beneficial in terms of CV outcomes, but this was presumably confounded by the disadvantages of the atenolol-based regimen.

However, we did not focus on the variable predictability of HR because that was not the purpose of the study. We wanted to know whether having a higher baseline HR attenuated the superior effects on major CV events of the amlodipine-based compared with atenolol-based regimen. We could find no evidence of any such attenuation, and hence we believe that an increased baseline HR should not be an indication for preferential use of beta-blockade in hypertensive populations without coronary heart disease. Even if baseline HR had not predicted CV outcomes in the ASCOT study, we believe that the same conclusion should be drawn.

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Bleeding Risk on Warfarin Among Elderly Patients With Atrial Fibrillation

Poli et al. (1) observed different rates of major hemorrhage between patients younger than 80 years of age and 80 years of age and older. As discussed by the authors, these rates differed considerably from the rates of major hemorrhage observed among similarly aged cohorts by Hylek et al. (2). We want to highlight an important methodological issue in the authors' calculation of event rates. The authors state, “the overall exposure to warfarin for each patient was calculated in relation to aging, before and after his/her 80th birthday.” Thus, the authors allowed crossover of prevalent warfarin survivors from the younger cohort to the age ≥80 years inception cohort. At the time of enrollment, the baseline age ≥80 years cohort numbered 180 patients. Yet, in Table 1 of their article (1), the authors provide baseline characteristics for 327 patients in the age ≥80 years group. The 2 age inception cohorts are distinct and should contribute person-years exclusively to their baseline assignment. Given this methodological error, the rates of hemorrhage provided for the 2 inception cohorts are flawed. The reader is also unable to compare baseline characteristics between the younger and age ≥80 years inception cohorts because the authors permitted crossover of 157 patients. In addition, the observation period in the study by Hylek et al. (2) was intentionally truncated at 1 year to provide the first-year experience on warfarin. Calculation of adverse event rates over years tends to enrich the person-year denominator with “survivors” because bleeding rates are highest in the first 90 days of warfarin therapy. To accurately report rates of major hemorrhage among elderly individuals newly starting warfarin, the authors need to recalculate the bleeding rates according to baseline group assignment without crossover between the groups. To enable comparison of the 2 studies, events and person-years of observation would need to be restricted to the patients’ first year of therapy. The anticipated results would be higher bleeding rates and deterioration of time “in-range” as reported.

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We studied a cohort of atrial fibrillation patients on oral anticoagulant treatment for stroke prophylaxis (1). Our patients were routinely followed by the Anticoagulation Clinic of our institution with a median follow-up of 2.7 years, and some of them for as long as 13 years. At the beginning of warfarin treatment, the mean age of our cohort was 75 years; therefore, many patients reached the age of 80 years during follow-up. As stated in the article, we decided to analyze the occurrence of adverse events in relation to aging to evaluate whether aging itself could be correlated with an increase in bleeding risk that exceeds the advantages of stroke prevention. In reporting clinical characteristics of patients, we
referred to baseline patients’ conditions as well as for those who switched from the younger to the older cohort.

Drs. Cowan and Hylek question that we found a bleeding rate far lower than that reported by Hylek et al. (2), suggesting that we should calculate event rates by limiting the observation to the first year of treatment. We recalculated the event rates in patients age 80 years and older, limiting the observation to the first year. We observed 3 major bleeding events among this group of patients (observation period 143 patient-years; rate 2.1 per 100 patient-years) and 4 major bleeding events among patients younger than 80 years (observation period 497 patient-years; rate 0.8 per 100 patient-years); the incidence rate ratio was 2.6 (95% confidence interval: 0.4 to 15.0; \( p = 0.23 \)). The statistical power of these data for the detection of differences between the 2 groups was limited due to the small number of events recorded in the first year of treatment. However, we also found a low bleeding rate in the first year of treatment, confirming the conclusions of our study.

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