

## Antiplatelet Therapy

# A Prospective, Blinded Determination of the Natural History of Aspirin Resistance Among Stable Patients With Cardiovascular Disease

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### **OBJECTIVES BACKGROUND**

This study was designed to determine if aspirin resistance is associated with clinical events. Aspirin resistance, defined by platelet function testing and presumed clinical unresponsiveness to aspirin, has been previously reported by our group and others. However, little information exists linking the laboratory documentation of aspirin resistance and long-term clinical events.

### **METHODS**

We prospectively enrolled 326 stable cardiovascular patients from 1997 to 1999 on aspirin (325 mg/day for  $\geq 7$  days) and no other antiplatelet agents. We tested for aspirin sensitivity by optical platelet aggregation using adenosine diphosphate (ADP) and arachidonic acid (AA). The primary outcome was the composite of death, myocardial infarction (MI), or cerebrovascular accident (CVA). Mean follow-up was  $679 \pm 185$  days. Aspirin resistance was defined as a mean aggregation of  $\geq 70\%$  with  $10 \mu\text{M}$  ADP and  $\geq 20\%$  with  $0.5 \text{ mg/ml}$  AA.

### **RESULTS**

Of the patients studied, 17 (5.2%) were aspirin resistant and 309 (94.8%) were not aspirin resistant. During follow-up, aspirin resistance was associated with an increased risk of death, MI, or CVA compared with patients who were aspirin sensitive (24% vs. 10%, hazard ratio [HR] 3.12, 95% confidence interval [CI] 1.10 to 8.90,  $p = 0.03$ ). Stratified multivariate analyses identified platelet count, age, heart failure, and aspirin resistance to be independently associated with major adverse long-term outcomes (HR for aspirin resistance 4.14, 95% CI 1.42 to 12.06,  $p = 0.009$ ).

### **CONCLUSIONS**

This study demonstrates the natural history of aspirin resistance in a stable population, documenting a greater than threefold increase in the risk of major adverse events associated with aspirin resistance. (J Am Coll Cardiol 2003;41:961-5) © 2003 by the American College of Cardiology Foundation