Viral Infection Seen in 'Idiopathic' Cardiomyopathy

More than two-thirds of endomyocardial biopsies show cardiotropic virus, German researchers find.

BY BRUCE JANCIN
Denver Bureau

VANCOUVER, B.C. — Mounting evidence points to a greatly expanded role for viral myocarditis as a cause of what has traditionally been classified as "idiopathic" dilated cardiomyopathy, Matthias Pauschinger, M.D., said at a meeting sponsored by the International Academy of Cardiology.

This revised conception of the pathogenesis of a surprisingly large percentage of cases of dilated cardiomyopathy is accompanied by growing—albeit not yet definitive—evidence for antiviral therapy as a novel and effective treatment strategy, added Dr. Pauschinger of Charité Hospital, Berlin, and the Free University of Berlin.

He and his coinvestigators detected evidence of persistent viral infection in more than two-thirds of endomyocardial biopsies obtained from 245 consecutive patients with idiopathic left ventricular (LV) systolic dysfunction.

This is a much higher prevalence than had been previously reported by others, probably because investigators in this study cast a wider net and used state-of-the-art polymerase chain reaction methods in the search.

Other studies looked chiefly for enterovirus and adenovirus in the myocardium. Dr. Pauschinger and his coworkers screened for a broader spectrum of cardiotropic viruses, including not only adenovirus and enterovirus but also parvovirus B19, human herpesvirus 6, human cytomegalovirus, herpes simplex virus, Epstein-Barr virus, and influenzas A and B.

There is good reason to believe these viruses are not innocent bystanders in the myocardium of patients with dilated cardiomyopathy.

Some of the viruses have direct cytopathic effects. Others have been shown to induce immune or autoimmune reactions, cause endothelial dysfunction, stimulate chronically increased expression of cytokines, and/or contribute to development of a chronic inflammatory state—all of which could cause destruction of the myocardium and ultimately heart failure, he explained.

Viral genomes were amplified from the endomyocardial biopsies of 67% of the 245 patients. Topping the list was parvovirus B19, present in 51% of biopsies, followed by human herpesvirus 6 in 22%, enterovirus in 9%, Epstein-Barr virus in 2%, adenovirus in 1.6%, and cytomegalovirus in fewer than 1%. Of note, 27% of patients had multiple myocardial viral infections.

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DR. PAUSCHINGER

All participants in this study had undergone angiography and echocardiography to exclude coronary artery disease, valve disease, and hypertension as causes of their LV systolic dysfunction.

In a similar study conducted by the German investigators in 37 patients with isolated LV diastolic dysfunction, 35 had endomyocardial biopsies that proved positive for cardiotropic viral genomes. Parvovirus B19 was present in 31 of the 35.

In an observational study soon to be published, Dr. Pauschinger and colleagues prospectively followed a group of patients with myocardial viral infection and dilated cardiomyopathy. Those who experienced spontaneous elimination of their viral infections showed a significant increase in LV ejection fraction; those with persistent viral infection did not.

On the treatment front, a phase III randomized clinical trial of interferon-β in dilated cardiomyopathy patients with evidence of persistent viral infection is planned for the United States and Japan.

By year's end, results of the phase II randomized placebo-controlled study Betaferon in Chronic Viral Cardiomyopathy (BICC), a multicenter trial in which Dr. Pauschinger was an investigator, should be available.

BICC was an outgrowth of an earlier pilot study conducted by the Berlin group. The pilot study involved 22 consecutive patients with a 44-month history of symptomatic LV dysfunction and myocardial enterovirus or adenovirus infection proved by polymerase chain reaction. After 24 weeks of subcutaneous interferon-β at a dose of 18×10^6, all 22 patients were cleared of myocardial viral genomes. LV ejection fraction climbed from a baseline mean of 44% to 53%, with 15 of 22 patients demonstrating improved LV function (Circulation 2003;107:2793-8). ■

Left Atrial Function Index Gives Cardiovascular Outcome Clues

BY DIANA MAHONEY
New England Bureau

BOSTON — Left atrial function is a sensitive predictor of cardiovascular outcome in patients with stable coronary heart disease, a prospective study has shown.

