

The ACTIVE Trial – Effect of clopidogrel added to aspirin in patients with atrial fibrillation

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Atrial fibrillation is a common cardiac condition, with higher incidence in elderly people. It often associates cardioembolic stroke. One of the principal directions of therapy is forethought oral anticoagulation with vitamin K antagonist. There is a large proportion of population in which oral anticoagulation is restricted and in whom aspirin alone does not protect against stroke. This study explores the possibility to add Clopidogrel to aspirin while comparing to aspirin alone in prevention of stroke .

7554 patients were enrolled in two arms, Clopidogrel 75 mg/day + aspirin in one arm, oral anticoagulation alone in the other. The follow-up was conducted for 3.6 years. The population's age was 71 years old, 58.1% men, with a mean CHADS₂ score of 2.0. The primary study outcome was any major vascular event (stroke, non-central nervous system systemic embolism, myocardial infarction, or death from vascular causes). The most important secondary outcome was stroke. Other secondary outcomes were the other individual components of the primary outcome (non-central nervous system systemic embolism, myocardial infarction, and death from vascular causes) and the

composite of the primary outcome and major hemorrhage.

The primary end point occurred in 832 patients receiving clopidogrel (6.8% per year) as compared with 924 patients receiving placebo (7.6% per year) relative risk reduction 11%, $P=0.01$. The reduction in the risk of major vascular events in the clopidogrel arm was mainly due to a reduction in stroke's incidence. Stroke occurred in 296 patients in the clopidogrel arm (2.4% per year) and 408 patients in the placebo (3.3% per year) relative risk reduction 27%, $P<0.001$. Myocardial infarction occurred in 90 patients receiving clopidogrel (0.7% per year) and in 115 patients receiving placebo (0.9% per year), relative risk reduction 22% $P=0.08$. The major burden was the increase in major bleeding, occurred in 251 patients receiving clopidogrel (2.0% per year) and in 162 patients receiving placebo (1.3% per year) relative risk increase 57%, $P<0.001$.

Conclusion

In patients with atrial fibrillation for whom vitamin K-antagonist therapy was unsuitable, the addition of clopidogrel to aspirin reduced the risk of major vascular events, especially stroke with an increased the risk of major hemorrhage. \square

Comment on the paper:

Connolly SJ, Pogue J, et al – Effect of Clopidogrel Added to Aspirin in Patients with Atrial Fibrillation, *NEJM*, 360 (2009); 20:2066-2078