

Self-testing of International Normalized Ratio

Maria Cristina CONSTANTINESCU, MD, PhD

Cardiology Department, Emergency University Hospital, Bucharest, Romania



Thromboembolic complications in patients with atrial fibrillation or mechanical heart valve(s) are dramatically reduced by anticoagulation, but in clinical practice oral anticoagulation is typically underused and/or the quality of anticoagulation management is poor, resulting in increased complications. The anticoagulation clinics may provide a high-quality management, but the patients have to travel to a specific location, limiting the frequency or even the access to anticoagulation treatment. Frequent home self-monitoring of the International Normalized Ratio (INR) by means of a point-of-care INR device is a promising strategy for improving outcomes and allows INR values that are outside the target range to be identified and addressed more quickly.

This trial was designed to test the hypothesis that weekly home INR testing would be superior to monthly clinic INR testing for improving the aggregate outcome of stroke, major bleeding or death. It was a prospective, randomized, nonblinded trial, in which 2922 patients who were taking warfarin because of mechanical heart valves or atrial fibrillation were randomly assigned to either weekly self-testing INR at home, or monthly high-quality testing in a clinic. The study took place from August 2003 through May 2008; enrollment took 2.75 years to complete the randomization process; the mean follow-up period was 3 years. Data were collected at 28 medical centers with anticoagulation clinics. Eligible patients had atrial fibrillation, a mechanical heart valve, or both, and needed to be deemed competent in perform-

ing self-tests using a special system, on the basis of training by the study staff.

The primary end point was the time to a first major event (stroke, major bleeding episode or death). Prespecified secondary end points included time within the INR target range, calculated on the basis of linear interpolation; patient satisfaction with anticoagulation, measured with the Duke Anticoagulation Satisfaction Scale (DASS); and quality of life, measured with the Health Utilities Index Mark.

Regarding the time to the first primary event, the difference between the two study groups was not significant, even after adjustment for duration of anticoagulation, presence or absence of a mechanical heart valve, and the interaction of these two factors, as well as for age. No significant difference was found for death, major bleeding episode with death as a competing risk, or stroke with death as a competing risk. The time to the first primary event also did not differ significantly between the two study groups in any of the subgroups examined including two prespecified subgroups (indication for warfarin, mechanical heart valve vs. atrial fibrillation without such a valve; duration of anticoagulation therapy, <3 months vs. \geq 3 months).

During the period of the trial, the percentage of time during which the INR was within the therapeutic range was modestly higher in the self-testing group than in the clinic-testing group ($p < 0.001$). At 2 years (the minimum duration of follow-up), patient satisfaction with anticoagulation was greater in the self-testing group than in the clinic-testing group ($p = 0.002$).

and the quality of life was considered to be better ($p < 0.001$). Costs were higher in the self-testing group but not significantly different from those in the clinic-testing group. The rate of loss to follow-up was the same in the two study groups, as was the percentage of patients who discontinued warfarin therapy. A significantly higher percentage of patients in the self-testing group reported minor bleeding episodes. No patient reported an adverse event as a result of physical interaction with the testing device.

The authors discuss that it can be ruled out with a high degree of confidence any important negative effect of self-testing on the primary end point. Furthermore, to a modest extent, home monitoring did improve some secondary outcomes (time in target INR range, general quality of life, and patient satisfaction with anticoagulation therapy, although the lack of blinding may have affected the latter two results). Although weekly self-testing did not reduce primary events to the extent suggested by

the results of earlier studies, the findings may be useful in considering whether to initiate anticoagulation for a specific patient. The time to the therapeutic INR range was moderately better for the patients in the self-testing group than for those in the clinic-testing group. Although this result did not translate into substantial reductions in event rates, it may offer some assurance to clinicians who are concerned that with self-testing the INR might not be properly monitored.

The authors conclude that the results of their study did not establish the superiority of self-testing over high-quality clinic testing in preventing major clinical outcomes, but did provide evidence of modest improvements in time within the therapeutic INR range, patient satisfaction with anticoagulation therapy, and quality of life, recommending that self-testing may be considered for patients whose access to high-quality anticoagulation care is limited.



Comment on a paper:

D. B. Matchar, A. Jacobson, R. Dolor, et al. – Effect of Home Testing of International Normalized Ratio on Clinical Events *N Engl J Med* 2010;363:1608-20.