Of 989 patients with heart disease recruited for the ongoing Heart and Soul Study at the San Francisco Veterans' Affairs Medical Center and the University of California at San Francisco, 8.5% of the 247 patients whose left atrial function index was in the lowest quartile had a cardiac event during the 1-year follow-up period, compared with 4% of the 742 whose indices fell into the upper three quartiles, reported Pamela Y.F. Hsu, M.D., in a poster presentation at the annual meeting of the American Society of Echocardiography.

"The association between a low index and cardiovascular outcomes persisted after adjusting for smoking, congestive heart failure, other comorbid illnesses, medication use, and left ventricular ejection fraction," said Dr. Hsu of the Mayo Clinic in Scottsdale, Ariz.

To determine the left atrial function index (LAFI), the investigators calculated the time-velocity integral for the left ventricular outflow tract, the left atrial end systolic volume (LAESV) and end diastolic volume (LAEDV), and the LAESV index measurements by using transthoracic echocardiography.

They also measured biplane left atrial volumes and calculated the left atrial ejection fraction (LAESV/LAEDV). The LAFI represents the left ventricular outflow tract time-velocity integral multiplied by the left atrial ejection fraction over the LAESV index, with the whole multiplied by 10 log 4.

Using logistic regression, the investigators evaluated the association between the lowest LAFI quartile and cardiovascular outcomes—including myocardial infarction, hospitalization for congestive heart failure, and coronary disease death—and adjusted for potential confounding variables.

In the lowest quartile, the age-adjusted odds ratio for having any cardiac event within 1 year was 3.3, while the specific odds ratios for myocardial infarction, heart failure, and coronary disease death were 3.3, 4.8, and 4.2, respectively.

In the multivariable adjusted model, the odds ratio for any cardiac event was 2.6 and the respective odds ratios for myocardial infarction, heart failure, and coronary disease death were 3.0, 3.3, and 2.2. All of the associations were statistically significant, Dr. Hsu said.

The findings indicate that the LAFI "is a simple, powerful, and clinically useful tool" for predicting 1-year cardiovascular outcomes in coronary heart disease patients, Dr. Hsu said.

It also adds to a growing body of evidence supporting the importance of left atrial function in determining cardiovascular prognoses, she added. ■

Carotid Plaque Burden Is Shown To Predict Cardiovascular Death

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Plaques in the carotid arteries were associated with an increased risk of death due to cardiovascular disease in a prospective 10-year study of 2,651 people chosen randomly from the general population.

Previous data have shown a significant association between carotid artery plaque burden and risk of cardiovascular death in people with known cardiovascular disease. The current study shows that carotid artery plaque burden provides independent prognostic information in the general population as well, Marina Krintel Christensen, M.D., said in a poster presentation at the annual meeting of the American Society of Hypertension.

The investigators examined the carotid arteries of apparently healthy people aged 41, 51, 61, or 71 years in 1993 and 1994 by using B-mode ultrasound. Ten years later, the investigators followed up by recording the number and causes of death.

At baseline, they found carotid artery plaques in 724 subjects—423 men and 301 women, said Dr. Christensen and her associates at Glostrup (Denmark) University Hospital.

The presence of plaques was linked to a 57% increase in the risk of cardiovascular death over the 10-year period after adjustment for conventional risk factors for cardiovascular death including age, cholesterol levels, smoking status, fasting glucose levels, gender, mean arterial pressure, pulse pressure, and prior cardiovascular disease.

Gender and smoking status did not alter the relationship between carotid artery plaques and cardiovascular death.

The study suggests that carotid artery plaques are another risk factor that might be assessed in deciding whether and how aggressively to treat patients with high blood pressure, Dr. Christensen said in an interview during the poster session. Conventional risk factors such as age, cholesterol, and smoking status provide plenty of information to guide management in most patients, but carotid ultrasound might be worth the added expense to look for plaques in borderline patients if physicians are having difficulty deciding on antihypertensive therapy, she said.

After 10 years, 3% of people with no plaques at baseline had died of cardiovascular causes, compared with 7% of people with one or two plaques and 19% of people with more than two plaques.

In men, the cardiovascular mortality rate at 10 years was 4% in those with no plaques at baseline, 7% in those with up to two plaques, and 25% in those with more than two plaques. In women, cardiovascular death rates were 1% with no plaques, 6% with up to two plaques, and 11% with more than two plaques. ■