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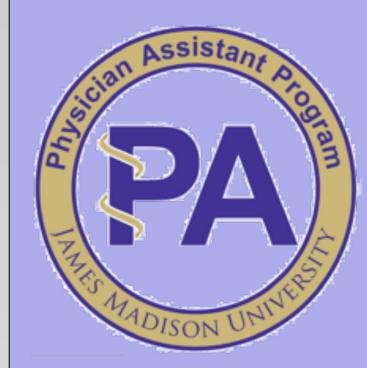
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Carter A, Deudne L, Stovall R. How much atrial fibrillation is too much? The net clinical benefit of anticoagulation therapy in atrial fibrillation patients with an intermediate CHA2DS2-VASc score. JMU Scholarly Commons Physician Assistant Capstones. http://commons.lib.jmu.edu/pacapstones/22. Published May 16, 2017.

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How Much Atrial Fibrillation Is Too Much?



The Net Clinical Benefit of Oral Anticoagulation Therapy in Atrial Fibrillation Patients With an Intermediate CHA₂DS₂-VASc Score

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INTRODUCTION

- Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia, affecting 33.5 million people worldwide
- Arterial thromboembolism, particularly ischemic stroke (IS), is a significant complication of AF
- The most widely recommended tool used to evaluate AF patient's risk of IS is the CHA₂DS₂-VASc score
- It assigns a numerical value to pre-determined IS risk factors and allows an overall estimation of the patient's risk
- Various organizations provide different recommendations for oral anticoagulation (OAC) therapy, making it difficult for providers to develop treatment plans for this patient population (see Table 1)

Table 1: Current Anticoagulation Guidelines for AF Patients

Sex Category	CHA ₂ DS ₂ -VASc Score						
	0	1	<u>≥</u> 2				
Men	No therapy	Oral anticoagulation, aspirin, or no therapy	Oral anticoagulation				
Women	N/A	Oral anticoagulation, aspirin, or no therapy	Oral anticoagulation				
Men	No therapy	Oral anticoagulation	Oral anticoagulation				
Women	N/A	No therapy	Oral anticoagulation				
	Men Women Men	Men No therapy Women N/A Men No therapy	Men No therapy Oral anticoagulation, aspirin, or no therapy Women N/A Oral anticoagulation, aspirin, or no therapy Men No therapy Oral anticoagulation Oral anticoagulation Oral anticoagulation				

OBJECTIVES

The purpose of this review is to evaluate the net clinical benefit (NCB) when comparing IS risk to that of hemorrhagic complications when prescribing OAC therapy to patients who have at least 1 non-gender (NGR) risk factor for IS or an intermediate CHA₂DS₂-VASc score.

