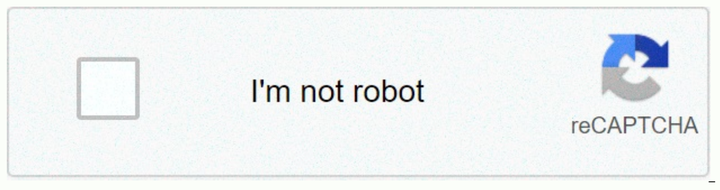

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2019 chest guidelines anticoagulation

To the editor:We write about the recently updated CHEST guidelines (November 2018) on antithrombotic atrial fibrillation therapy (AF).1Lip G.Y.H. Banerjee A. Boriani G. et al. Antithrombotic treatment of atrial fibrillation: CHEST guidance and expert opinion. These guidelines recommend the use of vitamin K-free antagonistic oral anticoagulants (NOAC) for the prevention of stroke in patients with AF. However, the recommendation to specifically use apixaban, dabigatran (110 mg twice daily) or edoxaban in patients with a prior unprovoked bleeding or high risk of bleeding is also included, based on the fact that all three substances showed a significantly lower risk of bleeding compared to warfarin. This is cited as a weak recommendation based on very low-quality evidence. In addition, the proposed anticoagulant selection scheme indicates the use of apixaban, dabigatane or edoxaban, but not rivaroxaban in Asian patients.1Lip G.Y.H. Banerjee A. Boriani G. et al. Antithrombotic treatment of atrial fibrillation: CHEST guidance and expert opinion. We believe that these recommendations could benefit from the many improvements, justifications and evidence that we are outlining here. It is not possible to directly compare the event rates observed with individual NOAC in Phase 3 studies comparing NOAC with warfarin for stroke prevention in patients with AF, and no Phase 3 studies have been conducted specifically to compare one NOAC with another. Therefore, it is not appropriate to indicate the existence of evidence on the relative safety of NOAC by recommending specific NOAC over others.2Camm A.J. Fox K.A.A. Peterson E. Challenges in comparing antagonistic oral anticoagulants not related to atrial fibrillation. The recommendations of the guidelines were mainly based on the results of two meta-analyses of phase 3 clinical studies comparing apixaban (Apixaban to reduce stroke and other thromboembolic events in atrial fibrillation [ARISTOTLE]), 3Granger C.B. Alexander J.H. McMurray J.J. et al. Apixaban versus warfarin in patients with atrial fibrillation. dabigatlan (randomised evaluation of long-term anticoagulant therapy with Dabigatan etexilate [RE-LY]),4Connolly S.J. Ezekowitz M.D. Yusuf S. et al. dabigatlan versus warfarin in patients with atrial fibrillation. edoxaban (Global Study to Assess the Safety and Efficacy of Edoxaban (DU-176b) vs. Standard Annealing Practice with Warfarin in Patients with Atrial Fibrillation [ENGAGE AF-TIMI 48]),5Giugliano R.P. Ruff C.T. Braunwald E. et al. Edoxaban versus warfarin in patients with atrial fibrillation. or rivaroxaban (Rivaroxaban once daily oral direct factor Xa inhibition compared to vitamin K antagonism for stroke prevention and embolism test for atrial fibrillation [ROCKET AF]6Patel M.R. KW Garg J. et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. and Japanese Rivaroxaban once daily oral direct factor Xa inhibition compared to vitamin K antagonism for stroke prevention and trial embolism in atrial fibrillation [J-ROCKET AF]7Hori M. Matsumoto M. Tanahashi N. et al. Rivaroxaban vs. Warfarin in Japanese patients with atrial fibrillation – J-ROCKET AF study.) warfarin for the prevention of stroke in patients with AF. 8Ruff C.T. Giugliano R.P. Braunwald E. et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: meta-analysis of randomised studies., 9Wang K.-L. Lips G.Y.H. Lin S.-J. Chiang C.-E. Antagonistic oral anticoagulants without vitamin K for the prevention of stroke in Asian patients with nonvalvular atrial fibrillation: meta-analysis. However, these meta-analyses did not compare safety outcomes between NOAC or conclude that the safety profiles of apixaban, dabigatran and edoxaban were more favourable than those of rivaroxaban, either in the overall patient population or in a subset of Asian patients. Meta-analyses only confirmed the efficacy and safety of NOAC as classes vs warfarin. Lips G.Y.H. Lin S.-J. Chiang C.-E. Antagonistic oral anticoagulants without vitamin K for the prevention of stroke in Asian patients with nonvalvular atrial fibrillation: meta-analysis. Moreover, it does not appear that the recommendation to use only apixaban, dabigatran or edoxaban in Asian patients does not take into account evidence from the ROCKET AF study that clearly demonstrated a reduced risk of intracranial haemorrhage and a trend toward a reduced risk of major bleeding with rivaroxaban vs. warfarin in Asian patients.6Patel M.R. Mahaffey K.W. Garg J. et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation., 9Wang K.