Atrial fibrillation (AF) remains a global health issue, carrying a great burden of stroke and systemic thromboembolism. In 2050, it is estimated that there will be 1 million AF patients in Japan. Previous randomized trials and meta-analyses have provided very solid evidence in regard to the efficacy of oral anticoagulants (OACs) such as warfarin, but a significant limitation of randomized trials has been the strict inclusion/exclusion criteria for selecting a representative population of patients. Therefore, in addition to well-controlled randomized trials, we need add-on data sets, “clinical registries”, to examine whether these data findings apply more broadly over the patient populations.

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To date, multiple AF registries have been published and include community, hospital, and emergency department settings. Of those we reported, the J-RHYTHM Registry, is a nationwide cohort study that enrolled 7,937 Japanese patients with AF (Figure 1). We found that nearly 90% of the patients were being treated with OACs because most of the patients were enrolled by cardiologists and electrophysiologists, and the major objective of this study was to determine the optimal anticoagulation levels for preventing thromboembolic and bleeding events.

The study by Akao et al in this issue of the Journal is timely for bettering our understanding of the actual situation of anti-thrombotic therapies and outcomes in the Japanese AF population (Figure 1). The Fushimi AF Registry is a community-based prospective survey of AF patients in an urban setting. The authors enrolled 3,282 AF patients and a 1-year follow-up was completed in 2,914 patients (a rate of nearly 90%). The

![Figure 1. Distribution of the CHADS2 score and rates of the anticoagulation therapy in the J-RHYTHM Registry and the Fushimi AF registry. CHADS2 comprises Chronic heart failure, Hypertension, Age ≥75 years, Diabetes, transient ischemic attack or Stroke. (Modified with permission from Atarashi H, et al and Akao M, et al.)*](image-url)
Risk-Treatment Paradox

Figure 2. The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. Categorization of physician-assigned risk and empirical risk of stroke (A) and bleeding (B). ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation. (Modified with permission from Steinberg BA, et al. 

strength of this registry was that most of the patients were enrolled by internal medicine/primary care physicians. The risk of stroke was assessed by CHADS2 score,\(^8\) overall, the mean CHADS2 score was 2.0, 55% of the patients were anticoagulated and 30% received an antiplatelet drug. They show a higher use of OACs in low-risk patients and relatively lower use of OACs in high-risk patients; this risk-treatment paradox continued after a 1-year follow-up.\(^9\) Although well-validated risk scores for stroke have been published, the real-world decisions on anticoagulation were quite different from the guidelines. The study provides other important data: an annual rate of stroke of 2.7% and mortality rate of 8%! We need to keep these data firmly in mind when managing AF patients.

Another important aspect of the study was the lack of effect between OAC treatment and outcome. We expected that OAC use would be associated with substantially lower rates of stroke and higher rates of major bleeding, but the rates of both stroke and major bleeding were similar, irrespective of OAC treatment. This result is probably related to under-dosage of OACs, in addition to under-usage of OACs. Of note, the authors found that the clinical factors that accounted for the physician’s decision to use anticoagulation were long-standing AF, stroke and heart failure, and there was a tendency to undervalue hypertension and diabetes, which make up CHADS2 as predictors of risk. Higher age (≥85 years) seemed to make physicians refrain from using anticoagulation. However, a 1-year follow-up was too short to draw any definite conclusions, and we would like the authors to present any bleeding risk data they may have, as well as the relationship between the CHADS2 score and rates of stroke.

Recently, a prospective registry of AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation registry, ORBIT-AF), enrolling approximately 10,000 patients from out-patient practices in the USA, was published.\(^8\) Those authors examined the factors related to the discrepancy between empirical stroke and bleeding risk, and the physician-assigned risk. They assessed the empirical stroke risk by CHADS2 score, and the bleeding risk by the ATRIA bleeding score.\(^9\) Separately, the physicians were asked to categorize their patients’ stroke and bleeding risks as low, intermediate or high. Overall, 72% of the patients were categorized as having a high-risk for stroke (CHADS2 score ≥2), but only 16% were assessed as having a high stroke risk by the physicians (Figure 2A). Further, 17% had a high ATRIA bleeding risk (≥5) but only 7% were considered so by physicians (Figure 2B). The study also showed that being frail\(^14\) and not living independently were strong factors associated with physician-empirical risk mismatch. These findings indicate the identification of patients perceived to be at risk of a stroke is often not based on evidence-based risk schemes, but rather on patient factors such as being frail or not living independently. We would like to know more about the accuracy between the evidence-based risk schemes and physician-assigned risk observed in this trial.

New OACs (NOAC) have been shown to potentially circumvent the many drawbacks of warfarin. Recent subanalyses of Phase 3 clinical trials in Asian patients consistently show that NOACs offer effective and safe options for stroke prevention when compared with warfarin.\(^15\) Despite this evidence, the Fushimi AF registry showed that the process of switching warfarin to NOACs is slow, and only 2.4% of patients were on dabigatran. The J-RHYTHM Registry 2 (UMIN-CTR 000007967) is now investigating the rate of switching of warfarin to NOACs and to improve the clinical guidelines for AF pharmacotherapy with warfarin and NOACs.

The Fushimi AF Registry\(^6\) demonstrated a significant risk-treatment paradox in the application of anticoagulation therapy in Japanese AF patients. There is still discord between the empirical validated scores that are used by the guidelines and physician-assigned risk. It seems clinicians have been slow to embrace the validity of the stroke or bleeding scores and better education might help with that. We look forward to the Fushimi AF Registry providing prospective data on how management strategies and patient outcomes evolve over time and thus bridge the gap between the guidelines and “real-world” clinical practice.
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References