Warfarin treatment quality in stroke prevention

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Aulan, utbildningslokalerna 1 trp, Sundsvalls sjukhus. Fredagen den 21 oktober, kl. 13:00. Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Docent, Christine Kremer, Institutionen för kliniska vetenskaper, Lunds universitet.
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Background
Ischemic stroke is a serious condition associated to presence of atrial fibrillation (AF). Use of anticoagulants in AF patients greatly reduces the risk of stroke. Warfarin is the most commonly used anticoagulant in Sweden. The aim of this thesis was to study the impact of warfarin treatment quality in Swedish stroke prevention.

Study I, II and IV were large multicentre, retrospective, cohort studies based on Swedish registries, especially AuriculA, a quality register for AF and anticoagulation. Study period was January 1, 2006, to December 31, 2011. Study III enrolled all warfarin treated AF patients in Sundsvall, registered in AuriculA on January 1, 2010. This smaller cohort was followed until discontinuation or study-stop December 31, 2013, and data used were collected from each patient’s medical record.

Results
The annual rate of major bleedings and thromboembolic events for warfarin treated patients, including all indications for warfarin, was relatively low (2.24% and 2.66%), with incidence of intracranial bleeding of 0.37% per treatment year. The overall mean time in therapeutic range (TTR) was 76.5%. Patients treated due to atrial fibrillation had a mean TTR of 68.6%, with an annual rate of major bleeding and thromboembolic events of 2.23% and 2.95%, and with 0.44% intracranial bleeding. No significant differences in overall complications were found comparing treatment monitored in anticoagulation clinics vs. primary health care centers. There were increased risk of both overall major bleedings and thromboembolic events for AF patients receiving additional acetylsalicylic acid (ASA) treatment, having individual TTR (iTTR) below 70%, or having high international normalized ratio (INR) variability. For AF patients with low INR variability, lower rates were seen for almost all events, compared with patients with high INR variability. For AF patients with iTTR ≥70% there were however no alteration of complication rates, due to INR variability. The overall proportion of persistence to warfarin treatment for stroke patients with AF was found to be 0.69 after 2 years treatment and 0.47 after 5 years. Stroke patients with diagnosed dementia at baseline were more than two-times likely of discontinuing warfarin than others. Excessive alcohol use, chronic obstructive pulmonary disease, cancer and chronic heart failure were baseline diagnoses each associated with over 20% increased risk of treatment discontinuation. Lower persistence to treatment was linked to increasing start-age and CHA2DS2-VASc scores. As documented reasons for warfarin treatment discontinuation in AF patients, we found regained sinus rhythm as the most common addressed cause (31.2%), followed by problematic monitoring and bleedings. We estimated that only half (49.5%) of those discontinuations were clinically well motivated.

Conclusions
Quality of Swedish warfarin treatment in initiated stroke prevention is high, with generally low rates of complications and high TTRs, no matter treatment in ACC or PHCC, including high long time persistence to warfarin in secondary stroke prevention. For better outcome in future warfarin stroke prophylactic treatment clinicians should aim for iTTRs over 70%, avoid additional ASA therapy, support fragile patients like those with excessive alcohol use and dementia, and base decisions on treatment discontinuations on solid medical arguments.

Keywords
Anticoagulation, atrial fibrillation, complications, international normalized ratio (INR) variability, persistence, stroke, time in therapeutic range (TTR), treatment quality, warfarin