

## Dyspnea in Diabetics Should Trigger Close CVD Work-Up

BY BRUCE JANCIN  
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SNOWMASS, COLO. — The complaint of shortness of breath in a diabetic patient without known coronary artery disease is a red flag that should trigger an extensive cardiovascular work-up including stress myocardial perfusion imaging, Dr. George A. Beller said at a conference sponsored by the Society for Cardiac Angiography and Interventions.

Recent studies strongly suggest that exertional dyspnea in a diabetic patient may actually be a much more ominous symptom than exertional angina, according to Dr. Beller, professor of internal medicine and chief of the division of cardiovascular medicine at the University of Virginia, Charlottesville.

"Whether this is an angina equivalent or a marker of silent ischemia with inducible ischemic left ventricular dysfunction reflecting more severe coronary artery disease, compared with diabetic patients presenting with angina, we really don't know yet. But I am very impressed that event rates are so much higher in diabetic patients presenting with dyspnea than when they present with angina," added Dr. Beller, a former president of the American College of Cardiology.

For example, investigators at Cedars-Sinai Medical Center in Los Angeles recently reported on 1,737 consecutive diabetic patients without known coronary artery disease (CAD) who underwent single-photon emission computed tomography (SPECT) myocardial perfusion imaging, of whom 1,430 were followed for a median of 2 years.

Objective evidence of CAD was found on SPECT in 39% of the 826 asymptomatic diabetic patients, in 44% of those with angina, and in 51% of the 151 patients with dyspnea.

The outcome was three times worse in diabetic patients with shortness of breath. The annual rate of cardiac death or nonfatal MI was 7.7% in patients with dyspnea as their predominant symptom, 3.2% in those



with angina, and 2.2% in asymptomatic diabetic patients. Among patients with SPECT evidence of CAD, the major event rate increased to 13.2% in patients with shortness of breath, 5.6% in those with angina, and 3.4% in asymptomatic diabetic patients (Eur. Heart J. 2004;25:543-50).

Dr. Beller noted that the cardiovascular import of dyspnea has also recently been underscored in nondiabetic patients. Another Cedars-Sinai study, this one involving 17,991 patients who underwent SPECT and were followed for a mean of 2.7 years, concluded that among patients with no known history of CAD, those with self-reported dyspnea were four times more likely to experience sudden cardiac death than asymptomatic patients and more than

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twice as likely to experience it as patients with typical angina (N. Engl. J. Med. 2005;353:1889-98).

But Dr. Beller focused mainly on dyspnea in diabetic patients, for two reasons: cardiovascular event rates in these patients are much higher than in nondiabetic patients, and the diabetic population is skyrocketing as a result of the obesity epidemic.

Since 1979, cardiovascular, cancer, and all-cause mortality rates have fallen in the United States. But age-adjusted mortality due to diabetes has climbed by 40% since 1987. Two-thirds of diabetic patients die of atherosclerotic disease, he noted.

Several recent studies highlight the existence of a large number of asymptomatic diabetic patients with severe CAD. In a Mayo Clinic study of more than 4,700 diabetic patients without clinically apparent CAD referred for SPECT, 58% of the asymptomatic patients and 60% of the symptomatic ones had abnormal scans. And 20% of asymptomatic and 22% of symptomatic diabetic patients had high-risk scans involving multi-vessel disease and/or extensive ischemia, compared with just 13% of more than 16,000 symptomatic nondiabetic patients and 11% of more than 6,000 asymptomatic nondiabetic patients. ■

## Intensive Insulin Control Cut Morbidity, Not Death in ICU

BY MIRIAM E. TUCKER  
Senior Writer

Targeting blood glucose levels to below 110 mg/dL with insulin therapy prevented morbidity but did not significantly reduce mortality among patients in a medical intensive care unit, said Dr. Greet Van den Berghe and her associates, of Catholic University of Leuven, Belgium.

A total of 1,200 adult patients who were predicted to require medical intensive care for at least 3 days were randomized to either strict normalization of glucose levels (80-110 mg/dL) with the use of infused insulin, or to conventional therapy in which insulin was given only when the blood glucose level exceeded 215 mg/dL and stopped below 180 mg/dL (N. Engl. J. Med. 2006;354:449-61).

The intensive treatment group experienced significantly fewer newly acquired kidney injuries than did the conventionally treated patients (9% vs. 6%), were weaned earlier from mechanical ventilation (hazard ratio 1.21), and were discharged earlier from both the ICU (1.15) and from the hospital (1.16). There was no significant effect on bacteremia, the researchers reported.

