

# Abstract

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## Incidence and clinical impact of dual nonresponsiveness to aspirin and clopidogrel in patients with drug-eluting stents.

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**OBJECTIVES:** This study sought to determine the incidence of aspirin nonresponsiveness in addition to clopidogrel nonresponsiveness and whether this association identifies patients at an increased risk of drug-eluting stent (DES) thrombosis.

**BACKGROUND:** Nonresponsiveness to clopidogrel is a predictor of DES thrombosis. No prospective data exist about the possible association of dual nonresponsiveness to clopidogrel and aspirin with DES thrombosis.

**METHODS:** Platelet function was assessed after a loading dose of 600 mg clopidogrel in 746 patients who had successful DES implantation followed by 6-month dual-antiplatelet therapy. Platelet reactivity was assessed by light transmittance aggregometry using adenosine 5'-diphosphate, arachidonic acid, and collagen. The primary end point was definite/probable DES thrombosis at 6 months. The secondary end point was the composite of cardiac mortality and DES thrombosis.

**RESULTS:** The incidence of dual nonresponsiveness to aspirin and clopidogrel was 6%. Definite/probable DES thrombosis was significantly higher in dual aspirin and clopidogrel nonresponders (11.1%) than in clopidogrel and aspirin responders (2.1%,  $p < 0.001$ ), isolated clopidogrel nonresponders (2.2%,  $p < 0.05$ ), or aspirin nonresponders (2.3%,  $p < 0.05$ ). The incidence of the secondary end point was 4.4% in isolated clopidogrel nonresponders, 2.3% in isolated aspirin nonresponders, and 13.3% in dual aspirin and clopidogrel nonresponders. **Dual clopidogrel and aspirin nonresponsiveness was an independent predictor of DES thrombosis** (hazard ratio: 3.18, 95% confidence interval: 1.14 to 8.83,  $p = 0.027$ ) and the composite of cardiac mortality and DES thrombosis (hazard ratio: 2.94, 95% confidence interval: 1.16 to 7.41,  $p = 0.022$ ).

**CONCLUSIONS:** **Dual nonresponsiveness to aspirin and clopidogrel is a relatively infrequent condition that identifies patients at a very high risk of DES thrombosis or death.**

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