

FOR RELEASE:  
3 p.m. CT/4 p.m. ET  
Monday, June 16, 2008



CONTACT: For journal copies only,  
please call: (214) 706-1396  
For other information, call:  
Karen Astle: (214) 706-1392  
Bridgette McNeill: (214) 706-1135  
Julie Del Barto (broadcast): (214) 706-1330

*Journal study highlights:*

- *Researchers found a strong association between insulin resistance and peripheral arterial disease, independent of the impact of diabetes and other cardiovascular risk factors.*
- *Odds of peripheral arterial disease increased by about 25 percent for each quartile of insulin resistance.*
- *People in the highest quartile of insulin resistance had nearly twice as much peripheral arterial disease.*

**American Heart Association rapid access journal report:**

**Insulin resistance linked to peripheral artery disease**

DALLAS, June 17 — For the first time, a strong association has been found between insulin resistance and peripheral arterial disease (PAD), a risk factor for heart attacks and stroke, researchers reported in *Circulation: Journal of the American Heart Association*. People with the highest levels of insulin resistance had twice as much PAD, regardless of other risk factors including diabetes.

The greatest statistical significance was among those with the highest levels of insulin resistance, said Reena L. Pande, M.D., lead author of the study and a researcher in the Brigham and Women's Hospital cardiovascular division in Boston, Mass.

Researchers analyzed data from 3,242 adults enrolled in the National Health and Nutrition Examination Survey 1999–2004. The nationally representative sample population study included data on arterial pressure in each person's ankle. Comparing the ankle and arm pressures (the ankle brachial index) can indicate restricted blood flow or PAD. Blood levels of c-reactive protein (CRP) and fasting insulin and glucose were also measured. Researchers compared PAD incidence and insulin sensitivity using a model of insulin resistance (HOMA-IR), a simple test derived from fasting glucose and insulin values.

The prevalence of PAD was 5.5 percent, and insulin resistance was independently associated with PAD after adjusting for age, gender, race/ethnicity, hypertension, hyperlipidemia, smoking, body mass index, chronic kidney disease and CRP, researchers said.

“We found a roughly 25 percent increase in risk of PAD for each one-quartile increase in HOMA-IR, a finding that remained consistent despite adjustment for typical atherosclerotic risk factors related to insulin resistance such as body mass index and glycemic control,” Pande said.

“Even after excluding subjects with diabetes, there were graded increases in PAD prevalence with increasing HOMA-IR quartiles, supporting prior observations that PAD is associated with the metabolic syndrome and glucose intolerance, both surrogate markers of insulin resistance.

“Further, the association persisted after adjustment for diabetes or hemoglobin A1c, another measure of blood sugar control, indicating that insulin resistance may play a role in PAD along the entire spectrum of insulin resistance, quite distinct from the impact of diabetes,” he said.

Insulin resistance contributes significantly to the development of diabetes, a known risk factor for PAD, and has been implicated in the development of atherosclerosis. But the role of insulin resistance in PAD is not well established, researchers noted.

“For doctors and patients, our study highlights the role of insulin resistance in PAD and gives us a snapshot of the association between the two diseases,” Pande said. “For this to play out, however, we still need prospective studies that follow over time insulin-resistant patients to determine their risk of developing PAD.”

Elevated C-reactive protein (CRP >3mg/L), an inflammation marker, was also strongly associated with PAD. But after grouping subjects based on their level of average insulin resistance, researchers found that CRP>3 was no longer significantly associated with PAD in subjects with insulin resistance.

“The association between heart disease and higher CRP levels has come predominantly from studies in healthy individuals,” Pande said. “We wanted to see if this was true in those with insulin resistance, too.”

Instead, they found that insulin resistance somehow modifies the association between inflammation and PAD. Nonetheless, the data establishes that insulin resistance plays some role in PAD, and highlights the relative importance of inflammation in patients with and without insulin resistance, Pande said.

PAD occurs when arteries in the legs become narrowed or clogged with fatty deposits, reducing blood flow to the legs. PAD affects about 8 million Americans and is associated with significant disease and death, according to the American Heart Association’s Heart Disease and Stroke Statistics – 2008 Update.

“PAD becomes more common as one gets older, and by age 65, about 12 to 20 percent of the population has it,” Pande said. “Diagnosis is critical, as people with PAD have a four-to-five times higher risk of heart attack or stroke.”

Co-authors are: Todd S. Perlstein M.D., M.M.Sc.; Joshua A. Beckman M.D., M.Sc.; and Mark A. Creager M.D.

The National Heart, Lung, and Blood Institute funded the study. Disclosures for individual authors are available on the manuscript.

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**Editor’s Note:** The American Heart Association is a member of the National Peripheral Arterial Disease Coalition, an alliance of approximately 50 leading health organizations, vascular professional societies and government agencies united to raise public and health awareness about PAD. For more information on the risk factors, symptoms and treatment of PAD, visit [americanheart.org/pad](http://americanheart.org/pad) and [padcoalition.org](http://padcoalition.org).

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NR08 – 1069 (Circ/Pande)

**Contact information:** Dr. Pande can be reached at (617) 732-5267 or [rpande@partners.org](mailto:rpande@partners.org).  
(Please do not publish contact information.)