JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. 64, NO. 23, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.09.051

Net Clinical Benefit of Antithrombotic Therapy in Patients With Atrial Fibrillation and Chronic Kidney Disease

A Nationwide Observational Cohort Study

Anders Nissen Bonde, MB,* Gregory Y.H. Lip, MD,† Anne-Lise Kamper, MD, DMSc,‡ Peter Riis Hansen, MD, PhD, DMSc,* Morten Lamberts, MD, PhD,* Kristine Hommel, MD, PhD,‡ Morten Lock Hansen, MD, PhD,* Gunnar Hilmar Gislason, MD, PhD,*§ Christian Torp-Pedersen, MD, DMSc,‖ Jonas Bjerring Olesen, MD, PhD*¶

JACC JOURNAL CME

This article has been selected as the month's *JACC* Journal CME activity.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Method of Participation and Receipt of CME Certificate

To obtain credit for *JACC* CME, you must:

1. Be an ACC member or *JACC* subscriber.
2. Carefully read the CME-designated article available online and in this issue of the journal.
3. Answer the post-test questions. At least 2 out of the 3 questions provided must be answered correctly to obtain CME credit.
4. Complete a brief evaluation.
5. Claim your CME credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME Objective for This Article: After reading this article the reader should be able to: 1) describe the association between chronic kidney disease and the risk of stroke and thromboembolism in atrial fibrillation; and 2) discuss the net clinical benefit of warfarin and aspirin, respectively, in patients with atrial fibrillation and chronic kidney disease.

CME Editor Disclosure: *JACC* CME Editor Ragavendra Baliga, MD, FACC, has reported that he has no financial relationships or interests to disclose.

Author Disclosures: The Capital Region of Denmark, Foundation for Health Research has financed this study through a research grant for Dr. Jonas Bjerring Olesen. Dr. Lip has served as a consultant for Bayer Healthcare, Astellas, Merck & Co., Inc., Sanofi, BMS/Pfizer, Daiichi-Sankyo, Biotronik, Medtronic, Portola, AstraZeneca, and Boehringher Ingelheim; and has served on the speakers bureaus for Bayer Healthcare, BMS/Pfizer, Boehringher Ingelheim, Daiichi-Sankyo, Medtronic, and Sanofi. Dr. Gislason has received research grants and speaking fees from AstraZeneca and Bristol-Myers Squibb. Dr. Torp-Pedersen has developed antiarrhythmic drugs; and has received fees for lecturing, serving on advisory boards, and steering committees for Cardiome, Sanofi, and Merck & Co., Inc. Dr. Bjerring Olesen has received speaking fees from Bristol-Myers Squibb; and funding for research from the Lundbeck Foundation, Bristol-Myers Squibb, and The Capital Region of Denmark, Foundation for Health Research. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz).

CME Term of Approval

Issue Date: December 16, 2014
Expiration Date: December 15, 2015

From the *Department of Cardiology, Copenhagen University Hospital Gentofte, Gentofte, Denmark; †University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; ‡Department of Nephrology, Copenhagen University Hospital Rigshospitalet, Rigshospitalet, Denmark; §The National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark; ‖Department of Health, Science and Technology, Aalborg University, Aalborg, Denmark; and the ¶Department of Cardiology, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark. The Capital Region of Denmark, Foundation for Health Research has financed this study through a research grant for Dr. Jonas Bjerring Olesen. Dr. Lip has served as a consultant for Bayer Healthcare, Astellas, Merck & Co., Inc., Sanofi, BMS/Pfizer, Daiichi-Sankyo, Biotronik, Medtronic, Portola, AstraZeneca, and Boehringher Ingelheim; and has served on the speakers bureaus for Bayer Healthcare, BMS/Pfizer, Boehringher Ingelheim, Daiichi-Sankyo, Medtronic, and Sanofi. Dr. Gislason has received research grants and speaking fees from AstraZeneca

JACC VOL. 64, NO. 23, 2014
DECEMBER 16, 2014:2471–82

Net Clinical Benefit of Antithrombotic Therapy in Patients With Atrial Fibrillation and Chronic Kidney Disease

A Nationwide Observational Cohort Study

ABSTRACT

BACKGROUND The balance between stroke reduction and increased bleeding associated with antithrombotic therapy among patients with atrial fibrillation (AF) and chronic kidney disease (CKD) is controversial.

