Also the very elderly benefit from warfarin in atrial fibrillation

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Warfarin therapy is the cornerstone in the prevention of thromboembolism in patients with atrial fibrillation. It reduces the risk of stroke by two thirds in comparison with no anticoagulation.¹ A weak alternative to warfarin is aspirin, which is also effective over placebo in the prevention of stroke in atrial fibrillation.¹ Aspirin is safer than warfarin in general use. The incidence of atrial fibrillation sharply increases with age, but also the risk of bleeding from warfarin shows the same pattern.² Many physicians are reluctant to prescribe warfarin to the very elderly patient with atrial fibrillation because of the risk of bleeding, and many are convinced that aspirin is a wise and acceptable alternative. This was established in a Dutch trial in the primary care of patients with atrial fibrillation showing equal efficacy of warfarin and aspirin.³ However, comparative data in the very elderly (over 75 years) are rather scarce.⁴ Therefore, the recently published BAFTA (Birmingham Atrial Fibrillation Treatment of the Aged) trial was very welcome.

In BAFTA 973 patients over the age of 75 with atrial fibrillation were randomised to warfarin (target INR 2-3), or aspirin 75 mg daily.⁵ Primary endpoint (fatal or disabling stroke, or clinically significant arterial embolism) was 1.8% / year with warfarin vs. 3.8% / year with aspirin (relative risk 0.48, 95% CI 0.28-0.80, $p=0.003$). The number of the very elderly to treat to prevent one endpoint per year was 50. Major bleeding was similar amongst the two treatment groups including the risk of intracranial haemorrhage.

This is the first randomised trial specifically in the aged population with atrial fibrillation comparing warfarin to aspirin. It clearly shows a benefit of warfarin over

aspirin with equal treatment risk. These data must be reassuring for physicians taking care of the elderly with atrial fibrillation and prescribing them warfarin. However, some remarks should be made. In the first place 40% of the patients were on warfarin before randomisation, which means that in nearly half of the patients allocated to aspirin the warfarin was discontinued, which may be responsible for the higher rate of events in the aspirin group. Secondly, over 80% of the patients were on either aspirin or warfarin prior to randomisation and thus experienced with antithrombotic therapy. This may explain the low bleeding risk in the trial, especially in the patients who were exposed to warfarin after randomisation. Finally, the patients were recruited in primary care, which is clearly different from hospital cardiology care or outpatient cardiology clinics, where most of the patients are seen with first atrial fibrillation and many are naive to antithrombotic therapy. Clearly, this is not the population observed in BAFTA.

Should cardiologists switch all patients over 75 with known atrial fibrillation already on an antithrombotic strategy to warfarin in the absence of contraindications? The question can be answered positively, but again this is not the population seen in BAFTA. However, the post-hoc evidence from other trials is clear. Should cardiologists seeing elderly patients with first atrial fibrillation put them on warfarin right away? This is much more difficult to answer since there are no clear data collected specifically in the elderly. But, if there are no clear contraindications to warfarin (gastro-intestinal ulceration, dementia or syncopal attacks), warfarin is an excellent therapy for this group of patients although their bleeding risk will probably be higher than in BAFTA.⁶ If there is an expected lack of cooperation by the patient, aspirin can be a good alternative. Even in BAFTA the bleeding rate in the elderly was below 4% per year on aspirin with an acceptable risk of stroke.

Despite the good results with warfarin in BAFTA better anticoagulant medication should be sought for. The direct oral thrombin inhibitor ximelagatran is as

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effective as warfarin and reduces major bleeding,^{7,8} but the drug is associated with liver toxicity. Another direct oral thrombin blocker dabigatran is currently under evaluation in comparison with warfarin in a megatrial in atrial fibrillation. Finally, oral direct factor Xa blockers are currently available and are effective in deep vein thrombosis and pulmonary embolism.⁹ Both rivaroxaban and apixaban are also under trial for stroke prevention in atrial fibrillation. Needless to say that besides efficacy, bleeding is a major safety endpoint of these agents when compared with warfarin. ■

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