'Mild' Nonobstructive CAD Is Often Anything But

BY BRUCE JANCIN
Denver Bureau

STOCKHOLM — The prognosis of nonobstructive coronary artery disease may be far less benign than generally assumed, according to two studies presented at the annual congress of the European Society of Cardiology.

Patients with less than 50% luminal stenosis upon diagnostic coronary angiography aren't considered candidates for percutaneous intervention; they are typically told they have "mild" CAD with a very good prognosis. For this reason, critical pathways for risk assessment and treatment of such patients have never been developed, according to Raffaele Bugiardini, M.D., of the University of Bologna, Italy.

The assumption that nonobstructive CAD carries a good prognosis is not based on hard data and had not been examined in a large study until recently. And now that it has, the assumption turns out to be incorrect, he said.

Dr. Bugiardini presented a secondary analysis of three published randomized clinical trials from the Thrombolysis in Myocardial Infarction (TIMI) program involving 10,915 patients with acute coronary syndromes (ACS) for whom angiographic data were available. The studies were the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT–TIMI 22), Orbofiban in Patients With Unstable Coronary Syndromes (OPUS–TIMI 16), and TIMI II-B studies.

The prevalence of nonobstructive CAD in this ACS population was 8.3%. Slightly more than half of the 910 affected patients had mild CAD as defined by a stenosis of less than 50%, whereas the remainder had angiographically normal, smooth coronary arteries.

The primary outcome measure in Dr. Bugiardini's analysis was the combined 1-year rate of death, MI, stroke, coronary revascularization, and/or unstable angina requiring rehospitalization. It occurred in 11.2% of patients with nonobstructive CAD. The incidence was 8.8% in ACS patients with angiographically normal arteries and 13.5% in those with less than 50% stenosis.

Those rates will strike most physicians as surprisingly high. Even more disturbing was the unexpectedly high rate of the most serious outcomes—death or nonfatal MI—in this supposedly low-risk population. The overall incidence was 2% at 1 year, with a 2.8% rate of death or nonfatal MI among patients with mild CAD and 1.3% in those with angiographically normal coronary arteries, Dr. Bugiardini said.

ACS patients with nonobstructive CAD with and without a primary study end point were evenly matched in terms of baseline demographic characteristics, as well as treatment.

Now that the prevailing assumption—that mild CAD carries a good prognosis—has been discredited, it becomes important for physicians to risk-stratify patients with nonobstructive CAD as to their likelihood of developing future coronary events so that their management can be tailored appropriately, he said. The validated and widely used TIMI risk score for patients with unstable angina/non–ST-segment elevation MI can play a useful role here, he added.

'When you go to a [TIMI] score of 3 points, you see [an] ... unacceptable 2.8% rate of death or MI.'

DR. BUGIARDINI

When he applied the TIMI risk score to the 665 eligible patients, the associated 1-year risk of death or MI climbed from 0% in those with a TIMI score of 0 to 4.1% in those with a score of 4 or more. (See box above.)

"The 0.6% death or MI rate seen with a TIMI score of 1 is the expected rate in the general population of asymptomatic subjects. But when you go to a score of 3 points, you see a completely unacceptable 2.8% rate of death or MI. That's unbelievable. So patients with a score of 3 or 4 are really at great risk," said Dr. Bugiardini.

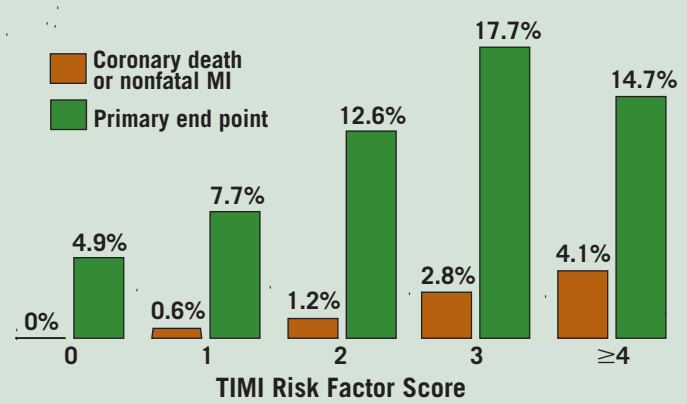
Separately, Sylvie Swales, M.D., presented data from the World Health Organization's Monitoring Trends and Determinants in Cardiovascular Disease project (MONICA) Belgian substudy. This prospective survey of the 130,000 residents of the Belgian province of Luxembourg identified all those who underwent coronary angiography for the first time in any Belgian hospital during 1985-1996.

