Heart, Lung and Circulation (2017) xx, 1–4
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2017.11.009

BRIEF COMMUNICATION

Identifying Warfarin Control With Stroke and Bleed Risk Scores

Nijole Bernaitis, BPharm [a,b], Chi Keong Ching, MBBS [c], Tony Badrick, PhD [d], Shailendra Anoopkumar-Dukie, PhD [a,b*]

[a]Menzies Health Institute and Quality Use of Medicines Network, Queensland, Griffith University, Brisbane, Qld, Australia
[b]School of Pharmacy & Pharmacology, Griffith University, Brisbane, Qld, Australia
[c]Cardiology Department, National Heart Centre Singapore, Singapore
[d]RCPA Quality Assurance Programs, New South Wales, Australia

Received 2 August 2017; received in revised form 25 October 2017; accepted 19 November 2017; online published-ahead-of-print xxx

Warfarin decreases stroke risk in atrial fibrillation patients, with efficacy and safety impacted by the quality of warfarin control, as measured by time in therapeutic range (TTR). Stroke and bleed risk scores are calculated prior to commencing warfarin, so it would be beneficial if these scores also identified likely warfarin control. Some studies have investigated $CHADS_2$, CHA_2DS_2VASc, and HASBLED individually for this purpose, but application of all scores to diverse ethnic populations and at sites with differing overall control has not been investigated. The aim of this study was to determine if these commonly used risk scores could identify poor warfarin control.

Retrospective data was collected for non-valvular AF patients receiving warfarin between January and June 2014 in Australia and Singapore. Patient data was used to calculate TTR and risk scores. Mean TTR was used for analysis and comparison to categorised scores.

There were 3199 patients in Australia and 1171 in Singapore. At both sites, mean TTR decreased according to HASBLED category, and there was a statistically higher percentage of patients achieving a TTR $> 65\%$ in the low HASBLED category. The association between HASBLED scores and TTR was independent of lower dosing in higher risk patients, particularly in Australia. No significant differences were found in mean TTR according to $CHADS_2$ at either site. Time in therapeutic range significantly decreased according to high CHA_2DS_2VASc category in Singapore, but no differences were found in Australia.

Of the bleed and stroke risk models, HASBLED is most suitable to identify a patient's potential TTR and ability to achieve TTR $> 65\%$. A high HASBLED score may assist prescribers in determining potential suitability to warfarin, and assist prescribers in deciding on the most suitable anticoagulant for patients.

Keywords Warfarin • Risk models • Time in therapeutic range

Introduction

Anticoagulant therapy has proven benefits in decreasing stroke risk in patients with atrial fibrillation (AF) [1]. Warfarin has long been used for this indication but there are now other non-vitamin K anticoagulant (NOAC) options, with clinicians needing to decide on the most suitable anticoagulant for individuals. Warfarin requires ongoing monitoring of International Normalised Ratio (INR) with time in therapeutic range (TTR) a recommended measure for quality of warfarin management [2]. Variations in warfarin TTR influences the efficacy and safety of warfarin, and has also been demonstrated to influence the comparative outcomes of warfarin to the NOACS [3]. Numerous patient factors including likelihood of achieving good warfarin control needs consideration in choosing suitable therapy.

*Corresponding author at: School of Pharmacy & Pharmacology, Gold Coast Campus, Griffith University, Qld 4222, Australia. Tel.: +61 07 555 27725, Fax: +61 07 555 28804., Email: s.dukie@griffith.edu.au

Please cite this article in press as: Bernaitis N, et al. Identifying Warfarin Control With Stroke and Bleed Risk Scores. Heart, Lung and Circulation (2017), https://doi.org/10.1016/j.hlc.2017.11.009

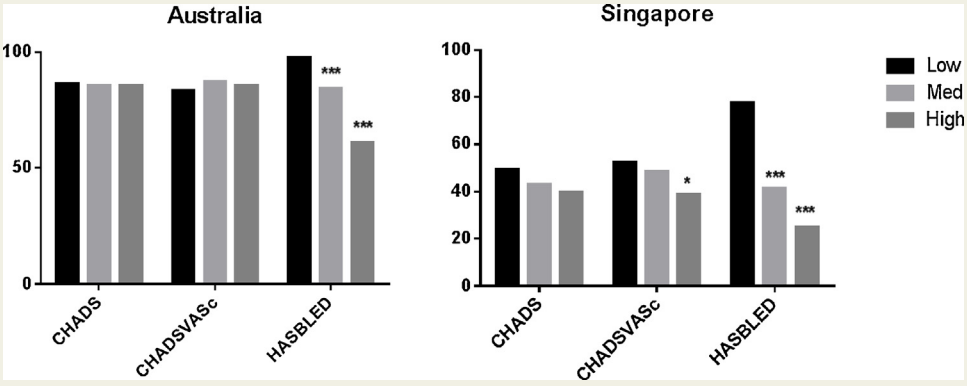

Figure 1 Percentage of patients achieving a TTR > 65% in Australia and Singapore for each risk score category. Significance defined as *p < 0.05, **p < 0.01, and ***p < 0.001.
Abbreviation: TTR = time in therapeutic range.

