Impact of NOAC and VKA on outcome of patients with diabetes and newly diagnosed atrial fibrillation – A report from the GARFIELD-AF registry

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BACKGROUND

◆ Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia associated with higher risks of ischaemic stroke/SE, all cause death, and bleeding due to antithrombotic therapy.

◆ Diabetes mellitus (DM) particularly type 2 diabetes mellitus (T2DM) is a growing worldwide epidemic[1,2] , and one of the most common comorbidities associated with AF. The interplay of these 2 conditions has the potential of worsening the outcome

◆ Few reports have explored the respective impact of direct oral anticoagulants (NOAC) and vitamin K antagonists (VKA) on the outcome of AF patients with diabetes[3-5].

PURPOSE

◆ In AF patients included in the prospective GARFIELD-AF registry we assessed (1) the outcome of DM patients compared with non-DM patients (2) the impact of OAC on outcome in both DM and non-DM patients, along with the relative effectiveness of NOAC and VKA.

METHODS

◆ The study population comprised 52,010 patients with newly diagnosed AF, 11,542 DM and 40,468 non-DM, who were enrolled in GARFIELD-AF, the largest multinational prospective AF registry.

◆ Adjusted hazard ratios (HRs) were obtained through Cox proportional-hazard models to quantify the effects of diabetes on death, ischaemic stroke/SE and major bleeding.

◆ Comparative effectiveness analyses between VKA and NOAC were restricted to 18,373 Safety and effectiveness of NOAC and VKA in DM and non-DM patients were assessed with propensity scores using an overlap weighting scheme. Weights were applied to Cox proportional-hazards models to estimate the effects of NOAC vs VKA use for each endpoint.

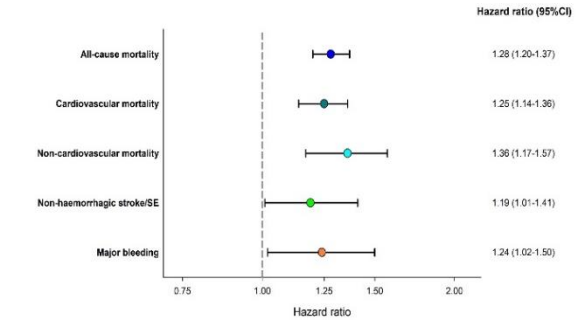
RESULTS

◆ Compared to non-DM patients, DM patients (39.3% with oral antidiabetic drug, 13.4% with insulin and 47.2% lifestyle recommendations only) had higher median BMI (28.7 vs 26.4), more frequent history of heart failure (24.8% vs 21.9%), acute coronary syndromes (15.9% vs 9.2%), vascular disease (32.6% vs 22.6%), ischaemic stroke/TIA/SE (12.8% vs 10.9%), hypertension (85.7% vs 73.7%), hypercholesterolemia (55.3% vs 37.7%), and moderate to severe CKD (14.4% vs 9.6%).

◆ Those with DM had higher rates of OAC use (70.5% vs 65.8%), consisting in VKA (44.0% vs 38.0%), or AP in combination with OAC (28.9% vs 19.1%), DM and non-DM patients respectively. AP monotherapy was used in 20.2 % of DM and 21.2 % of non-DM patients. The median CHA2DS2-VASc score was [3.0 (2.0;4.0)] in both DM and non-DM patients.

◆ At 2-year follow-up the risk of all-cause death, ischaemic stroke/SE, and major bleeding was significantly higher in DM than in non-DM patients (Figure 1).

Figure 1. Adjusted[1] hazard ratios diabetes vs no diabetes (ref.) within 2-year follow-up



[1]Adjusted by sex, age, ethnicity, type of AF, congestive heart failure, vascular disease, hypertension, prior stroke/TIA/SE, prior bleeding, moderate to severe, current smoking, heavy alcohol consumption, baseline anticoagulation and antiplatelet therapy.

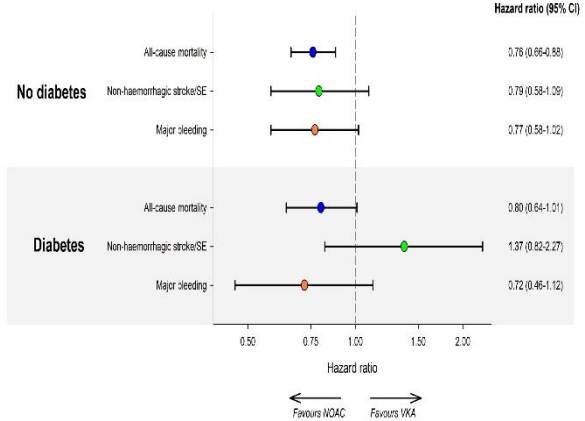
◆ Overall, OAC led in both non-DM and DM populations to similar risk reduction for death [HR 0.75 (0.69-0.83) vs 0.74 (0.64-0.86)], ischaemic stroke/SE [0.69 (0.58-0.83) vs 0.70 (0.53-0.93)], and similar increase in major bleeding risk [HR 1.40 (1.14-1.71) vs 1.37 (0.99-1.89)].

◆ NOAC use was associated with significantly lower rate of all-cause death, in non-DM patients, [0.76 (0.66-0.88)] and marginally non-significant lower rate in DM patients [0.80 (0.64-1.01)]. (p-value 0.6098 for interaction between NOAC and diabetes).

◆ Major bleeding associated with NOAC use trended to lower rates than with VKA in both non-DM and DM patients

◆ A non-significant increase in ischaemic stroke/SE rates was observed in DM patients (Figure 2).

Figure 2. Adjusted1 hazard ratios NOAC vs VKA (reference) at two years of follow-up.



[1]Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, cirrhosis, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.

CONCLUSIONS

◆ At baseline, DM patients had higher rates of OAC prescription than non-DM patients.

◆ At 2-year follow-up the risk of all-cause death, stroke/SE, and major bleeding was significantly higher in DM than in non-DM patients.

◆ OAC led to similar risk reduction for death and ischaemic stroke/SE, and similar increased risk of bleeding in both DM and non-DM patients.

◆ The rates of all-cause death and of major bleeding tended to be lower, though not significantly, with NOAC compared to VKAs in both DM and non-DM patients.

◆ These results show that the efficacy / safety profile of oral anticoagulation, including NOAC use, is similar in DM and non-DM patients.

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AF Garfield global anticoagulant registry in the field