

A HISTORY OF STROKE, NOT OF TRANSIENT ISCHAEMIC ATTACK, PREDICTS A HIGHER RISK FOR MORTALITY AND STROKE IN NEWLY DIAGNOSED ATRIAL FIBRILLATION PATIENTS, REAL-WORLD EVIDENCE FROM GARFIELD-AF SHOWS

- *Findings based on baseline characteristics and one year-follow up data on 51,670 GARFIELD-AF patients*
- *Patients with a history of only stroke have an increased risk for all-cause mortality, non-cardiovascular (CV) mortality and stroke/SE*
- *No significantly increased hazards in patients with a history of only TIA*

Montreal, Canada, 18 October 2018 – A history of stroke only or of both stroke and transient ischaemic attack (TIA) are associated with an independent increase in risk of one-year mortality and stroke/systemic embolism (SE) in atrial fibrillation (AF) patients, while a history of TIA only is a much weaker predictor, according to a new data analysis from the Global Anticoagulant Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF), the largest multinational prospective registry in AF, presented today at the 11th World Stroke Congress 2018.

Previous stroke/TIA has been identified as a marker for increased risk of death and ischemic events. This analysis aimed to further characterise the risk of mortality, stroke/systemic embolism and bleeding events associated with a history of stroke/TIA in patients with AF. Baseline characteristics and one-year follow-up of patients from all 5 GARFIELD-AF cohorts were analysed.

During a Late Breaking Trials session,¹ Professor Werner Hacke, Senior Professor of Neurology at the University of Heidelberg, Heidelberg, Germany, commented: “These data show that while patients with a history of stroke only or both stroke and TIA have an elevated risk of mortality and stroke, a history of TIA only could be removed from scores estimating the risk for stroke and systemic embolism in AF patients. Furthermore a history of TIA only is not a reliable predictor of increased risk for events and should not be used to define subcohorts at higher risk in prevention trials.”

The GARFIELD researchers compared the outcome occurrence of patients with no prior stroke nor TIA (N=46,053) and patients with a history of stroke or TIA (N=5,617). They also analysed the subsets of patients with history of stroke only (without TIA, N=3,362), of TIA only (without stroke, N=1,788) and of both stroke and TIA (N=467). Patients with a history of stroke or TIA were on average 4 years older. They had, by definition, higher baseline CHA₂DS₂-VASC and HAS-BLED as well as more prevalence of common risk factors such as hypertension, diabetes or vascular disease. These patients had a higher risk of all-cause mortality (adjusted hazard ratio [HR]: 1.26; 95% confidence interval [CI]: 1.12-1.42), CV (adjusted sub-hazard ratio [SHR]: 1.22; 95% CI: 1.01-1.48) and non-CV mortality (SHR:1.39; 95% CI: 1.15-1.68) and stroke/SE (SHR: 2.17; 95% CI: 1.80-2.63), while the risk for major bleeding was not significantly increased.

The weak predictive power of a history of TIA only is probably caused by the low reliability of establishing the diagnosis of TIA retrospectively, Professor Hacke commented.

About the GARFIELD-AF Registry

GARFIELD-AF is a worldwide observational programme that aims to enhance the breadth and depth of understanding of stroke prevention in atrial fibrillation (AF), ultimately informing strategies to improve patient outcomes, safety and utilisation of healthcare resources.

It offers a unique opportunity to obtain a comprehensive and contemporary description of the spectrum of patients with AF and their management worldwide as they evolve over time. The registry is important in bridging the gap between research and clinical practice, serving to increase awareness of the importance of thrombosis and its treatment.

GARFIELD-AF recruited patients with newly diagnosed nonvalvular AF and at least one risk factor for stroke. A total of 57,262 patients were recruited from 1352 centres in 35 countries worldwide, including the Americas, Europe, Africa and Asia-Pacific, over five sequential cohorts. Follow-up is over a minimum of 2 years and up to 8 years after diagnosis, to create a comprehensive database of treatment decisions and outcomes in everyday clinical practice.

GARFIELD-AF is a pioneering, independent academic research initiative led by an international steering committee under the auspices of the TRI, London, UK.

Contemporary understanding of AF is based on data gathered in controlled clinical trials. Whilst essential for evaluating the efficacy and safety of new treatments, these trials are not representative of everyday clinical practice and, hence, uncertainty persists about the real-life burden and management of this disease. GARFIELD-AF seeks to provide insights into the impact of anticoagulant therapy on thromboembolic and bleeding complications seen in this patient population. It will provide a better understanding of the potential opportunities for improving care and clinical outcomes amongst a representative and diverse group of patients and across distinctive populations. This should help physicians and healthcare systems to appropriately adopt innovation to ensure the best outcomes for patients and populations.

