PREDICTING STROKE IN ADULTS WITH NON-RHEUMATIC ATRIAL FIBRILLATION: SYSTEMATIC REVIEW OF VALIDATION OF $CHADS_2$ CLINICAL PREDICTION RULE

(Preliminary results)

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Background

Non-rheumatic atrial fibrillation (NRAF) is the most common cardiac arrhythmia, with a population prevalence of 0.5-1%.[1] It results in a fivefold increased risk of thrombotic stroke. Stroke is a major cause of morbidity and mortality worldwide. There are several risk score/clinical prediction rules (CPRs) used to predict thrombotic stroke risk in patients with NRAF. The most well known and implemented risk score is $CHADS_2$. The $CHADS_2$ CPR, derived by Gage et al (2001) [2], involves a 6 point scoring system whereby one point is given for any of: **C**ongestive heart failure, **H**ypertension (or treated hypertension), **A**ge>75, **D**iabetes mellitus and two points for a past history of **S**troke/ TIA. A higher risk score is said to be indicative of a higher risk of stroke. This CPR may be used by clinicians to risk stratify patients with NRAF to inform decisions regarding treatment with anti-platelet or anti-thrombotic treatment.

Introduction

The objective of this study was to assess the performance of the $CHADS_2$ score in terms of whether or not it accurately predicts thrombotic stroke by assessing the predicted: observed ratio across the CHADS2 risk strata.

Methods

Data sources

A systematic electronic search was performed in Pub Med from January 2001 to October 2009 and in EMBASE from January 2001 to October 2009. Search terms included 'venous thromboembolism', 'cerebral infarction', 'stroke', 'atrial fibrillation', 'risk assessment', 'risk adjustment', 'risk factors', 'prognosis', '$CHADS_2$' and 'clinical prediction rule'. Supplementary electronic searches were carried out in Cochrane library, MEDION, Cinahl and Google scholar. Hand searches of relevant articles' references were also performed. No restrictions were placed on language.

Inclusion criteria

Inclusion criteria were adults with NRAF (both inpatients and outpatients) who were risk stratified utilising the $CHADS_2$ CPR and the outcome of interest was thrombotic stroke. Two researchers independently reviewed all retrieved articles and disagreements were resolved by discussion.

Quality assessment

The QUADAS quality analysis score was used to assess the quality of each included study.

Data extraction

Data were extracted directly from individual studies wherever possible. Authors who used the score but did not publish the corresponding data were contacted and the appropriate data was obtained, where possible.

Data synthesis

The initial $CHADS_2$ derivation study was used as the predictive model to which all validation studies were compared. The number of strokes predicted was compared to the observed number of strokes across three strata of risk ($CHADS_2$ 0 (low), 1-2 (medium), >/=3 (high)). In order to calculate the predicted number of strokes according to $CHADS_2$, the proportionate stroke estimate from the original derivation study was calculated. Review Manager 5 software from the Cochrane collaboration was used to perform the analysis, determine heterogeneity and produce forest plots of observed: predicted risk across the $CHADS_2$ risk strata. Patients with NRAF were grouped according to the treatment they were taking i.e. aspirin or warfarin.

Results

Warfarin group

In the warfarin group, five validation studies were included with a total of 28,693 patients.

