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Real-World Direct Oral Anticoagulants Experience in Atrial Fibrillation: Falls Risk and Low Dose Anticoagulation are Predictive of both Bleeding and Stroke Risk

Running Head: Real-World Experience of DOAC in AF

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Abstract

Background: Clinical trials have demonstrated that direct oral anticoagulants (DOAC) are non-inferior to vitamin K antagonist for stroke prevention in non-valvular atrial fibrillation (AF) with comparable safety outcomes; however real-world Australian data is limited.

Aims: We aim to evaluate local real-world DOAC use focusing on safety, particularly in high-risk patients.

Methods: A retrospective evaluation of 658 patients commenced or continued on DOAC between September 2013-September 2016 for non-valvular AF at Northern Hospital, a tertiary hospital in Victoria, Australia was performed.

Results: Factor Xa inhibitors were more commonly prescribed than direct thrombin inhibitor (83.3% vs 16.7%) for AF management. The median patient age was 75 years. The rate of clinically significant bleeding on anticoagulation was 3.13 per 100 person-years (including four deaths) with risk factors including history of bleeding (HR 3.52, 95% CI 1.22-10.17), concurrent antiplatelet therapy (HR 2.62, 95% CI: 1.11-6.20) and high falls risk (HR 2.76, 95% CI: 1.26-6.08). Patients on low dose DOAC had significantly higher bleeding risk compared to those on full dose (5.05 vs 1.82 per 100 person-years). The rate of thrombotic stroke despite anticoagulation was 1.34 per 100 person-years with risk factors including low dose anticoagulation (p=0.034), high falls risk (p=0.046) and previous stroke (p=0.028).

Conclusions: DOAC use in real-world Australian practice is safe and effective, consistent with international data. Low dose anticoagulation and falls risk are associated with increased bleeding

and thrombotic risk demonstrating overlapping risk factors. Careful individualised patient risk assessment is still required as low dose anticoagulation is not without risks.

Key Words

Anticoagulants; Atrial fibrillation; Thrombosis; Haemorrhage; Frailty

INTRODUCTION

Atrial fibrillation (AF) is a prevalent chronic disease in Australia affecting 5.4% of adults age ≥55 years, with significant risk of embolic stroke and consequent morbidities and mortalities as well as healthcare burden, estimated to be over AUD $874 million a year [1,2]. The mainstay of treatment for AF is stroke prevention with anticoagulation and the introduction of direct oral anticoagulants (DOACs) has revolutionised anticoagulation management. DOACs are currently the treatment of choice in many patients with non-valvular AF, with more than 60% of patients being commenced on DOACs[3], largely because of the ease of oral administration without the requirement for regular drug level monitoring.

The seminal clinical trials have shown that DOACs are non-inferior to vitamin K antagonists in stroke prevention efficacy and at least as safe as warfarin from the major bleeding safety perspective [4-7] . In addition, an increasing body of literature including large international real-world analysis suggest improved safety profile for some DOACs e.g. apixaban and dabigatran when compared to warfarin [8-14]. However, the challenge faced by clinicians remains selecting the optimal choice and dose of DOAC in order to maintain the delicate equilibrium between thrombosis and bleeding risk in patients, especially those with multiple medical co-morbidities. One added advantage of DOACs is the

availability of lower dose option for patients with relevant co-morbidities such as advanced age and renal impairment, although this adds another layer of complexity to clinical risk assessment [15,16]. Criteria for dose reduction are outlined in the Australian Medical Handbook (AMH) guidelines for prescribing DOACs based on age, weight and renal function [15,16].

Nonetheless, there remains limited local data regarding the efficacy and safety of DOACs in Australian real-world practice particularly in high-risk groups such as those with renal impairment and the geriatric population, which are not well represented in clinical trials. Unique to our institution, all prescriptions of DOACs require a computer stewardship program approval prior to supply of medications. This program aims to guide prescribers according to the Pharmaceutical Benefits Scheme (PBS) and AMH guidelines [15,16]. In this audit, we aim to evaluate the local real-world use of DOACs with a focus on safety outcomes particularly in high-risk patient groups.

MATERIALS AND METHODS

A retrospective evaluation of patients continued or commenced on DOACs for AF between September 2013 and September 2016 at a tertiary teaching hospital in Melbourne servicing the Northern suburbs. Patients were identified using the 'iGuidance' program, a health service wide stewardship program to assist with appropriate prescription of DOACs. Approval numbers generated from the system are mandatory for inpatient, discharge and outpatient scripts of DOACs, allowing the capture of the majority of patients being prescribed or continuing on DOACs through the hospital. Patients who have contraindications or do not meet criteria for prescription were discussed with Clinical Haematology for suitability of DOACs, and in some cases, approvals were given outside

of the recommended guidelines. This project was registered with the Northern Health Governance Office as a Quality Improvement & Innovation project (ALR23.2017).

Patient medical records were retrospectively audited between August 2016 and February 2018 – hospital presentations, outpatient attendances and external correspondence were reviewed. Patient demographics were collected along with relevant safety data of major complications while on anticoagulation. Clinically significant bleeding and thrombotic stroke are the primary endpoints for this study. Patients who did not re-present to our medical service or have subsequent documentation of thrombotic stroke or bleeding in our medical records, were considered not to have had an event.