The registry started in December 2009. Four key design features of the GARFIELD-AF protocol ensure a comprehensive and representative description of AF; these are:

- Five sequential cohorts of prospective, newly diagnosed patients, facilitating comparisons of discrete time periods and describing the evolution of treatments and outcomes;
- Investigator sites that are selected randomly within carefully assigned national AF care setting distributions, ensuring that the enrolled patient population is representative;
- Enrolment of consecutive eligible patients regardless of therapy to eliminate potential selection bias;
- Follow-up data captured for a minimum of 2 and up to 8 years after diagnosis, to create a comprehensive database of treatment decisions and outcomes in everyday clinical practice.

Included patients must have been diagnosed with nonvalvular AF within the previous 6 weeks and have at least one risk factor for stroke; as such, they are potential candidates for anticoagulant therapy to prevent blood clots leading to stroke. It is left to the investigator to identify a patient's stroke risk factor(s), which need not be restricted to those included in established risk scores. Patients are included whether

or not they receive anticoagulant therapy, so that the merit of current and future treatment strategies can be properly understood in relation to patients' individual risk profiles.

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG, Berlin, Germany.

For more information, visit our website: www.garfieldregistry.org

The burden of AF

Up to 2% of the global population has AF,² including around 8.8 million people in Europe³ and 5–6.1 million in the United States.⁴ It is estimated that its prevalence will at least double by 2050 as the global population ages.⁴ AF is associated with a five-fold increase in stroke risk, and one out of five strokes is attributed to this arrhythmia.² Ischaemic strokes related to AF are often fatal, and those patients who survive are left more frequently and more severely disabled and have a greater risk of recurrence than patients with other causes of stroke.² Hence, the risk of mortality from AF-associated stroke is doubled and the cost of care is 50% higher.²

AF occurs when parts of the atria emit uncoordinated electrical signals. This causes the chambers to pump too quickly and irregularly, not allowing blood to be pumped out completely.⁵ As a result, blood may pool, clot and lead to thrombosis, which is the number one cardiovascular killer in the world.⁶ If a blood clot leaves the left atrium, it could potentially lodge in an artery in other parts of the body, including the brain. A blood clot in an artery in the brain leads to a stroke; 92% of fatal strokes are caused by thrombosis.⁶ Stroke is a major cause of death and long-term disability worldwide – each year, 6.5 million people die⁷ and 5 million are left permanently disabled.⁸ People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.⁹

About the TRI

The TRI is dedicated to bringing new solutions to patients for the detection, prevention and treatment of blood clots. The TRI's goal is to advance the science of real-world enquiry so that the value of real-world data is realised and becomes a critical link in the chain of evidence. Our pioneering research programme, across medical disciplines and across the world, continues to provide breakthrough solutions in thrombosis.

For more information, visit: <http://www.tri-london.ac.uk/>.

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1. Hacke W, *et al.* In newly diagnosed atrial fibrillation patients, a history of stroke is a better predictor of events than a history of TIA. Late Breaking Trials 2 World Stroke Congress 2018.
 2. Camm AJ, *et al.* Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010; 31(19):2369-429.
 3. Krijthe B P, Kunst A, *et al.* Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013; 34:2746-51.
 4. Colilla S, Crow A, Petkun W, *et al.* Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *Am J Cardiol* 2013; 112(8):1142-7.
 5. National Heart, Lung, and Blood Institute. What is Atrial Fibrillation? Available at: <http://www.nhlbi.nih.gov/health/health-topics/topics/af/>. [Last accessed: August 9 2018].
 6. World Thrombosis Day. Know Thrombosis. Available at: <http://www.worldthrombosisday.org/issue/thrombosis/>. [Last accessed: 16 October 2018].
 7. World Stroke Organization. World Stroke Campaign. Available at: <http://www.worldstrokecampaign.org/>. [Last accessed: 16 October 2018].
 8. Stroke Centre. Stroke Statistics. Available at: <http://www.strokecenter.org/patients/about-stroke/stroke-statistics/>. [Last accessed: 16 October 2018].
 9. American Heart Association. Why Atrial Fibrillation (AF or AFib) Matters. Available at: http://www.heart.org/HEARTORG/Conditions/Arrhythmia/AboutArrhythmia/Why-Atrial-Fibrillation-AF-or-AFib-Matters_UCM_423776_Article.jsp. [Last accessed: 16 October 2018].