Clinical Digest

CARDIOLOGY

Paradoxical Findings on Smoking and AMI Mortality

The "smokers' paradox," a phenomenon that seems to defy conventional medical wisdom by highlighting an apparent benefit of tobacco smoking, was used first to explain why the rate of mortality after an acute myocardial infarction (AMI) is lower among smokers than among nonsmokers. In the National Register of Myocardial Infarction 2, a study of 510,044 patients, researchers found smoking to be an independent variable for mortality with a protective effect—even after adjusting for such variables as age and general health. And now, consistent with these findings, a researcher from the Hospital de Poniente, El Ejido, Almeria, Spain—along with colleagues from Virgen de las Nieves University Hospital, the Hospital San Cecilio, the Carlos Haya University Hospital, and the University of Granada, all in Granada, Spain—noted a similar effect when they conducted a multicenter analysis of 17,761 patients from the ARIAM (Análisis del Retraso en el Infarto Agudo de Miocardio) Register in Spain—a database of 29,532 patients with a diagnosis of AMI or unstable angina who were admitted to the intensive care unit (ICU) or critical care unit (CCU) of one of 119 Spanish medical centers within 24 hours of symptom onset.

The investigators analyzed clinical outcomes based on smoking status (classifying subjects as smokers, nonsmokers, or ex-smokers), age (under 55 years, 55 to 64 years, 65 to 74 years, and over 75 years), and various cardiovascular risk factors. They found that the smokers with AMI were younger, with a higher incidence of inferior/inferoposterior AMI and Q-wave infarction and a lower incidence of such complications as cardiogenic shock, reinfarction, and refractory postinfarct angina. On the one hand, smokers with AMI had a higher frequency of high cholesterol and family history of cardiovascular risk. On the other, they had a lower incidence of diabetes, hypertension, and previous angina, and had required fewer angioplasty procedures and coronary artery bypass grafts prior to the hospital admission under investigation.

By contrast, the nonsmokers with AMI required more diagnostic therapeutic techniques, such as insertion of a Swan-Ganz catheter, mechanical ventilation, and temporary pacemakers.

Regarding the primary result—intra-ICU/CCU mortality—nonsmokers with AMI were more than twice as likely to die (13% versus 5%) than were smokers with AMI. Even ex-smokers seemed to be somewhat protected by their former habits, with a 9% mortality rate.

Smoking appeared to have a protective benefit for patients with unstable angina as well. Hypercholesterolemia, hypertension, diabetes, and cerebrovascular accidents were more frequent in the nonsmokers. The smokers required fewer reperfusion techniques, such as angioplasty, stent insertion, and aortocoronary bypass. And again, smoking had its paradoxical effect on mortality: In nonsmokers, the mortality rate was 1.5%, compared with 1% for ex-smokers, and 0.7% for smokers.

The paradoxical effect could not be explained by age, sex, other cardiovascular risk factors, Killip and Kimball classification, or treatment received. (Treatment differences were considered minor with smokers who had AMI or unstable angina given beta-blockers and lipid lowering drugs more often—and ACE inhibitors less often—than ex-smokers and nonsmokers with those conditions.)

It may be, the researchers say, that the type of coronary artery disease induced by smoking is different from that seen in nonsmokers. They also note that their study was limited to patients who were admitted to the ICU/CCU. Thus, it didn't include patients who received no hospital or prehospital care. And the researchers don't know how many patients died before receiving care.

Source: *Chest*. 2004;125: 831–840.

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RHEUMATOLOGY

A New Twist on Gout Risk

A diet containing foods that are both purine-rich and high in protein—including organ meats, some seafood, and beans—has long been considered a major risk factor for gout. But according to a large, prospective cohort study by researchers from Massachusetts General Hospital, Brigham and Women's Hospital, Harvard Medical School, and Harvard School of Public Health, all in Boston, your patients may not need to scratch all purine- and protein-rich foods from their shopping lists just yet.

The researchers conducted a 12-year prospective study to determine the relationship between purported dietary risk factors for gout and new cases among 47,150 men who had no history of gout at baseline. Through a semiquantitative questionnaire sent out every two years, the participants reported their average consumption of over 130 foods and beverages, as well as their weight, regular use of medications, and, if applicable, gout diagnosis. Those who reported a diagnosis of gout were sent a supplementary questionnaire to confirm the report and to establish whether their case met the criteria for gout outlined by the American College of Rheumatology.

Over the course of the study, 730 new cases of gout were documented. Severe foot pain was noted by 642 individuals (88%); high levels of uric acid, by 526 (72%); midfoot involvement, by 256 (35%); and tophus, by 80 (11%). The incidence of gout increased with age and peaked between ages 55 and 69, a range within which 260 cases were diagnosed.

Beef, pork, and lamb as a main dish raised the risk of gout, as did seafood. Each additional daily serving of meat was associated with a 21% increase in gout risk, and each additional daily serving of seafood, a 7% increased risk. And the risk may be even greater in patients who already have gout, since gout tends to impair renal clearance of urate.