METHODS

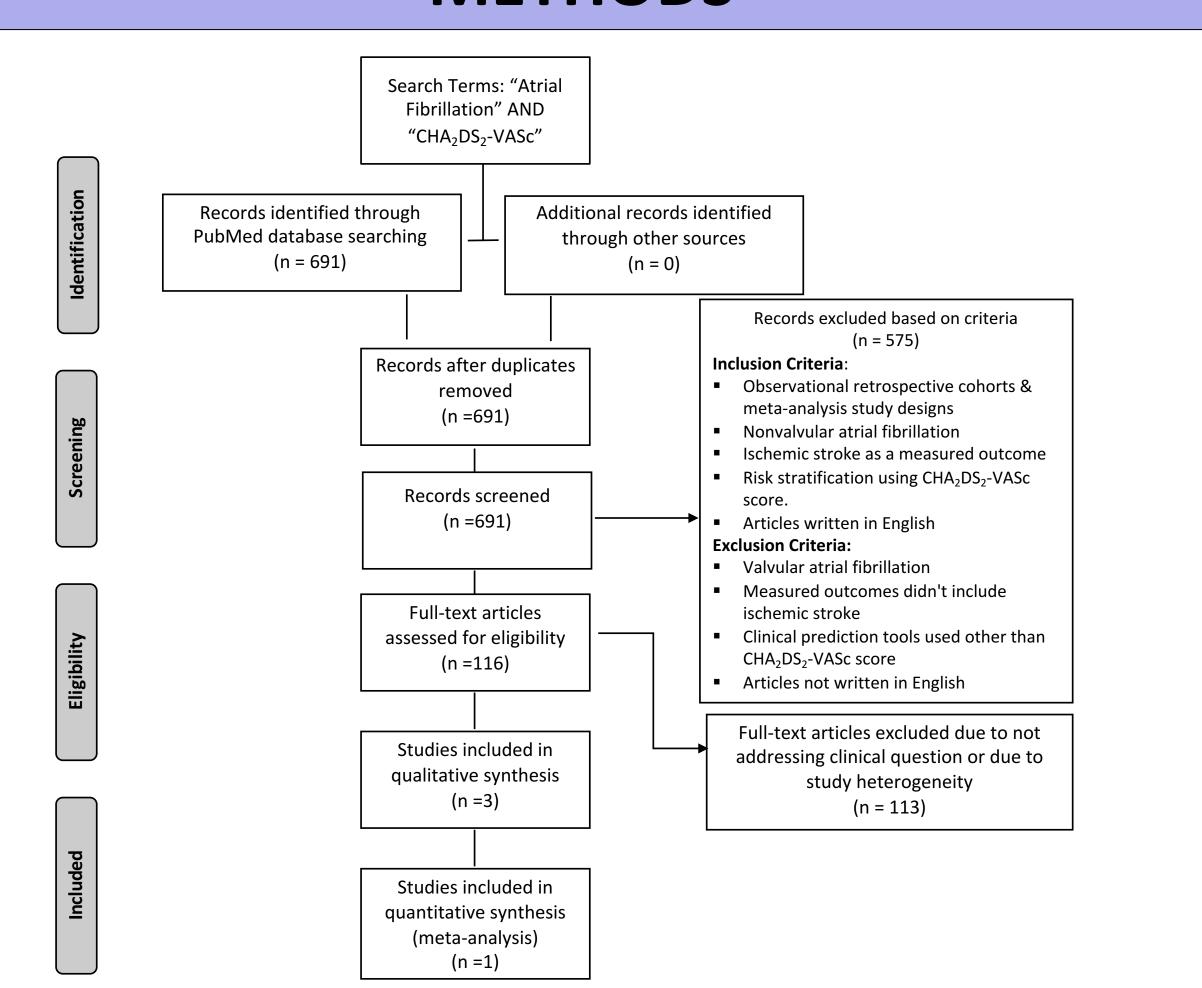


Figure 1: PRISMA Article Selection Criteria

RESULTS

-Study 1-

Should Atrial Fibrillation Patients With 1 Additional Risk Factor of the CHA₂DS₂-VASc Score (Beyond Sex) Receive Oral Anticoagulation?

Objective: To determine whether the presence of a single NGR risk factor increases the annual rate of IS in Taiwanese AF patients aged 20 years and older.

Study Design: Retrospective cohort using data from the National Health Insurance Research Database (NHIRD) regarding AF patients. They were assigned a CHA₂DS₂-VASc score based on their risk factors and outcome of IS was evaluated.

Results: The average annual IS rate for males with a CHA₂DS₂-VASc score of 1 was 2.75% and for females with a CHA₂DS₂-VASc of 2 was 2.55%.

Study Critique: It's the first population based investigation addressing our clinical question setting the stage for research to come. However it could be undermining the annual stroke rate due to inclusion of patients who could have been prescribed antithrombotic therapy 90 days after the diagnosis of AF.

-Study 2-

Should Atrial Fibrillation Patients With Only 1 Nongender-Related CHA₂DS₂₋VASc Risk Factor be Anticoagulated?

