Guideline-directed medical therapies for comorbidities among patients with atrial fibrillation: results from GARFIELD-AF

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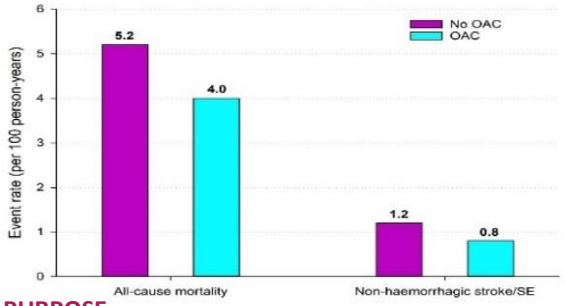
BACKGROUND

◆ The GARFIELD-AF registry is a prospective, multicentre, observational study of adults with recently diagnosed non-valvular atrial fibrillation (AF) and at least one risk factor for stroke[1].

◆ In GARFIELD-AF anticoagulation is associated with a rate of all-cause mortality which is 1.2 deaths per 100 person years less than in those not anticoagulated, but this cannot be completely attributed to the effect on strokes, since this is lower by only 0.4 per 100 person years (Figure 1).

◆ One potential explanation is improved treatment, with the use of comprehensive guideline-directed medical therapies (GDMT), in patients with AF receiving oral anticoagulant (OAC) therapy[2].

Figure 1. ***Event rates (per 100 person-years) over 2-year follow-up in patients with CHA_2DS_2-VASc ≥2 by baseline anticoagulation***



PURPOSE

◆ To identify the potential relationships between anticoagulation status, GDMT use and clinical outcomes.

METHODS

◆ GARFIELD-AF patients with CHA_2DS_2-VASc ≥2 and with at least one of these five comorbidities: coronary artery disease, diabetes mellitus, heart failure, hypertension and peripheral vascular disease.

◆ Use of GDMT was determined on the basis of published European Society for Cardiology guidelines operative between 2010 and 2016 [3,4].

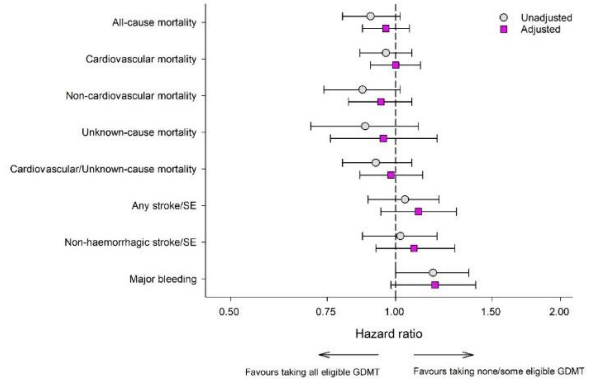
◆ Association between GDMT use and clinical outcome events was evaluated with Cox-proportional hazards models. A robust covariance estimate is included in order to account for correlation within country. The models included stratification by all possible combinations of the five comorbidities used to define GDMT eligibility.

RESULTS

◆ Among the 39,946 patients, 9041 (22.6%) received none of the GDMT, 15,414 (38.6%) received some, and 15,491 (38.8%) received all of the GDMT for which they were eligible.

◆ Patients on OAC tended to receive all the GDMTs more frequently compared to patients not on OAC (40.8% vs 34.8%, respectively, p-value <0.0001).

Figure 2. ***Unadjusted and adjusted[1] hazard ratios for GDMT use at two years of follow-up in patients with CHA_2DS_2-VASc ≥2.***

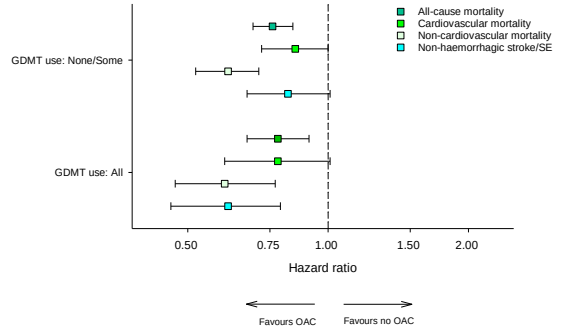


[1]Hazard ratios are adjusted for age, sex, ethnicity, type of AF, prior stroke/TIA/SE, history of bleeding, moderate-to-severe CKD, anticoagulation at baseline, smoking status and heavy alcohol consumption. The reference category is patients taking none/some eligible GDMT.

◆ Patients who received all of the GDMT were not found to have a different risk of mortality, stroke/SE or major bleeding compared to patients who received none or some GDMT (HR: 0.96 [0.87-1.06], 1.10 [0.94-1.29], 1.18 [0.98-1.40], respectively) (Figure 2).

◆ The effect of OAC was beneficial for mortality and stroke risk whether receiving comprehensive GDMT or not (Figure 3).

Figure 3. ***Adjusted[1] hazard ratios for baseline OAC treatment at two years of follow-up by GDMT use.***



[1]Hazard ratios are 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 specialty and location, acute coronary syndromes, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypercholesterolemia, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use. The reference category is patients taking no OAC.

DISCUSSION

No significant reduction of CV outcomes associated with GDMT for CV disease and the finding of significant reduction of non-CV mortality associated with anticoagulants are counterintuitive, but there are potential explanations, which cannot be resolved from GARFIELD-AF data:

◆ Patients who received all eligible GDMT may have had more serious CV disease than those who did not receive such therapy, thus explaining less than expected improvement in CV outcomes associated with GDMT.

◆ Patients who received comprehensive CV disease GDMT may also have received better non-CV disease management accounting for lower non-CV outcomes.

◆ Anticoagulation may be associated with lower non-CV mortality by revealing cancer at an earlier stage and reducing venous thromboembolic disease.

CONCLUSIONS

◆ OAC therapy is associated with a lower risk of all-cause mortality, non-cardiovascular mortality and stroke/SE in comparison with no OAC, irrespective of GDMT use in patients with CHA_2DS_2-VASc ≥2.

◆ The use of GDMT is associated with non-statistically significant lower rate of mortality, but there is little evidence that this explains the decrease in mortality with the use of OAC.

REFERENCE

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TRI Thrombosis Research Institute

www.garfieldregistry.org

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AF Garfield global anticoagulant registry in the field