OBJECTIVES This study assessed the risk associated with CKD in individual CHA_2DS_2-VASc (Congestive heart failure; Hypertension; Age ≥75 years; Diabetes mellitus; previous Stroke, transient ischemic attack, or thromboembolism; Vascular disease; Age 65 to 74 years; Sex category) strata and the net clinical benefit of warfarin in patients with AF and CKD in a nationwide cohort.

METHODS By individual-level linkage of nationwide Danish registries, we identified all patients discharged with non-valvular AF from 1997 to 2011. The stroke risk associated with non-end-stage CKD and end-stage CKD (e.g., patients on renal replacement therapy [RRT]) was estimated using Cox regression analyses. The net clinical benefit of warfarin was assessed using 4 endpoints: a composite endpoint of death/hospitalization from stroke/bleeding; a composite endpoint of fatal stroke/fatal bleeding; cardiovascular death; and all-cause death.

RESULTS From nonvalvular AF patients (n = 154,259), we identified 11,128 patients (7.2%) with non-end-stage CKD and 1,728 (1.1%) receiving RRT. In all CHA_2DS_2-VASc risk groups, RRT was independently associated with a higher risk of stroke/thromboembolism, from a 5.5-fold higher risk in patients with CHA_2DS_2-VASc score = 0 to a 1.6-fold higher risk in patients with CHA_2DS_2-VASc score ≥2. In patients receiving RRT with CHA_2DS_2-VASc score ≥2, warfarin was associated with lower risk of all-cause death (hazard ratio [HR]: 0.85, 95% confidence interval [CI]: 0.72 to 0.99). In non-end-stage CKD patients with CHA_2DS_2-VASc score ≥2, warfarin was associated with a lower risk of a composite outcome of fatal stroke/fatal bleeding (HR: 0.71, 95% CI: 0.57 to 0.88), a lower risk of cardiovascular death (HR: 0.80, 95% CI: 0.74 to 0.88), and a lower risk of all-cause death (HR: 0.64, 95% CI: 0.60 to 0.69).

CONCLUSIONS CKD is associated with a higher risk of stroke/thromboembolism across stroke risk strata in AF patients. High-risk CKD patients (CHA_2DS_2-VASc ≥2) with AF benefit from warfarin treatment for stroke prevention. (J Am Coll Cardiol 2014;64:2471–82) © 2014 by the American College of Cardiology Foundation.

The optimal management of thromboprophylaxis in patients with atrial fibrillation (AF) and chronic kidney disease (CKD) is complex. Whereas CKD patients are at high risk of stroke and thromboembolism (TE), these patients are also at high risk of death and major bleeding. This is particularly true of patients with end-stage CKD treated with renal replacement therapy (RRT), whether as dialysis or renal transplantation (1–4). Thromboprophylaxis in this high-risk group is therefore complex, and clinical decision making requires interpretation of the balance between the

and Bristol-Myers Squibb. Dr. Torp-Pedersen has developed antiarrhythmic drugs; and has received fees for lecturing, serving on advisory boards, and steering committees for Cardiome, Sanofi, and Merck & Co., Inc. Dr. Bjerring Olesen has received speaking fees from Bristol-Myers Squibb; and funding for research from the Lundbeck Foundation, Bristol-Myers Squibb, and The Capital Region of Denmark, Foundation for Health Research. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

You can also listen to this issue's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

Manuscript received April 28, 2014; revised manuscript received August 19, 2014, accepted September 16, 2014.