Among the 1,200 patients in the intention-to-treat analysis, ICU and in-hospital mortality were not significantly reduced by intensive insulin therapy. At day 3, mortality was 2.8% of the 605 patients randomized to conventional treatment, compared with 3.9% of the 595 in the intensive treatment group. Total in-hospital deaths occurred in 40% and 37%, respectively.

However, when the 767 patients who stayed in the ICU for more than 3 days were examined separately, the in-hospital mortality was reduced significantly, from 53% of the 381 conventionally treated patients to 43% of the 386 in the intensive treatment group, Dr. Van den Berghe and her associates reported.

In contrast, among the 433 patients

who stayed in the ICU less than 3 days, mortality was slightly—but not significantly—higher in the intensive treatment group. After censoring 65 patients for whom intensive care had been limited or withdrawn within 72 hours after ICU admission, the in-hospital mortality was 15% for the conventional treatment group and 17% with intensive treatment.

The most likely explanation for the difference in the effect of insulin therapy in the group as a whole compared with those staying in the ICU at least 3 days is that benefits from intensive insulin therapy take time to be realized. Because the intervention is aimed at preventing complications that occur during—and perhaps as a result of—intensive care, it wouldn't be expected to work if the patient has a high risk of death from the disease that prompted the ICU admission, they said.

The mortality findings from these medical ICU patients differ from what the authors reported previously in a study of 1,548 surgical ICU patients, for whom mortality at 12 months was 8% with conventional treatment versus 4.6% with intensive insulin therapy (N. Engl. J. Med. 2001;345:1359-67).

When complications resulting from intensive care contribute to an adverse outcome, a preventive strategy like intensive glucose control is likely to be effective. This would explain why patients with long stays in the medical ICU benefit more than those with short stays, as was shown in the surgical ICU, they said.

Hypoglycemia was more common among the intensively treated patients and was also identified as an independent risk factor for death. However, among those who had hypoglycemia, the intensively treated patients were less likely to die in the ICU than were the conventional treatment patients (46% vs. 67%). ■

Contributing writer Giancarlo La Giorgia assisted with this report.

## Rapid Glycemic Control May Complicate Cataract Surgery

BY MICHELE G. SULLIVAN  
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Rapid glycemic correction before cataract surgery should be avoided in patients with moderate to severe diabetic retinopathy because it might increase the risk of retinopathy or maculopathy progression.

Blood glucose levels that are quickly corrected in the 3 months before surgery might actually contribute to macular damage, wrote Dr. Chikako Suto of the department of ophthalmology at Tokyo Women's Medical University, and associates (Arch. Ophthalmol. 2006;124:38-45).

"Early [postoperative] worsening might be due to irreversible invasive damage to the macula resulting from vascular hyperpermeability in patients with rapid correction of glycemic control who have maculopathy before surgery. On the basis of these findings, rapid reduc-

tion of blood glucose levels should not be advocated" for these patients, they said.

The researchers examined disease progression 1 year after cataract phacoemulsification and lens replacement surgery in 87 patients with type 2 diabetes (mean age 63 years). The same surgeon performed all of the operations.

The patients were divided into three groups. The rapid control group consisted of 27 patients with elevated (9% or higher) glycosylated hemoglobin (HbA<sub>1c</sub>) levels, which were reduced by at least 3% at 3 months before surgery. The poor control group consisted of 30 patients with consistently elevated HbA<sub>1c</sub> levels that remained high (8.5% or higher) until surgery. The good control group consisted of 30 patients with normalized HbA<sub>1c</sub> levels (mean 7%).

Postoperative progression of retinopathy occurred in 30% of the rapid control group, 17% of the poor control group, and 13% of the good control group; there were no significant differences between groups. In a multi-

variate analysis of risk factors, only the presence of preoperative maculopathy was significantly associated with progression (odds ratio 4).

"[This] indicates that the postoperative rate of retinopathy progression is the same regardless of whether rapid correction is attempted," the authors wrote.

Postoperative progression of maculopathy occurred in 33% of the rapid control group, 13% of the poor control group, and 3% of the good control group. In the multivariate analysis, rapid preoperative glycemic correction increased the risk of progression by more than 8 times; preexisting maculopathy increased the risk by more than 11 times. "To achieve a good visual outcome, it may be important to perform surgery in cooperation with physicians who are advised to avoid [rapid glycemic correction] in patients with moderate to severe [nonproliferative diabetic retinopathy] or maculopathy," the researchers concluded. ■