

Antibody May Raise Heart Attack, Stroke Risks

Lupus anticoagulant said to be 'a major risk factor for arterial thrombotic disease' in young women.

BY JANE SALODOF MACNEIL

The presence of lupus anticoagulant, an antiphospholipid antibody, increased the risk of stroke by 40-fold and of heart attack by 5-fold in a Dutch study that compared young women who had survived these conditions with a healthy control group.

Smoking and use of oral contraceptives drove the risk of these arterial thrombosis events yet higher in the survivors who tested positive for lupus anticoagulant, according to a report posted online in the *Lancet Neurology*.

"Our data suggest that lupus anticoagulant is a major risk factor for arterial thrombotic disease. . . . Screening for lupus anticoagulant in young women with ischemic stroke seems to be warranted," wrote Rolf T. Urbanus, Ph.D., of University Medical Centre Utrecht (the Netherlands) and associates (*Lancet Neurol.* 2009 [doi:10.1016/S1474-4422(09)70239-X]).

Most important is the elucidation that young women with antiphospholipid antibodies should be informed "about the serious risks of cigarette smoking and use of oral contraceptives," according to an accompanying editorial by Dr. Kathryn F. Kirchoff-Torres and Dr. Steven R. Levine, both of the Stroke Center at Mount Sinai School of Medicine, New York (*Lancet Neurol.* 2009 [DOI:10.1016/S1474-4422(09)70263-7]).

Lupus anticoagulant is one of several antibodies implicated in antiphospholipid syndrome, an autoimmune disease that is an acquired risk factor for arteri-

al thrombosis. The syndrome is known to be more prevalent in young women. Diagnosis is based on thrombotic events and repeated positive tests for antiphospholipid antibodies, such as those against the phospholipid cardiolipin or the plasma protein beta₂-glycoprotein I, as well as the lupus anticoagulant.

For this analysis, the investigators drew participants from the multicenter RATIO (Risk of Arterial Thrombosis In relation to Oral contraceptives) study, which enrolled women aged 49 years and younger who had been hospitalized with their first ischemic stroke or MI between January 1990 and October 1995. Dr. Urbanus and colleagues also included 50 women who presented with ischemic stroke between 1996 and 2001 at the Utrecht center.

All told, the population comprised 175 women with ischemic stroke, 203 women with MI, and 628 healthy controls who were identified by random-digit dialing of telephone numbers and invited to participate. The average age was 42 years for the MI group and 39 years for the stroke patients and healthy controls.

More than a quarter of the MI and stroke groups but only 6% of the controls had hypertension. Use of oral contraceptives was higher in the stroke group (53%) than in the MI (39%) and control (33%) groups. The MI patients were most likely to be current smokers (82%), followed by those in the stroke (60%) and control (42%) groups.

Analysis of blood samples found lupus anticoagulant in 6 (3%) MI patients and

30 (17%) stroke patients, but only 4 (0.6%) healthy controls. Comparing the women with lupus anticoagulant to those who did not have the antibody produced odds ratios of 5.3 (95% confidence interval, 1.4-20.8) for MI and 43.1 (12.2-152.0) for ischemic stroke, Dr. Urbanus and his associates reported.

In women who used oral contraceptives and carried the lupus anticoagulant risk factor, the odds ratios became 21.6 (1.9-242.0) for MI and 201.0 (22.1-1,828.0) for stroke. Similarly, smoking increased the odds of MI to 337 (6.0-189.0) and of stroke to 87.0 (14.5-523.0), the investigators said.

The authors did not find increased risks with anticardiolipin or antiprothrombin antibodies. Presence of beta₂-glycoprotein I antibodies doubled the risk of stroke (OR 2.3) but did not add to the risk of MI. In women with lupus anticoagulant, the presence of a second antiphospholipid antibody did not increase risk.

The investigators noted that the study had limitations, and the editorial emphasizes that "a few methodological issues . . . deserve attention." The odds ratios are much higher than previously reported by other researchers who found increased risk with antiphospholipid antibodies (*Stroke* 2002;33:2396-400 and *Stroke* 2004;35:736-41). This may have been a reflection of the low prevalence of lupus anticoagulant in the healthy controls compared with historic data.

Other issues include the timing of the testing for antiphospholipid antibodies, which occurred as long as 10 years after the thrombotic events. "Some aPL [antiphospholipid antibody]-positive patients in the study by Urbanus and col-

leagues might not, therefore, have been aPL-positive at the time of the thrombotic event, and vice versa, making any claims of causality speculative," wrote Dr. Kirchoff-Torres, a senior vascular neurology fellow and postdoctoral researcher, and Dr. Levine, professor of neurology and director of the cerebrovascular research training program at Mount Sinai.

