Optimizing stroke prevention in atrial fibrillation: better adherence and compliance from patients and physicians leads to better outcomes

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For adequate stroke prevention, most patients with non-valvular atrial fibrillation (AF) would need oral anticoagulant therapy (OAC), with either vitamin-K antagonists (VKAs) or non-vitamin-K oral anticoagulants (NOACs).1 Once AF has been diagnosed (OAC), with either vitamin-K antagonists (VKAs) or non-vitamin-K oral anticoagulants (NOACs), the very first priority is effective stroke prevention based on guidelines, but physicians’ adherence to the guidelines for AF management is still suboptimal.4–7 Indeed, guideline adherent therapy is associated with better outcomes.5 An equally important step is the patient’s actual uptake of recommended therapy, as well as good adherence and persistence to long-term treatment, which makes the patient a key proactive part of the process.6

Current AF guidelines mandate discussion with patients about their values and treatment preferences.1 In order to reach an informed decision about treatment acceptance (or refusal), AF patients need to understand not only AF, but also the benefits and risks of recommended therapy. In a recent study, AF patients generally perceived moderate or severe stroke as equal to or worse than death, respectively, and were willing to experience 4.4 major bleeds just to prevent one stroke.7

Perhaps knowledge and understanding is crucial. Given the variable knowledge levels among AF patients,8 many educational interventions have been developed to improve their perception of AF and understanding of treatments implemented to prevent AF-related complications.9 Indeed, an active structured interaction between AF patients and responsible physicians or other healthcare providers may be crucial to achieve better outcomes in AF management.

In the current issue of Europace, Vrijens et al. nicely highlight a changing perception of relationships between patients and health providers, from a passive patient role to ‘simply follow the physician’s instructions’ (that is, patient compliance) to an active bilateral participation in the process termed medication adherence by which the patients take their medications as prescribed.10 As emphasized in this article, poor adherence to medications with a narrow therapeutic range such as the VKAs11 may result in serious consequences, including increased rates of both thromboembolism and bleeding. Compared with VKAs, the NOACs offer several advantages including fixed dosing and the lack of anticoagulant monitoring.12

At least in theory, this should facilitate medication adherence and persistence (that is, adherence during the whole treatment period).

However, before the transition to NOACs, a careful analysis of individual patient reasons for non-adherence to VKAs is warranted, since simply switching the patient from VKA to an NOAC might not necessarily result in better adherence. Given the shorter half-lives of NOACs, medication adherence to NOACs is even more important compared with VKAs.12,13

In this issue of Europace, Beyer-Westendorf et al. reported prospective results from the Dresden NOAC Registry on persistence with rivaroxaban in AF patients.14 These are some of the first ‘real-world’ prospective data on persistence to an NOAC therapy in daily care setting, generally showing a high overall persistence to rivaroxaban, with a discontinuation rate of ~15% in the first year of treatment and a declining discontinuation thereafter (with overall persistence of 81.5% during the median treatment duration of 544 days).

Could these results be attributed solely to once-daily dosing of rivaroxaban? The percentage of doses taken generally increases with less frequent dosing regimens.15 As Vrijens et al. rightly point out, once-daily dosing may require a near-perfect medication adherence to achieve the expected clinical results whilst twice-daily dosing, due

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to a greater continuity duration of drug action and a smaller peak-to-trough plasma concentration ratio, might appear more tolerant to occasional non-adherence—at least in theory. As estimated pharmacokinetically, a single missed once-daily dose equals to ~2–3 consecutively missed doses from a twice-daily drug regime.\textsuperscript{10}

What are the implications? Neither once-daily nor twice-daily dosing should be automatically considered as a better option for all AF patients, and only after a detailed assessment of individual patient preferences the final drug choice should be made. In addition, a structured follow-up of AF patients taking an NOAC, with interventions to improve medication adherence and sufficient patient education are necessary to manage NOAC adherence in clinical practice, as also suggested by Vrijens et al.\textsuperscript{15}

Of 1204 AF patients taking rivaroxaban in the Dresden registry, 39.3% previously used warfarin, and the main reason for VKA discontinuation (in 53.7% of cases) was a labile international normalized ratio (INR), whilst rivaroxaban was mostly discontinued following the bleeding events (30% of discontinuations), which were predominantly non-major clinically relevant bleeds.\textsuperscript{14} Importantly, >90% of all AF patients taking rivaroxaban had high stroke risk (CHA\textsubscript{2}-DS\textsubscript{2}-VS\textsubscript{c} score ≥2), but after rivaroxaban discontinuation, a worrying 15.7% of patients were left without any antithrombotic therapy, 1.8% received dual antiplatelet therapy and as many as 30% of patients were prescribed single antiplatelet therapy. Perhaps there is the physicians misperception that antiplatelet drugs are safer compared to OAC or the risk of recurrent bleeding with OAC was (often erroneously) estimated to be higher than the benefit from OAC.\textsuperscript{12,16} Thus, practitioners would also benefit from initiatives directed towards better adherence to AF guidelines.

Indeed, interdisciplinary AF expert programs coordinated by clinical nurse specialists may improve patient knowledge on AF therapies and the adherence of physicians to AF guideline recommendations.\textsuperscript{17} Prospective randomized trials such is the ongoing AEGEAN (Assessment of Education and Guidance Programme for Eliquis Adherence in Non-Valvular AF, NCT01884350), which randomizes patients taking apixaban to usual care or with added structured education and follow-up by a virtual clinic, will facilitate the elicitation of patient-related factors which need further management.

With such integrated approaches, AF patients are increasingly becoming active players in optimising stroke prevention. Ultimately, the goal is better medication adherence and improved long-term outcomes.

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