Using Aspirin Resistance to Predict Long-Term Cardiovascular Outcomes

Chen WH, Cheng X, Lee PY, et al. Aspirin resistance and adverse clinical events in patients with coronary artery disease. Am J Med 2007;120:631–5.

Study Overview

Objective. To determine whether patients with aspirin resistance have higher rates of cardiovascular complications compared with patients without aspirin resistance.

Design. Prospective cohort study.

Setting and participants. 468 patients with stable coronary artery disease (CAD) who used 80 to 325 mg of aspirin for ≥ 4 weeks. Patients were tested for aspirin resistance, defined as Aspirin Reaction Unit ≥ 550, using a point-of-care assay.

Main outcome measures. The primary endpoint was a composite of cardiovascular death, myocardial infarction (MI), stroke, transient ischemic attack, and unstable angina requiring hospitalization.

Main results. Aspirin resistance was found in 128 (27.4%) patients and was associated with increased age, female gender, renal insufficiency, a lower hemoglobin level, and a lower prescribed dose of aspirin. After a mean follow-up of 379 days, aspirin-resistant patients were at dramatically increased risk of the primary outcome compared with aspirin-sensitive patients (15.6% vs. 5.3%; hazard ratio [HR], 3.12 [95% confidence interval {CI}, 1.65–5.91]; $P < 0.001$). Aspirin resistance, diabetes, prior MI, and a low hemoglobin level were independently associated with major adverse long-term outcomes based on Cox proportional hazard regression modeling (HR for aspirin resistance, 2.46 [95% CI, 1.27–4.76]; $P = 0.007$).

Conclusion. Aspirin resistance is an independent predictor of increased risk of adverse clinical outcomes in patients with stable CAD. Prospective randomized trials are needed to determine whether patients with aspirin resistance need additional antiplatelet therapy.

Commentary

Cardiovascular disease (CVD) is the leading killer of U.S. adults, and antiplatelet therapy, especially aspirin, is a cornerstone of therapy for patients with CVD. Aspirin is cheap and generally effective, reducing the risk of ischemic events by 22% [1]. Unfortunately, aspirin is not uniformly effective, and studies have shown that up to 45% of patients do not receive an adequate antiplatelet response from aspirin therapy [2–6]. Even among patients who adequately respond to aspirin's effects, 10% to 20% appear to develop recurrent vascular events [7]. However, it is still unclear whether aspirin resistance (ie, failure to receive an adequate antiplatelet response) contributes to vascular events in patients with CVD. This study by Chen et al begins to fill this gap.

Chen et al examined patients with established CVD and determined the rate of aspirin resistance using a point-of-care assay (VerifyNow Aspirin, Accumetrics Inc, San Diego, CA). Aspirin-resistant patients had two- to threefold higher rate of cardiovascular outcomes than aspirin-sensitive patients. There are several limitations to this analysis. First, the findings could be explained by other unmeasured confounders. For instance, aspirin-resistant patients were older and had higher rates of renal disease and anemia, suggesting that this was a sicker population. It is possible that "aspirin resistance" is a marker for more severe CVD in ways that were not measured (and therefore not adjusted for) by the authors. Stratifying patients by types of CVD (ie, prior MI) would help by allowing us to examine patients with similar baseline risk.

Another important limitation is that the study does not provide information on how to treat patients with aspirin resistance. Although this point-of-care test seems to identify a higher-risk subgroup, it is unknown whether patients should continue aspirin therapy or be switched to another antiplatelet agent. Because this information is lacking, it is difficult to know whether to test patients for aspirin resistance.

Applications for Clinical Practice

Antiplatelet therapy is a cornerstone of treating patients with CVD. It is critically important to understand which patients with CVD are likely to be unresponsive to first-line therapy (aspirin). The study by Chen and colleagues sheds light on identifying this high-risk group. However, given the limitations of their analysis, the exact level of increased risk for

aspirin resistance is not well understood. Until we know how to treat patients identified as having aspirin resistance, testing patients for aspirin resistance is likely of little value.

—Review by Ashish K. Jha, MD, MPH

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