-L. Lips G.Y.H. Lin S.-J. Chiang C.-E. Vitamin K-free antagonistic oral anticoagulants for stroke prevention in Asian patients with nonvalvil atrial fibrillation: meta-analysis,, 10Goodman S.G. Wojdyla D.M. Piccini J.P. et al. Factors associated with major bleeding events: observations from rocket af study (rivaroxaban oral direct factor Xa inhibition compared to vitamin K antagonism for stroke prevention and atrial fibrillation embolism studies). In addition, no differences in primary efficacy or safety outcomes were observed in any of the Phase 3 studies comparing individual NOAC with warfarin in Asian or non-Asian AF patients. 3Granger C.B. Alexander J.H. McMurray J.J. et al. Apixaban versus warfarin in patients with atrial fibrillation,, 4Connolly S.J. Ezekowitz M.D. Yusuf S. et warfarin in patients with atrial fibrillation, 5Giugliano R.P. Ruff C.T. Braunwald E. et al. Edoxaban versus warfarin in patients with atrial fibrillation., 6Patel M.R. Mahaffey K.W. Garg J. et al. Rivaroxaban vs. warfarin for nonvalvular atrial fibrillation., 11Hori M. Connolly S.J. Zhu J. et al. Dabigatran versus warfarin: effects on ischaemic and haemorrhagic stroke and bleeding in Asians and non-Asians with atrial fibrillation. Real-world evidence of rivaroxaban cited in the anticoagulant selection scheme1Lip G.Y.H. Banerjee A. Boriani G. et al. Antithrombotic treatment of atrial fibrillation: CHEST guidance and expert opinion. was a nationwide retrospective cohort study based on data from taiwan's national health insurance research database. This study showed that the risk of gastrointestinal bleeding hospitalisation was higher for rivaroxaban compared to dabigatran, but this difference was not maintained in the analysis during treatment and the authors concluded that either rivaroxaban or dabigatran would be more appropriate than warfarin in Asian patients in this environment.12Chan Y.H. Kuo C.T. Yeh YH. et al. Thromboembolic, bleeding and mortality risk of rivaroxaban and dabigataban in Asians with nonvalvular atrial fibrillation. In addition, the scheme did not consider two relevant studies providing real-world information on rivaroxaban. Xarelto for the prevention of stroke in patients with atrial fibrillation in Asia (XANAP) was a prospective, observational study that showed low bleeding rates in Asian patients with AF, who received rivaroxaban for the prevention of stroke, in accordance with the results of the ROCKET AF study, as well as other real studies such as Xarelto for the prevention of stroke in patients with atrial fibrillation (XANTUS).13Kim Y.H. Shim J. Tsai C.T. et al. XANAP: real, prospective, observational study of patients treated with rivaroxaban for the prevention of stroke in atrial fibrillation in Asia,, 14Camm A.J. Amarenco P. Haas S. et al. XANTUS: a real, prospective, observational study of patients treated with rivaroxaban for the prevention of stroke in atrial fibrillation. The dynamic cohort study, which also used data from the Taiwan National Health Insurance Research Database, showed a lower risk of stroke/systemic embolism, major bleeding, intracranial haemorrhage, gastrointestinal bleeding and all-cause mortality of rivaroxaban compared to warfarin.15Lee H.F. Chan Y.H. Tu H.T. et al. Efficacy and safety of low-dose rivaroxaban in Asians with non-avalual atrial fibrillation. Overall, we consider that preferential use of individual NOAC in patients at high risk of bleeding cannot be recommended and that evidence supports the use of rivaroxaban in Asian patients. Indeed, the recently updated American Association / American College of of Rhythm Guidelines for the Management of Patients with AF recommend the use of NOAC over warfarin for eligible patients without any criteria for preferential use of individual NOAC.16January C.T. Wann L.S. Calkins H. et al. AHA/ACC/HRS focused on updating the 2014 AHA/ACC/HRS guidance on the management of atrial fibrillation patients. In our opinion, this should be reflected in all relevant guidelines to support the selection of evidence-based anticoagulants in patients with AF at risk of stroke, which will ultimately improve patient outcomes. Antithrombotic treatment of atrial fibrillation: CHEST guidance and expert opinion. Chest. 