The subsequent 5-year incidence of coronary death among 274 subjects with mild CAD as defined by a less than 50% stenosis was 7.8%, similar to the 8.1% rate among 377 others with angiographically significant single-vessel disease not treated with angioplasty or bypass surgery. The 5-year rate of coronary death or nonfatal MI was 10.3% in the group with mild CAD and 14.8% in those with significant single-vessel CAD as defined by a 50% or greater stenosis.

The prognosis was far better for the 763 individuals whose angiogram showed smooth vessels. Their 5-year rate of coronary death was just 0.7%, while their rate of coronary death or nonfatal MI was 1.2%, noted Dr. Swales of the Catholic University of Leuven (Belgium).

Dr. Bugiardini said that although it's possible some cases that are labeled as "nonobstructive" CAD represent misclassification of the angiogram, it has been his clinical observation that poor patient compliance with secondary prevention measures is a much bigger factor. ■

TIMI Score Can Stratify Risk in Nonobstructive CAD



Note: Based on data from 665 patients with acute coronary syndromes. Primary end point was combined 1-year rate of death, MI, stroke, unstable angina requiring rehospitalization, and/or coronary revascularization.
Source: Dr. Bugiardini

CV Biomarkers Not Set for Wide Use

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — None of the newer biomarkers being evaluated as possible predictors of cardiovascular risk has been studied enough to be considered ready for clinical use, Michael H. Alderman, M.D., said at the annual meeting of the American Society of Hypertension.

Conventional risk factors such as blood pressure, insulin resistance, diabetes, obesity, lipids, and family history account for 50% of cardiovascular risk, so any biomarkers that could further gauge risk would be useful. A biomarker is a substance that can be measured precisely in serum or urine and is related to subsequent occurrence of cardiovascular disease—such as cholesterol, said Dr. Alderman of Albert Einstein College of Medicine, New York.

A handful of newer, more precise biomarkers appears to be more intimately associated with the development of cardiovascular disease, and they look like they will be useful. These include C-reactive protein, neurocytokines, and uric acid. So far, however, there is "suggestive, but for the most part not yet convincing, evidence that these new biomarkers add to the predictive value already contained in the markers that we have," Dr. Alderman said at a press briefing during the meeting, where he gave a summary of reports on the newer biomarkers.

To be useful, a new risk marker would have to make a contribution beyond what's obtained from conventional risk markers. "I don't think that's been formally tested" with the newer biomarkers, he said.

Tests for the new risk marker would have to be reproducible at different times and in different populations, and would have to define an important amount, or proportion, of risk, he said. Lastly, an assay for the biomarker would need to be feasible and cost effective when applied to a population.

"Those kinds of questions have been asked of blood pressure screening and cholesterol screening, but haven't been asked of cytokines," for example, he said.

Dr. Alderman said he believes that uric acid is an independent risk factor for cardiovascular events, particularly in hypertensive patients, but the data supporting this are inconsistent. Other data showing that uric acid is predictive of elevated blood pressure may be more interesting and useful, he said.

"For most of these [new biomarkers], we're not at the point where they're useful, but I think that we're awfully close," Dr. Alderman said. ■

Incidence of Unrecognized MI Proves High in Older Patients

STOCKHOLM — A high proportion of MIs occurring in patients after age 55 go clinically unrecognized, Anneke de Torbal, M.D., reported at the annual congress of the European Society of Cardiology.

This observation from the prospective, population-based Rotterdam Study raises the possibility that periodic screening ECGs ought to be routine in older adults. It would result in identification of patients with previously unrecognized MI so they could have the benefit of placement on an intensive secondary prevention regimen, added Dr. de Torbal of Erasmus Medical Center, Rotterdam, the Netherlands.

The Rotterdam Study includes 4,187 men and women above age 55 who are free of evidence of prevalent MI by 12-lead ECG at baseline and who had a follow-up ECG a mean of 6.4 years later.

During the follow-up period, 141 subjects experienced a clinically recognized MI. This translated into an incidence of 5.0 cases/1,000 patient-years. The rate in men—8.4 cases/1,000 patient-years—was significantly greater than the 3.1/1,000 patient-years in women.

The incidence of clinically unrecognized MI picked up only by the screening ECGs performed as part of the Rotterdam Study protocol was 4.2 cases/1,000 patient-years in men and 3.6/1,000 patient-years in women. The investigators determined that the proportion of all MIs that were unrecognized was 54% in women, compared with 33% in men.

—Bruce Jancin