Dr. Kirchoff-Torres also cited the wide confidence intervals and noted during an interview that the original study on oral contraceptive risk was not designed to look at antiphospholipid antibodies. In addition, there is no information on young women with fatal MIs or fatal ischemic strokes. It also is not reported how many women with stroke or MI had only the lupus anticoagulant as a risk factor and nothing else.

The data do not justify screening all women being prescribed oral contraceptives at this time, she said, calling such a wide generalization of results premature. Testing might be appropriate, however, in women who have lupus, a personal or family history of autoimmune or thrombotic disease, or abnormalities in normal blood work, she said, suggesting low platelet or elevated activated partial thromboplastin time (aPTT) could be cause for concern.

The study "definitely raises awareness of the importance of taking a careful history and cautioning any women on oral contraceptives not to smoke," Dr. Kirchoff-Torres said.

The Netherlands Heart Foundation and Leducq Foundation supported the study, and the U.S. National Institutes of Health grants supported the editorial. The authors said that they had no conflicts of interest. ■

Regional Initiative Speeds Reperfusion Treatment Time

BY HEIDI SPLETE

BOSTON — A statewide program to get patients with severe heart attacks to hospitals faster significantly reduced disparities in reperfusion treatment times for women and elderly patients, based on a study of more than 900 patients in North Carolina.

Disparities exist in the use and timing of reperfusion therapy for ST-segment elevation myocardial infarction (STEMI), Dr. Seth Glickman said at the annual meeting of the American College of Emergency Physicians. "Recent national efforts have focused on the regionalization of STEMI care to reduce time to reperfusion," he noted.

The impact of regionalization on STEMI care for hospitals that don't provide percutaneous coronary intervention (PCI) is unknown, but studies have shown that middle-aged white patients are more likely to benefit than other demographic groups, said Dr. Glickman of the University of North Carolina, Chapel Hill.

In the study, Dr. Glickman and colleagues reviewed data from 923 patients treated at 55 hospitals without PCI services during the Reperfusion of Acute Myocardial Infarction of North Carolina Emergency Departments (RACE) initiative from 2005 to 2007.

The RACE program divided the state of North Carolina into five regions, with at least one PCI-capable

hospital in each region. The investigators compared 518 patients treated prior to the RACE initiative and 405 patients treated after the initiative. The patients ranged in age from 51 to 73 years.

Overall, median door-to-ECG times before and after RACE dropped from 10 minutes to 8 minutes in men, and from 15 minutes to 8 minutes in women.

The median door in/door out times for men dropped from 85 minutes to 55 minutes, and times for women dropped from 124 minutes to 65 minutes. Median door-to-needle times decreased from 33 minutes to 29 minutes in men, and from 42 minutes to 30 minutes for women. Before the intervention, women's times were significantly longer than men's. After the intervention, however, the times for both genders were nearly identical, Dr. Glickman noted.

There was a slight increase in the use of prehospital ECG as part of the RACE initiative, he added.

The median door-to-ECG time for patients younger than 70 years dropped from 10 minutes to 7 minutes before and after RACE, and the time for patients 70 and older dropped from 18 minutes to 9 minutes.

Median door in/door out times for patients younger than 70 years dropped from 81 minutes to 48 minutes, and times for patients 70 years and older dropped from 117 minutes to 76 minutes. Median door-to-needle times for patients younger than 70 years dropped from 32 minutes to 28 minutes, and from 48 minutes to 36 minutes for patients aged 70 years and older.

The results were limited by a lack of regional comparators during the study period, but the findings showed a reduction in baseline care disparities between men and women, Dr. Glickman said. Disparities persist in the

elderly, despite improvements after the RACE initiative, Dr. Glickman noted, which suggests the need for additional study and intervention focused on older patients.

The research was supported by the American Heart Association, the Robert Wood Johnson Foundation, and Blue Cross Blue Shield of North Carolina. For more details on RACE, visit www.nccacc.org/race.html. ■

Overall, median door-to-ECG times before and after North Carolina's RACE program dropped from 10 minutes to 8 minutes in men, and from 15 minutes to 8 minutes in women.

☞ To watch a video interview with Dr. Glickman, go to www.youtube.com/user/FamilyPracticeNews#p/a/u/0/oZ_aXx-8kqU.