Objective: To measure whether a single NGR CHA₂DS₂-VASc risk factor confers a significant risk of IS and if the use of OAC can reduce IS risk with minimal hemorrhagic complications. **Study Design:** Retrospective community cohort investigating adverse outcomes of OAC use in nonvalvular AF patients with just one NGR risk factor in accordance with CHA₂DS₂-VASc risk assessment. Adverse outcomes included rates of IS, intracranial hemorrhage, major extracranial bleeding, and myocardial infarction. Net clinical benefit was calculated using 2 methodologies: Singer et al and Connolly et al formula.

Results: A positive net clinical benefit was measured in favor of vitamin K antagonists when comparing the benefit of IS reduction against the increased risk of ICH in patients with 1 NGR risk factor and nonvalvular AF. This was consistent across both the Singer and Connolly methodologies.

Critique: Real world registry data from a large cohort of consecutive patients recruited and data is complementary to data reported in randomized clinical trials. However, patients are at risk for changes in treatment during follow-up which was impossible to make adjustments for in a multivariable analysis.

-Study 3-

Ischemic Stroke Risk in Patients with Atrial Fibrillation and CHA₂DS₂-VASc score of 1; Systematic Review and Meta-analysis.

Objective: To reduce uncertainty about OAC therapy in patients with a CHA₂DS₂-VASc score of 1 by comparing annual IS rates in AF patients to pre-determined OAC therapy thresholds. **Study Design:** Systematic review and meta-analysis

Results: Patients with a CHA₂DS₂-VASc score of 0 do not meet the treatment threshold for OAC therapy. Patients with a CHA₂DS₂-VASc score of 1 meet the treatment threshold for novel OAC therapy but not warfarin. Patients with a CHA₂DS₂-VASc score of 2 meet the treatment threshold for both novel OAC and warfarin.

Study Critique: Weaknesses of this meta-analysis include wide confidence intervals, significant heterogeneity, several types of bias, and a lack of discussion regarding the quality of the included studies. Strengths of the study include its recent publication date, its large population size, and the variety of countries represented by the data.

RESULTS Cont.

Table 2: Study Characteristics

Study	Study Type	Location	Number of Patients in Study	Study Recommendation
Study 1	Retrospective Cohort	Taiwan	20,838 patients	Recommend anticoagulation therapy in patients
Study 2	Retrospective Cohort	France	2,208 patients	with 1 or more NGR risk factors for IS (CHA ₂ DS ₂ -VASc score of 1 for males and 2 for females)
Study 3	Systematic Review and Meta-Analysis	Studies Included in the Meta-Analysis: Banerjee et al: Denmark Chao et al: Taiwan Friberg et al: Sweden Hobbs et al: United Kingdom Huang et al: China Komatsu et al: Japan Larsen et al: Denmark Lip et al: Multi-Country Siu et al: China Suzuki et al: Japan	Studies Included in the Meta-Analysis: Banerjee et al: 132,372 Chao et al: 186,570 Friberg et al: 182,678 Hobbs et al: 665 Huang et al: 548 Komatsu et al: 332 Larsen et al: 1,603 Lip et al: 5,599 Siu et al: 9,727 Suzuki et al: 3,588	Recommend considering OAC therapy in patients with a total CHA ₂ DS ₂ -VASc score of 1 or higher for males and females.

CONCLUSIONS

Based on our review of the current literature, we found that the presence of even 1 NGR risk factor significantly increases a patient's risk of IS. Therefore, we agree with the European Society of Cardiology (ESC) and the National Institute for Health and Care Excellence (NICE) guidelines that support considering anticoagulation therapy in AF patients with 1 NGR risk factor, and we suggest that the American College of Cardiology, American Heart Association, and the Heart Rhythm Society (ACC/AHA/HRS) guidelines follow suit.

ACKNOWLEDGEMENTS

We would like to thank Dr. Erika Kancler, Ms. Carolyn Schubert, and the James Madison University Graduate School and Physician Assistant Program for their assistance and contributions to our research.

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