2018; 154:1121-1201View in article Challenges in comparing non-vitamin K antagonist oral anticoagulants for atrial fibrillation-related stroke prevention. Europace. 2018; 20: 1-11Se in the article Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011; 365: 981-992Se in dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009; 361: 1139-1151Eeas a view in the article Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013; 369: 2093-2104View in the article Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011; 365: 883-891Eear view in article Rivaroxaban vs Warfarin in Japanese patients with atrial fibrillation – J-ROCKET AF study. Circ J. 2012; 76: 2104-2111View in the article Comparing the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised studies. Lancet. 2014; 383: 955-962View in the article Antagonist without vitamin K oral anticoagulants for the prevention of stroke in Asian patients with nonvalvular atrial fibrillation: meta-analysis. Stroke. 2015; 46: 2555-2561Ease in the article Factors associated with major bleeding events: observations from the study ROCKET AF (rivaroxaban once a day oral direct factor Xa inhibition compared to vitamin K antagonism for the prevention of stroke and embolism in the atrial fibrillation study). J Am Coll Cardiol. 2014; 63:891-900View in the article Dabigatran versus warfarin: effects on ischemic and hemorrhagic stroke and bleeding in Asians and non-Asians with atrial fibrillation. Stroke. 2013; 44: 1891-1896Se in the article Thromboembolic, bleeding, and the risk of mortality of rivaroxaban and dabigatan in Asians with nonvalvular atrial fibrillation. J Am Coll Cardiol. 2016; 68: 1389-1401View in Article XANAP: a real, forward-looking, observational study of patients treated with rivaroxaban for the prevention of stroke in atrial fibrillation in Asia.J Arrhythm. 2018; 34: 418-427View in the article XANTUS: real-world, prospective, observational studies of patients treated with rivaroxaban for the prevention of stroke in atrial fibrillation. Eur Heart J. 2016; 37: in article Efficacy and safety of low doses asians with non-valvular atrial fibrillation. Int J Cardiol. 2018; 261: 78-83View in the AHA/ACC/HRS article focused updates to the 2014 AHA/ACC/HRS guidelines for managing patients with atrial fibrillation. Circulation. 2019; () article FINANCIAL/NON-FINANCIAL DISCLOSURES: None declared. DOI: antithrombotic therapy for atrial fibrillationIn briefThe risk of stroke is heterogeneous in different groups of patients with atrial fibrillation (AF), it depends on the presence of various risk factors of stroke. We provide recommendations for antithrombottic treatment based on pure clinical benefit for Patients with AF at different levels of stroke risk and in many common clinical scenarios. Full-TextPDFResponseIn BriefWe thank Kim et al for their comments on the 2018 CHEST guidelines.1 We acknowledge that there are no randomized controlled trials (RCTs) comparing one non-vitamin K antagonist oral anticoagulant to another that we only give a (very) weak recommendation. However, the recommendation is not unreasonable because apixaban, edoxaban and a lower dose of dabigatban (110 mg twice daily) showed significantly less severe bleeding than warfarin, which was a common comparator, while rivaroxaban and a higher dose of dabigattrane (150 mg twice daily) showed similar bleeding. Full-TextPDF Page 2To editor: Thank you Kim et al for their comments on the 2018 CHEST guidelines.1Lip G.Y.H. Banerjee A. Boriani G. et al. Antithrombotic therapy for atrial fibrillation: CHEST guidelines and expert panel report. We recognize that there are no randomized controlled trials (DCtS) comparing one antagonist without vitamin K oral anticoagulants with another, which is why we only give (very) weak recommendations. However, the recommendation is not unreasonable because apixaban, edoxaban and a lower dose of dabigatban (110 mg twice daily) showed significantly less severe bleeding than warfarin, which was a common comparator, while rivaroxaban and a higher dose of dabigattrane (150 mg twice daily) showed similar bleeding. In addition, a meta-analysis of RCTs2Ruff C.T. Giugliano R.P. Braunwald E. et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised