

Optimal International Normalised Ratio Target For Warfarin Therapy In Asian Patients With Atrial Fibrillation With And Without Mitral Stenosis: A Real-World Cohort Study In Hong Kong

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Introduction

The current recommended international normalised ratio (INR) in guidelines is mainly derived from trials in Western populations. The optimal INR target in Asian patients with atrial fibrillation (AF) remains unclear. This study aimed to determine the optimal INR target for Asian patients receiving warfarin with nonvalvular AF (NVAF) with and without mitral stenosis (MS).

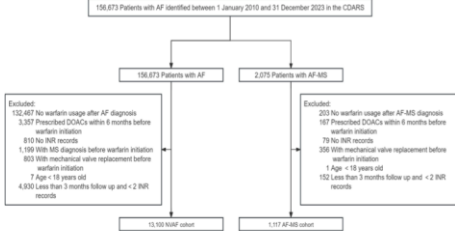


Figure 1. Study Flow Chart

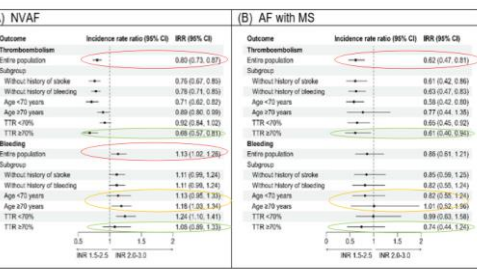


Figure 2. Incidence rate ratio of thromboembolism and bleeding of low versus standard intensity anticoagulation

Results and findings

A total of 11,518 patients with AF without MS and 1,070 patients with AF-MS were identified. The incidence rate of thromboembolism decreased sharply as the INR increased from 1.5-1.99 to 2.0-2.49, both in patients with AF without MS (6.3 to 4.2 events per 100 person-years) and AF-MS (6.1 to 3.2 events per 100 person-years). The lowest bleeding incidence (2.4 events per 100 person-years) in patients with AF without MS was observed at INR of 2.0-2.49, rising to 3.4 events per 100 person-years at INR of 2.5-2.99. In patients with AF-MS, the incidence rate of bleeding remained relatively low when INR was in the range of 1.5-2.99, with a slight increase at 3.0-3.49. Both conditional Poisson regression and GEE models found a significant risk of bleeding among patients with AF without MS when INR≥2.5 but it increased among patients with AF-MS when INR≥3.

Ethical Approval: The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (Reference number: UW 20-114). Informed consent was not necessary for this study as we used anonymised data.

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Methods

This retrospective cohort study included patients newly diagnosed with AF with and without MS between 1 January 2010 and 31 December 2023 using territory-wide electronic health records in Hong Kong. The INR-specific incidence rates of thromboembolism and bleeding were computed using the Rosendaal method. The incidence rate ratio (IRR) was calculated by conditional Poisson regression. The association between repeated INR measurements and outcomes was further evaluated using the generalised estimating equation (GEE) model.

Table Baseline Characteristics

Characteristics	NVAF (n=13100)	AF with MS (n=1070)
Age, years - mean (SD)	70.9 (11.7)	62.6 (10.0)
Sex, male	7289 (55.6)	513 (48.0)
CHA ₂ DS ₂ -VASc score - mean (SD)	2.5 (0.7)	2.0 (0.9)
HAS-BLED score - mean (SD)	2.5 (0.8)	2.0 (0.8)
Concomitant - no. (%)		
Congestive heart failure	2936 (22.4)	240 (22.5)
Renal disease	1316 (10.0)	27 (2.4)
Liver disease	723 (5.5)	21 (1.9)
Cancer	660 (5.0)	42 (3.9)
Hypertension	5388 (41.1)	158 (14.6)
Diabetes	2727 (20.8)	84 (7.8)
Obesity	297 (2.3)	7 (0.6)
History of thromboembolism	2077 (15.8)	567 (52.0)
History of bleeding	1848 (14.1)	181 (16.9)
History of myocardial infarction	1073 (8.2)	41 (3.7)
Medication in the last three months		
Aspirin	7000 (53.4)	303 (27.1)
Antiplatelet	1179 (9.0)	57 (5.1)
NOACs	2311 (17.6)	159 (14.8)
Antithrombotic	1053 (7.9)	137 (12.6)
Calcium channel blocker	6703 (51.2)	331 (29.8)
β-blocker	7788 (59.4)	484 (44.2)
ACE/ARB	6279 (47.9)	331 (29.8)
PPV	3659 (27.9)	258 (23.1)

Abbreviations: NVAF, non-valvular atrial fibrillation; AF, atrial fibrillation; MS, mitral stenosis; SD, standard deviation; NOACs, non-vitamin K-dependent oral anticoagulants; ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PPV, proton pump inhibitor.

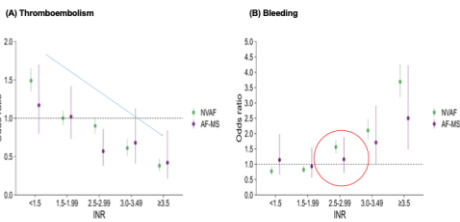


Figure 3. Association between INR value and risk of thromboembolism and bleeding

Conclusions

INR 1.5-2.5 is non-inferior to INR 2.0-3.0 for Asian patients with NVAF and an INR range of 2.0- 2.49 may be an optimal target. Standard-intensity anticoagulation (INR 2.0-3.0) is still preferable for Asian patients with AF-MS, considering the low risk of bleeding at INR of 2.5-2.99.

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