Diabetic Cardiomyopathy Drugs In Pipeline Will Boost Identification

BY JOYCE FRIEDEN
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WASHINGTON — Diabetic cardiomyopathy is likely to become a more common problem in diabetic patients, but several new therapies in the pipeline look promising, Dr. Francisco Villarreal said at a meeting sponsored by the National Hispanic Medical Association. “This is something we will have to watch for in our young people developing diabetes, and it takes a long time to evolve,” said Dr. Villarreal of the division of cardiology at the University of California, San Diego.

The term “diabetic cardiomyopa- thy” will become much better known in the near future, Dr. Villarreal predicted. The term “refers to pathological changes in the hearts of certain diabetics in the absence of an underlying identifiable cause.”

“Very frequently we associate diabetes with atheroocclerosis, but in these patients we could not identify problems with blood vessels or the presence of hypertension. But we could document changes that occurred at the cellular level—be it muscle cells or cells that produce fibrous tissue—and also at the tissue level. These structural changes are characterized by myocardial hypertrophy and also by the presence of excess fibrotic tissue—in particular, collagen,” he explained.

Diabetic cardiomyopathy appears to play a role in the increased rate of heart failure in diabetic patients, according to Dr. Villarreal. The Strong Heart Study concluded that the extent and frequency of diabetic dysfunction was directly proportional to the level of hemoglobin A1c (Circulation 2000;101:2271-6). The Framing- ham heart study led to similar conclu- sions (Prog. Cardiovasc. Dis. 1985;27:235-70).

“When they looked at the risk of heart failure in diabetics and nondiabetes, in adult diabetic males, the risk was about two times that of (nondiabetic males), and in females, it was about five times,” he said. “But even more, these risks multiplied about 2.5% when observing young individ- uals—in young males, it was a four times higher risk, and in young fe- males, eight times higher. It was also noted that each 1% elevation in HbA1c levels led to an increase of about 30% in the risk of heart failure.”

In one study, Doppler echocardiography documented the presence of diastolic dysfunction in up to 60% of well-controlled type 2 di- abetic patients, Dr. Villarreal noted (Diabetes Care 2001;24:5-10).

“Two compounds in the therapeu- tic pipeline appear promising, he not- ed. Early studies of ruboxistaurin, a novel highly selective inhibitor of protein kinase C, suggest that it may curb diabetes related blindness, nephropathy, and neuropathy. None of these trials involved cardiac dis- eases, but “it is likely that these drugs probably will also benefit the heart,” he said. Also, minoxidil (ALT-711), may help collagen become more compliant, Dr. Villarreal said.

Age, Gender May Flag Risk for Serious Infections in Diabetics

BY PATRICE WENDLING
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NICE, FRANCE — Male gender, advanced age, and a history of several office visits in the past year were among the risk factors for a complicated urinary tract infection in a retro- spective-cohort study of older primary care pa- tients with type 2 diabetes mellitus.

The findings were used to create a clinical prediction rule that could improve manage- ment of UTIs in patients aged 45 years and older, Leonie Muller said at the 16th European Congress of Clinical Microbiology and Infectious Diseases. Patients with type 2 diabetes are known to be at greater risk for urinary tract in- fections. But little is known about predictors of a complicated course.

Although the rule still needs to be validated in other populations, the idea is to use it to identify patients at high risk for serious UTI and educate them about the signs and risk fac- tors for complicated infection, she said.

In a second retrospective cohort study, Ms. Muller and colleagues at the University Med- ical Center Utrecht, the Netherlands, created a similar rule for predicting complicated lower respiratory tract infections, which also are common in older patients with diabetes.

Using data from the Second Dutch National Survey of General Practice, the investigators conducted a 12-month, prospective cohort study that identified 6,343 patients, 45 years or older, with type 2 diabetes. The primary outcome was death or hospitalization as a complication of UTI, defined as an episode of acute pyelonephritis or prostatitis, and re- current cystitis. The mean age was 67 years, 46% were male, and 36% recurrent cystitis.

Multivariate logistic regression analysis was used to develop a clinical prediction rule. There were 179 (2.8%) complicated UTIs, 1 per 100 patient-years in females and 2 per 100 patient-years in males. Independent predictors were increasing age (odds ratio 1.7), male gen- der (OR 1.8), 12 or more office visits in the pre- vious year (OR 11.5), urinary incontinence (OR 2.4), cerebrovascular disease or dementia (OR 2.1-4), and renal disease (OR 3.6).

A cut-off score of 4 points or more on a 12-point scale, 60% of patients would be selec- ted for tailored care, and 8% of patients with a complicated course of UTI would be missed. An example of how the rule might be ap- plied in a diagnostic setting would be that a 75- year-old (1 point) male (1 point) patient with diabetes and renal disease (3 points) would be considered high risk, whereas his 73-year-old (1 point) wife with diabetes and urinary inconti- nence (2 points) would not.

Ms. Muller, a doc- toral student at the university, acknowledged that the model has the potential to identify a large percentage of high-risk patients, adding that future studies should focus on the cost-effec- tiveness of the rule.

In the second study, the investigators evaluat- ed 20 predictors of death and/or 30-day hospi- talization following an episode of lower respi- ratory tract infection in a subgroup of 1,693 patients, aged 65 years and older, with diabetes, from the same database. Among 645 episodes of lower respiratory tract infections including acute bronchitis, exacerbation of chronic obstructive pulmonary disease, asthma, or pneumonia, 13 were fatal and 55 required hospitalization.

Positive predictors of death and/or hospitalization were pneumonia (adjusted odds ra- tio 5.3), age greater than 80 years (OR 2.2), presence of heart failure (OR 2.1), and pred- ictor use (OR 2.4). The hospitalization/death rate was 5.2% among patients found to be at low risk and 36.6% among high-risk patients, Ms. Muller reported.