studies. there was evidence that there was statistical heterogeneity as regards the vitamin K-free antagonistic oral anticoagulant effect on major bleeding, which claims that there are statistical and therefore potentially clinically significant differences between substances at least in case of major bleeding. Clinical trials are extended to real observation cohorts, largely in accordance with RCTs.3Bai Y. Deng H. Shantsila A. Lip G.Y. Rivaroxaban versus dabigatran or warfarin in real-world stroke prevention studies in atrial fibrillation: systematic review and metaanalysis., 4Proietti M. Romanazzi I. Romiti G.F. Farcomeni A. Lip G.Y.H. Real-world use of apixaban to prevent stroke in atrial fibrillation: systematic review and meta-analysis. Various meta-analyses and more recent large real-world data show the consistency of G.5Li G. Lip G.Y.H. Holbrook A. et al. Direct comparative efficacy and safety between vitamin K-free antagonistic oral anticoagulants for the prevention of stroke in non-calvary atrial fibrillation: systematic review and meta-analysis of observational studies., 6Lip G.Y.H. Keshishian A. Li X. et al. Efficacy and safety of oral anticoagulants in nonvalvular patients with atrial fibrillation, 7Li X.S. Deitelzweig S. Keshishian A. et al. Efficacy and safety of apixaban versus warfarin in nonvalvular atrial fibrillation patients in real clinical practice. Analysis of inclinations of 76,940 patients. similar bleeding between rivaroxaban and warfarin (consistent with RCT) and lower bleeding risks for dabigatane, apixaban and edoxaban compared to warfarin. Since patients with atrial fibrillation are not all homogeneous, and we have several anticoagulant options available, we have the option to fit the drug on the clinical profile of the patient (or vice versa). Antithrombotic therapy for atrial fibrillation: CHEST guidelines and expert panel Report.Chest. 2018; 154: 1121-1201Se in the article Comparing the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised studies. Lancet. 2014; 383: 955-962View in Rivaroxaban versus dabigatran or warfarin in real-world stroke prevention studies in atrial fibrillation: systematic review and meta-analysis. Stroke. 2017; 48: 970-976View in the article Real-world use of apixaban to prevent stroke in atrial fibrillation: systematic review and meta-analysis. Stroke. 2018; 49: 98-106View in the article Direct comparative efficacy and safety between vitamin K-free antagonistic oral anticoagulants for the

prevention of stroke in nonvalvular atrial fibrillation: systematic review and meta-analysis observational studies. Eur J Epidemiol. 2019; 34: 173-190Neglicking in the article Efficacy and safety of oral anticoagulants in non-vavalular fibrillation patients of atrials. Stroke. 2018; 49: 2933-2944View in the article Efficacy and safety of apixaban versus warfarin in patients with nevalvular atrial fibrillation in real world clinical practice. Analysis of inclinations of 76,940 patients. Thrombin hemost. 2017; 117: 1072-1082View in article DISCLOSURES: See the above article for author conflicts conflicts 2019 American College of Chest Physicians. Published by Elsevier Inc. All Rights Reserved. Access to this article on ScienceDirect New Chest Guidelines for Antithrombotic Atrial Fibrillation Therapy should consider recent data on RivaroxabanIn BriefS we are writing about the recently updated CHEST guidelines (November 2018) on antitrombo treatment of atrial fibrillation (AF).1 These guidelines recommend the use of vitamin K-free antagonistic oral anticoagulants (NOAC) to prevent stroke in patients with AF. However, the recommendation to specifically use apixaban, dabigatran (110 mg twice daily) or edoxaban in patients with a prior unprovoked bleeding or high risk of bleeding is also included, based on the fact that all three substances showed a significantly lower risk of bleeding compared to warfarin. Full-TextPDFAntithrombotic Therapy for Arial FibrilationIn BriefThe risk of stroke is heterogeneous in different groups of patients with atrial fibrillation (AF), dependent on the presence of various risk factors of stroke. We provide recommendations for antithrombottic treatment based on pure clinical benefit for Patients with AF at different levels of stroke risk and in many common clinical scenarios. Full-TextPDF scenarios. Full-TextPDF