adults with type 1 diabetes followed for 2.5 years, Dr. Maahs and coworkers showed that serum cystatin C predicted progression of subclinical coronary atherosclerosis as reflected by coronary artery calcification better than serum creatinine, estimated glomerular filtration rate, or albumin excretion rate (Diabetes 2007;56:2774-9).

That being said, data on cystatin C's performance in pediatric populations with diabetes remain lacking, he noted.

Serum cystatin C goes up as the GFR goes down. Cystatin C is thought to better reflect GFR than does serum creatinine because it is independent of age, sex, and muscle mass. Cystatin C is a stable protein produced by nucleated cells at a constant rate. Furthermore, freely filtered at the glomerulus because of its small molecular mass, it is not reabsorbed, and it is eliminated by the kidneys.

Putting aside for the future the question of cystatin C as potential tool for following GFR in diabetic patients, Dr. Maahs stressed the importance of following guidelines for screening for diabetic nephropathy in young patients. About 20%-40% of patients with diabetes develop nephropathy. Indeed, diabetic nephropathy has become the number-one cause of end-stage renal disease in the United States, accounting for 40% of all new cases, he said.

The earliest clinical evidence of nephropathy is persistent microalbuminuria. Among 3,259 participants in the SEARCH for Diabetes in Youth study, Dr. Maahs and coworkers found that the prevalence of an elevated albumin-to-creatinine ratio indicative of microalbuminuria was 9.2% among type 1 and 22.2% in type 2 diabetic individuals under age 20 (Diabetes Care 2007;30:2593-8).

Because persistent microalbuminuria is the reversible stage of diabetic nephropathy if treated with an ACE inhibitor or angiotensin receptor blocker along with intensified glycemic control, smoking cessation, and treatment of hypertension if present, the American Diabetes Association recommends performing an annual test to assess urine albumin excretion in all patients who've had type 1 diabetes for at least 5 years and in all type 2 diabetes patients starting at the time of diagnosis.

The screening for microalbuminuria can be performed by one of three methods: measurement of the albumin to creatinine ratio in a random spot urine; a 24-hour urine collection; or a timed urine collection, often done overnight. A diagnosis of persistent microalbuminuria requires a positive result on two of three tests conducted within a 3-6 month period.

The American Diabetes Association guidelines also call for measurement of serum creatinine at least annually in all adults with diabetes regardless of their degree of urine albumin excretion. The serum creatinine is to be used to estimate GFR.

Because it's important to identify progression to microalbuminuria in a timely way in patients with type 1 diabetes, Dr. Maahs and his coworkers have developed and validated a prediction rule that identifies a subset of patients at high risk. The idea is that a few relatively easily obtainable patient characteristics can be used to help physicians identify a patient subgroup likely to benefit from screening for microalbuminuria more frequently than once yearly.

The prediction rule was developed using data from 1,115 patients in the European Diabetes Prospective Complications Study, then validated in the Finnish Diabetic Nephropathy Study, the Coronary Artery Calcification in Type 1 Diabetes Study, and the Pittsburgh Epidemiology of Diabetes Complication Study. The key variables used in the prediction rule are the albumin excretion rate, body mass index, waist:hip ratio, and a history of ever having smoked.

Thirteen percent of patients progressed to microalbuminuria during 7 years of follow-up. A high-risk subgroup consisting of 8% of the patient population was identified as having a risk of progression of 32% (Diabetologia 2010;53:254-62). ■

Disclosure: *Dr. Maahs disclosed receiving research support from Merck & Co. Inc. and Eli Lilly.*