

Stroke Prevention in Patients with Atrial Fibrillation: Inappropriate Anticoagulation and Poor INR Control

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Background

- ◆ Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder. AF can lead to formation of left atrial thrombi, which if dislodged, may result in ischaemic stroke.
- ◆ AF increases the risk for ischaemic stroke nearly 5-fold above the general population risk and approximately 15% of all strokes are attributable to AF.¹
- ◆ Guidelines for stroke prevention in AF patients recommend antithrombotic prophylaxis with an oral anticoagulant (OAC), or antiplatelet thromboprophylaxis (APT). Choice of the agent depends on the risk of stroke for each patient; patients at moderate to high risk of stroke should receive an OAC, while patients at low risk may be managed with APT.²
- ◆ Inadequate anticoagulation can result in stroke in patients with AF; conversely, anticoagulation can also lead to bleeding events.³ Until recently, the vitamin K antagonists (VKAs), primarily warfarin, were the only OACs available. Due to its narrow therapeutic window, warfarin requires close monitoring of blood clotting using the International Normalised Ratio (INR) test.
- ◆ Given the limitations of warfarin, OAC is often underused, and less effective APT is prescribed instead or patients remain untreated.
- ◆ Further, a recent Canadian analysis showed that many well-controlled AF patients are considered "difficult to treat" due to factors such as concomitant chronic disease or increased INR monitoring frequency.⁴

Objectives

- ◆ 1) To measure the appropriateness of AF management by determining the type of antithrombotic prophylaxis (OAC±APT, APT alone, or none) used by AF patients as stratified by stroke risk (using CHADS₂ scores) in developed countries and comparing results to treatment recommended by guidelines.
- ◆ 2) To assess quality of treatment with OAC by time in therapeutic range (TTR) of international normalised ratios (INR).

Methods

Extensive literature searches were conducted using PubMed for:

- 1) AF patients and treatment level categorised by CHADS₂ score
 - ◆ **Limits:** Studies with European, North American and Australian information; human; adults; published 2002-2010.
 - ◆ **Inclusion:** Only studies that delineated OAC±APT, APT alone and untreated in their AF patient population were included.
 - ◆ **Exclusion:** Randomised clinical trials (RCTs), case studies.
 - ◆ **Data reporting:** For each treatment subgroup, the mean percent and range of the AF population within each CHADS₂ score subcategory is presented.
- 2) time in therapeutic range (TTR) for AF patients
 - ◆ **Limits:** published 1997-2010
 - ◆ **Inclusion:** Studies reporting poor INR control among AF patients in "real world" clinical settings in terms of TTR
 - ◆ **Exclusion:** RCTs, case studies.
 - ◆ **Data reporting:** The proportion of AF patients on warfarin poorly controlled are reported as pooled means and ranges for TTR <50% or greater, <60% or greater, or <75% or greater benchmarks.

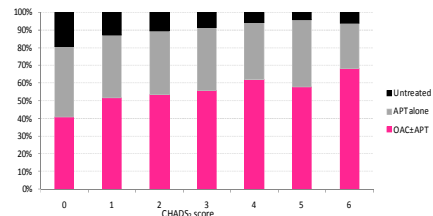
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Results

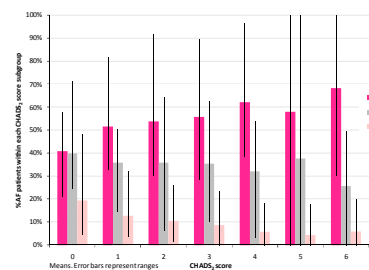
1 AF treatment according to CHADS₂ score

- ◆ Six studies were identified that had information about AF treatment— OAC±APT, APT alone, or no treatment—according to CHADS₂ score.⁵⁻¹⁰
- ◆ In line with guidelines for AF treatment, as CHADS₂ scores increased (i.e., higher risk for stroke), the percentage of patients receiving OAC±APT increased and of patients receiving APT alone, or no treatment, decreased.
- ◆ The variability reported within CHADS₂ score groups was large



2 A large percentage of AF patients receive inappropriate treatment

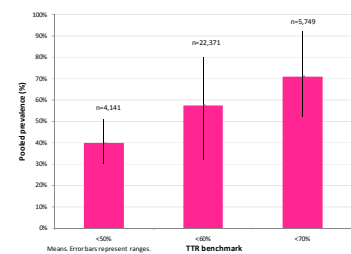
- ◆ However, a large number of moderate to high risk patients (based on CHADS₂ scores >2) who should have received OAC±APT were treated with APT alone (means: 25.6–37.6%; range: 0–100%) or were untreated (means: 4.4–10.6%; range: 0.0–26.3%). Thus, up to 48% of AF patients at high risk for stroke were treated inappropriately.
- ◆ Several factors may contribute to lower than recommended use of OAC, such as risk of bleeds, inconvenience (regular INR monitoring, dietary restrictions), and contraindications.^{11,12}
- ◆ For AF patients with a CHADS₂ score of 0 who should be using APT or no treatment, therapy with OAC±APT by 40.8% (range: 21.4%–57.9%) showed further inappropriate use.



3 AF patients on warfarin were mostly out of therapeutic range

- ◆ Fourteen studies were identified that reported the proportion of patients deemed poorly controlled in terms of TTR.
- ◆ The definition of 'control' varied among studies: 50–60% TTR was the most common benchmark, followed by 70–100% TTR
- ◆ There was no clear relationship between benchmark and prevalence of poor control across studies.
- ◆ Pooling of data that defined poorly controlled anticoagulation to be <50% TTR yielded a proportion of 39.9% of 4,141 patients being inadequately controlled;¹³⁻¹⁵ <60% TTR, 57.5% of 22,371 patients;^{13,14,16-19} and <75% TTR, 71.1% of 5,749 patients.^{13,14,20-22}

- ◆ Of note, in this "real world" top-line analysis, RCTs were excluded, and patient populations may not be comparable due to a number of factors, including patient level (comorbidities, length of time on warfarin, number of concomitant medications), organizational (e.g. frequency of INR testing, method of calculating TTR, practice type) and cultural (regional, economic).



Conclusions and Discussions

- ◆ A large proportion of AF patients at moderate to high risk for stroke do not receive guideline recommended thromboprophylaxis.
- ◆ Among those who do receive OAC thromboprophylaxis, many are not optimally controlled.
- ◆ Widespread adoption of the CHA₂DS₂-VASc score, a more recent and more inclusive risk assessment tool, would likely result in even higher numbers of patients who would be OAC candidates.²³
- ◆ Safe and effective treatments that do not require complicated management (INR monitoring), would likely promote higher compliance with guideline recommendations and patient persistence with prescribed anticoagulant prophylaxis.

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