Dairy products—especially low fat dairy—lowered the risk of gout, something that's been suggested in earlier research. And neither consumption of purine-rich vegetables nor a greater total protein intake—including animal protein intake—was associated with increased risk of gout. In fact, say researchers, their results suggest that vegetable protein intake may have a protective effect, though smaller than that afforded by dairy protein.

In general, gout risk didn't vary according to body mass index (BMI) or alcohol intake, both of which previously were believed to elevate risk. The exception was seafood intake, which had a significantly stronger association with gout among men who had a BMI of less than 25, than among men whose BMI was 25 or above.

Little is known about the precise identity and quantity of individual purines in most foods, the researchers maintain, especially when the foods are cooked or processed. In addition, they point out, the purported link between purine-rich diets and gout has been based on metabolic experiments that examined the effect of artificial short-term loading of purified purine on the serum uric acid level—not on gouty arthritis. Since many patients with high levels of uric acid won't have gouty arthritis, it's hard to predict whether a certain food or food group actually affects the risk of gout and to what extent.

Source: *N Engl J Med.* 2004;350:1093–1103.

DIABETES CARE

Patients in the Know Keep it Low

Give patients more information about their glucose values, and they may keep serum levels in better balance, say researchers from the University of Colorado Health Sciences Center, Denver; the Diabetes and Glandular Disease Research Associates, San Antonio, TX, and the University of California, San Diego. They studied 15 adult patients with type 1 diabetes (mean age, 37 years; mean duration of disease, 21 years) who tested a new, implantable glucose sensor (DexCom, San Diego, CA) that provides continuous, real-time glucose data.

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The sensor—about the size and shape of an AA battery—contains a microprocessor, radiotransmitter, and biosensor covered with a multilayered membrane. It's surgically implanted in the subcutaneous tissue of the abdomen. The sensor determines glucose levels in subcutaneous tissue every 30 seconds and transmits the data every five minutes to an external receiver that's about the size of a pager. The receiver is programmed with software that allows data to be uploaded to a personal computer, viewable by both the health care providers and the patients. In addition to wearing the sensor, throughout the study, patients were asked to take at least two measurements daily using a self-monitored blood glucose meter and to upload the meter readings to the receiver.

The study had blinded and unblinded phases. During the blinded control period, data were not displayed to the patient. During the unblinded period, data were displayed to the patient in real time as a number (in mg/dL or mmol/L) as well as one-, three-, and nine-hour glucose trend graphs, and the receiver alerted the patient by vibration or sound when glucose levels were high or low. High and low alerts were set at 11.1 and 5.6 mmol/L, respectively; an additional alarm was triggered when the glu-

cose levels fell below 3.1 mmol/L.

When patients could see their glucose levels in real time, they spent 47% less time per day in the hypoglycemic range and 25% less time in the hyperglycemic range than when they relied on self-monitored blood glucose meters. Moreover, the implantable sensor helped these patients spend 88% more time per day in the euglycemic range of 4.4 to 7.8 mmol/L.

Initial concerns about "confusing" the patient with too much information were unfounded, say the researchers. The patients received no special training, but their progress was tracked closely with biweekly visits to the clinics. No device- or procedure-related adverse events were reported during any part of the study, including the unblinded portion.

The fact that the patients visited the clinic with the same frequency during both the blinded and unblinded phases of the study, say researchers, is further evidence that the improvements in glycemic control were not simply a benefit of participating in a study that required more intensive oversight than is customarily provided with routine care but were in fact due to real-time viewing of continuous glucose data and trends during the unblinded period. The researchers call for further study of the implantable devices to confirm their findings and, potentially, to obtain such significant clinical outcomes as reduced glycosylated hemoglobin levels.

Source: *Diabetes Care.* 2004;27:734–738.

UROLOGY

Is BPSA Better than PSA?

A form of free prostate-specific antigen (PSA) known as benign PSA (BPSA) may be better than free PSA at predicting clinically significant prostatic enlargement in men who do not have prostate cancer, say researchers from Baylor College of Medicine, Houston, TX; the University of Texas Southwestern Medical Center, Dallas; and Hybritech Corporation, San Diego, CA. Their study of 91 consecutive patients with a median age of 64 and no prostate cancer demonstrated that the serum concentration of BPSA, unlike PSA, could predict clinical parameters of benign prostatic hyperplasia (BPH)—independent of patient age.

One of the processes involved in age-related prostate enlargement is diffuse enlargement of the transition zone (TZ) tissue. The researchers identified BPSA at levels three to four times higher in the nodular hyperplastic TZ tissue from patients with BPH than in normal TZ tissue from patients without BPH, or from peripheral zone tissue. They also found that the specificity of BPSA for predicting TZ enlargement at all sensitivity levels was better than that of PSA.

In an accompanying editorial, a physician from the department of urology at the University of Texas Southwestern Medical Center at Dallas questions whether BPSA—which he acknowledges is superior to PSA in predicting clinically significant enlargement of the prostate's TZ—is also superior to total PSA in predicting the natural history of the disease. If so, he contends, it would be "a most welcome addition to our diagnostic armamentarium." In response, the study authors point out that their current study is just the first of many planned trials of the properties and performance capacity of BPSA as a novel serum marker to advance the diagnosis and management of BPH. ●

Source: *Urology*. 2004;63: 905–911.