
To the Editor:

With interest we read the article of Medi et al about stroke risk and antithrombotic strategies in atrial fibrillation. We have several comments on the emerging therapies to prevent stroke that are mentioned in the article:

1. Achieving good control of international normalized ratio (INR) values is a matter of concern in patients undergoing therapy with vitamin K antagonists. A subanalysis of the ACTIVE trial has shown that considerable national differences exist in the quality of oral anticoagulation (OAC). Most probably, these differences are caused by organization of the health care system and by differences in the reimbursement of physicians and institutions who take care of patients on vitamin K antagonists. Thus, an improvement in the quality of OAC is a matter of public health, and initiatives should be directed toward these institutions on national and international levels.

INR self-monitoring improves the quality of OAC. Patients capable of self-monitoring therapy with vitamin K antagonists have fewer thromboembolic events, a higher proportion of INR values within the therapeutic range, and lower mortality than do patients under conventional monitoring of OAC. Instead of only complaining that INR values are frequently outside the therapeutic range, atrial fibrillation patients should be encouraged to perform INR self-monitoring.

2. Whether dabigatran, rivaroxaban, or apixaban will solve the problems associated with vitamin K antagonists is uncertain. These drugs are substrates of the intestinal P-glycoprotein transport system. A variety of drugs and food components affect the P-glycoprotein system, thus influencing serum levels of these drugs. It has been shown that P-glycoprotein-affecting drugs are prescribed to 42% of hospitalized atrial fibrillation patients. The relevance of these drug and food interactions are unknown. There is an urgent need to collect data on this issue, a task that will be impeded by the lack of easily available laboratory testing of antithrombotic effects.

Furthermore, the long-term effects of thrombin-generation inhibition are unknown. Thrombin plays an important role in infection, immune response, angiogenesis, tumor growth, and endothelial function. Reported adverse effects of new antithrombotic drugs were restricted to hemorrhagic, gastrointestinal, and vascular events; however, they did not consider conditions like cancer, sepsis, or infection. Furthermore, in the RE-LY study, dabigatran was discontinued in 21% of the patients after 2 years. Which alternative therapy should these patients receive?

3. Occlusion of the left atrial appendage (LAA), as stressed by the authors, has a high procedural complication rate and an uncertain long-term effect. Because of the high compliance of the LAA myocardium, leaks between the wall and the occluder may develop months, or even years, after occluder implantation, and may be a new source of embolism. Furthermore, the LAA protects the left ventricle from pressure and volume overload. The long-term consequences of LAA-occlusion or resection on cardiac function and on the development of heart failure are largely unknown.

From these considerations, we conclude that stroke prevention in atrial fibrillation should be directed primarily toward improving the quality of standard OAC by enhancing INR self-monitoring as well as initiatives in public health. Whether new antithrombotic drugs are useful for stroke prevention outside randomized clinical trials is still uncertain. There is an urgent need to assess the relevance of drug and food interactions and potential adverse effects of these drugs. LAA occlusion is an experimental procedure of yet unproven benefit, carries potential risk, and thus should not be performed until all open questions have been answered.

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