Risk scores are widely used to assess stroke and bleed risk in patients with AF, namely $CHADS_2$[1] and/or CHA_2DS_2-VASc[2] scores for stroke, and HASBLED[3] score for bleeds [4]. Recently, studies have investigated the ability of these scores to perform a dual purpose of identifying warfarin control. Poor warfarin control and high risk scores have been demonstrated for $CHADS_2$ [5] and HASBLED [6] scores, but these studies involved only individual scores and did not assess TTR with other risk models. Hellyer et al. [7] demonstrated decreasing TTR across increasing CHA_2DS_2VASc and HASBLED scores, however this was in an American population with relatively low mean TTR i.e. <60%. Therefore, the aim of this study was to determine if commonly used risk scores, i.e. $CHADS_2$, CHA_2DS_2VASc, or HASBLED, could identify poor warfarin control in diverse ethnic populations and at sites with differing overall control.

Methods

Ethics approval was obtained from SingHealth Centralised Institutional Review Board (CIRB 2015/2435) and Griffith University Human Research Ethics Committee (PHM/08/15/HREC). A retrospective analysis of non-valvular AF patients receiving warfarin was conducted between January and June 2014 at Sullivan Nicolaides Pathology Queensland, Australia and the National Heart Centre in Singapore. Data collected included INR test dates/results, patient demographics, medical history, concurrent medications, and warfarin doses. Risk scores were calculated as of June 2014, and each patient categorised into low-, moderate-, and high-risk groups. Time in therapeutic range was calculated using the Rosendaal method with mean TTR and weekly warfarin dose used for analysis and comparison across risk categories. Comparisons were made using ordinary analysis of variance through non-parametric methods, including Kruskal-Wallis test, Dunn's multiple comparisons test, and chi-squared test. Data were analysed using GraphPad InStat version 3 and figures drawn using GraphPad Prism version 6.0.

[1] **$CHADS_2$** = Congestive Heart failure (1 point), Hypertension (1 point), Age ≥ 75 years (1 point), Diabetes mellitus (1 point), Stroke/TIA (2 points).
[2] **CHA_2DS_2VASc** = Congestive Heart failure (1 point), Hypertension (1 point), Age ≥ 75 years (2 points), Diabetes mellitus (1 point), Stroke/TIA (1 point), Vascular disease (1 point), Age 65–74 years (1 point), Female sex (1 point).
[3] **HASBLED** = Hypertension (1 point), Abnormal renal/liver function (1-2 points), Stroke history (1 point), Bleeding history or predisposition (1 point), Labile INR (1 point), Age > 65 years (1 point), Drugs/Alcohol concomitantly (1–2 points).

Results

The study included 3199 patients in Australia and 1171 in Singapore, with a higher proportion of males at both sites (52.3% in Australia, 60.4% in Singapore). The mean age of patients was 77.2 ± 9.1 years in Australia and 69.7 ± 10.0 years in Singapore, and the mean TTR was 82.3 ± 15.6% and 57.7 ± 34.2% respectively. In Australia, no significant differences were found in mean TTR according to $CHADS_2$ or CHA_2DS_2VASc category, but mean TTR significantly decreased according to HASBLED category with no significant difference in doses according to HASBLED category (Table 1). In Singapore, significant differences were found in mean TTR across all HASBLED categories and with high CHA_2DS_2VASc, with a non-significant trend to decreasing mean TTR according to $CHADS_2$. At this site all risk scores were associated with a significant decrease in warfarin dose between the low-risk and both the medium- and high-risk categories. At both sites, the percentage of patients achieving a TTR >65% was statistically higher for low HASBLED scores (Figure 1).

Discussion

The quality of warfarin control impacts therapy, with superior outcomes from higher TTRs. Identifying patients likely

Please cite this article in press as: Bernaitis N, et al. Identifying Warfarin Control With Stroke and Bleed Risk Scores. Heart, Lung and Circulation (2017), https://doi.org/10.1016/j.hlc.2017.11.009