PREDICTING STROKE IN ADULTS WITH NON-RHEUMATIC ATRIAL FIBRILLATION: SYSTEMATIC REVIEW OF VALIDATION OF CHADS\textsubscript{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.\textsuperscript{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 scores/clinical prediction rules (CPRs) used to predict thrombotic stroke risk in patients with NRAF. The most well known and implemented risk score is CHADS\textsubscript{2}. The CHADS\textsubscript{2} CPR, derived by Gage et al (2001)\textsuperscript{2}, involves a 6 point scoring system whereby one point is given for any of: Congestive heart failure, Hypertension (or treated hypertension), Age>75, Diabetes mellitus and two points for a past history of Stroke/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.

Methods

Data sources


Quality assessment

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

Inclusion criteria

Inclusion criteria were adults with NRAF (both inpatients and outpatients) who were risk stratified utilising the CHADS\textsubscript{2} CPR and the outcome of interest was thrombotic stroke. Two researchers independently reviewed all retrieved articles and disagreements were resolved by discussion.

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\textsubscript{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\textsubscript{2} 0 (low), 1-2 (medium), >3 (high)). In order to calculate the predicted number of strokes according to CHADS\textsubscript{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\textsubscript{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.

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} score</th>
<th>Risk Ratio (RR)</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (low risk)</td>
<td>1.94</td>
<td>[0.85, 4.43]</td>
</tr>
<tr>
<td>1-2 (moderate risk)</td>
<td>1.25</td>
<td>[1.04, 1.51]</td>
</tr>
<tr>
<td>&gt;3 (high risk)</td>
<td>1.20</td>
<td>[1.00, 1.44]</td>
</tr>
</tbody>
</table>

Table 1: Warfarin group: risk Ratios adjusted for warfarin

Discussion

This study further validates the CHADS\textsubscript{2} tool as a predictor of thrombotic stroke in patients with NRAF. Our work shows that the CHADS\textsubscript{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\textsubscript{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\textsubscript{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