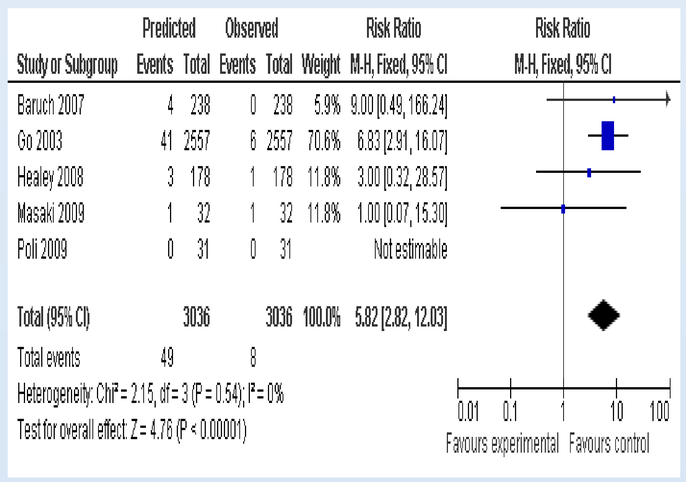

Figure 1. $CHADS_2$ score=0, Low risk, Warfarin group

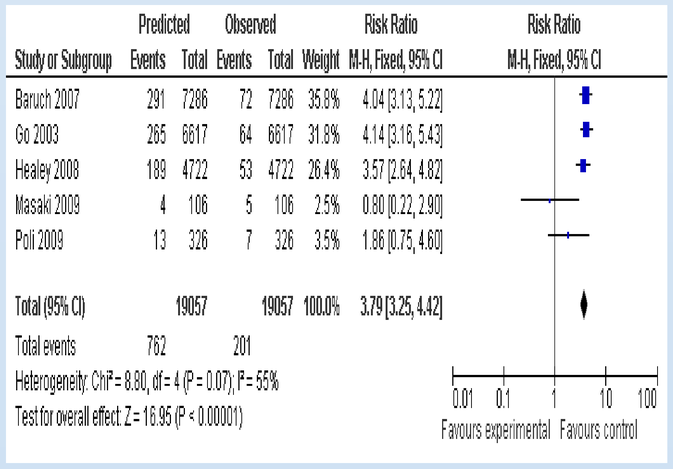

Figure 2. $CHADS_2$ score 1-2, Moderate risk, Warfarin group

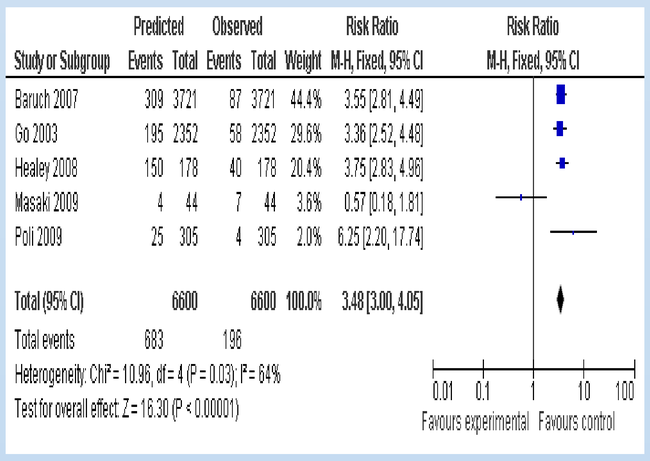

Figure 3. $CHADS_2$ score >/=3, High risk, Warfarin group

In this population all patients were taking warfarin. In order to comment on the predictive ability of the $CHADS_2$ score it is necessary to adjust for effect of warfarin in reducing thrombotic stroke. The relevant literature suggests warfarin reduces thrombotic stroke by approximately 68%. [3] Adjusting for warfarin allows an approximation of the true predictive ability of the $CHADS_2$ score with regard to thrombotic stroke in patients not taking any anti-thrombotic agent.

Results

CHADS2 score	Risk Ratio (RR)	CI
0 (low risk)	1.94	[0.85, 4.43]
1-2 (moderate risk)	1.25	[1.04, 1.51]
>/=3 (high risk)	1.20	[1.00, 1.44]

Table 1. Warfarin group: Risk Ratios adjusted for warfarin

Discussion

This study further validates the $CHADS_2$ tool as a predictor of thrombotic stroke in patients with NRAF. Our work shows that the $CHADS_2$ score tends to over-predict the risk of thrombotic stroke across all risk strata in patients receiving warfarin.

When results are adjusted to account for warfarin treatment the magnitude of over-prediction is reduced but still persists. Considering the adjustment for warfarin treatment should render the group similar to an untreated population, this over-prediction may lead to unnecessary treatment of certain patients with NRAF with anti-thrombotic therapy.

Warfarin therapy, though very effective, can be associated with significant morbidity and requires careful monitoring. Clinicians need to exert caution with uncritical application of this CPR for this reason.

This study is limited by the need to adjust for warfarin, though in real clinical settings many NRAF patients are taking warfarin so this limitation is predictable.

Ongoing work

To date we only have data for two studies which risk stratify using $CHADS_2$ and allow for calculation of annual thrombotic stroke rate in patients with NRAF taking aspirin. Further data is pending which should allow for meta analysis of this subgroup. Further data is also expected for the warfarin group. Quality analysis of included studies is ongoing.

Conclusions

Preliminary results from our study show that the $CHADS_2$ score tends to over-predict the risk of thrombotic stroke across all risk strata.

Clinicians need to make decisions regarding treatment of patients with NRAF on an individual patient basis evaluating the benefits and risks of treatment.

References:

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2.Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ . Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA* 2001;285 (22): 2864–70.

3.Guidelines for the Prevention of Stroke in Patients with Ischemic Stroke or Transient Ischemic attack: A statement for Healthcare professionals from the American Heart Association Council on Stroke. *Stroke* 2006;37:577-617.