Full dose anticoagulation was defined as rivaroxaban 20mg daily, apixaban 5mg twice daily (BD) and dabigatran 150mg BD respectively, with all other doses (rivaroxaban 15mg daily, apixaban 2.5mg BD and dabigatran 110 mg BD) classified as low dose. Bleeding complications were evaluated based on the International Society on Thrombosis and Haemostasis (ISTH-SSC) bleeding assessment tool with events scoring 3 or more points considered clinically significant [17]. Ischaemic strokes were defined by imaging or clinical assessment by a consultant neurologist, and transient ischaemic attacks were excluded. Falls risks were evaluated using the "The Northern Hospital Modified Stratify Falls Risk Assessment Tool", a validated local adaptation of the St Thomas' Risk Assessment Tool and Modified St Thomas' Risk Assessment Tool with a score of ≥3 being classified as high falls risk (Table 1)[18,19].

Statistical Analysis

Descriptive statistics were prepared to present the number of clinically significant bleeding or thrombotic stroke events. Counts and frequencies were used to present categorical variables, while continuous variables were presented as median and range (minimum to maximum). The differences in baseline characteristics and the risk of clinically significant bleeding or thrombotic stroke events were evaluated using the Chi-square test, or Fisher's Exact test on occasions of frequencies of less than 5. Time to event analysis was conducted with the two primary endpoints considered separately, with mortality treated as a competing risk to the primary endpoints. Due to the consideration of a competing risk event of mortality, cumulative incident curves were prepared to compare groups. Patients who were alive or lost to follow-up before an event were censored at the date of last follow-up. Univariate and multivariable cox proportional hazards competing risk regression analyses was used to identify and quantify associations between clinically significant bleeding or stroke and patient/clinical variables. The variables identified with a p-value of less than 0.20 on univariate analysis were included in the multivariable model and manual backwards step-wise regression techniques were employed to identify those variables independently associated with clinically significant bleeding or stroke. A two-tailed p-value of less than 0.05 was considered to indicate statistical significance. STATA statistical analysis software (version 12.1) was used (StataCorp, College Station, TX, USA).

RESULTS

A total of 683 patients were identified as having an 'iGuidance' approval generated for DOAC use for the treatment of AF during the included period – 25 patients who had no documented evidence that a DOAC was subsequently prescribed to them were excluded. The median duration of follow-up

period was 17 months (range: 3-34), and the demographic variables of the 658 included patients are outlined in Table 2. Overall, factor Xa inhibitors, rivaroxaban (43.9%) and apixaban (39.4%) were more commonly prescribed than direct thrombin inhibitor, dabigatran (16.7%). The overall median age of the patients was 75 years (range: 31-96), comparable across all three DOACs (apixaban 78 years, rivaroxaban 72 years, dabigatran 76 years) with an even split of genders. The median CHA_2DS_2-VASC score was 4. Low dose anticoagulation was prescribed in 43.3% with apixaban being the most popular option for low dose anticoagulation.

Patients classified as high falls risk (scoring ≥3 on the modified falls assessment tool) made up 24.6% (n=162) of patients with 64.2% (n=104) of them being prescribed low dose anticoagulation, representing 36.5% (104/285) of the total low dose population. Patients on low dose anticoagulation were also older (81 years vs 69 years; p= <0.001), more likely to have renal impairment (p=<0.001) and higher CHA_2DS_2-VASC score (p=<0.001). From the total study population, 30.2% (n=199) of patients did not have all the required data to retrospectively assess for suitability of DOAC dosing as per guidelines due to no recorded weight in the medical history.

Of the 459 patients whose dose could be analysed against the AMH guidelines, 63.8% (n=293) were on the recommended dose. Ten patients were on DOACs despite lower calculated creatinine clearance than recommended by the guidelines of whom 50% (n=5) had clinically significant bleeding. Of the assessed 209 patients on low dose anticoagulation, 30.1% (n=138) did not meet criteria for dose reduction – there was 3.6% (n=5) significant bleeding complications and 2.2% (n=3) episodes of thrombotic stroke. 7.2% (n=18) of patients who met criteria for dose reduction but were on full dose anticoagulation did not report any complications.

Clinically Significant Bleeding

There were 26 (4.0%) episodes of clinically significant bleeding (ISTH-SSC bleeding assessment score of ≥3[17]) while on anticoagulation with an overall rate of 3.13 per 100 person-years. On univariant analysis (Table 3), significant risk factors for clinically significant bleeding included low dose anticoagulation (p=0.023), reduced renal function (eGFR 30-59 ml/min/1.73m^2) (p=0.042), history of bleeding (p=0.017), high falls risk (p=0.032) and CHA_2DS_2-VASC score ≥4 (p=0.018). Interestingly, the event rate of patients on low dose DOACs was higher, 5.05 per 100 person-years compared to 1.82 per 100 person-years for full dose (Figure 1a). There was also a trend towards increased risk with concurrent antiplatelet therapy (p=0.05). Upon multivariable analysis, only four variables retained their independent statistically significant association: history of bleeding (Hazard ratio (HR) 3.52, 95% Confidence interval (CI): 1.22-10.17, p=0.011), concurrent antiplatelet therapy (HR 2.62, 95% CI: 1.11-6.20, p=0.028) and high falls risk (HR 2.76, 95% CI: 1.26-6.08, p=0.011).

The initial 3 months on anticoagulation conferred the highest rate of bleeding complications with an event rate of 7.80 per 100 person-years. For patients who did not bleed in the first 3 months the rate of bleeding decreased significantly to 2.07 per 100-person-year. No significant difference was observed in bleeding rates between the different DOACs.

Thrombotic stroke

There were 11 (1.7%) episodes of thrombotic stroke despite anticoagulation with an event rate of 1.34 per 100 person-years (Figure 1b). On univariate analysis, risk factors for stroke included low dose anticoagulation (p=0.034), high falls risk (p=0.046) and previous stroke (p=0.028) (Table 4). Of the 17.3% (n=114) of patients on concurrent antiplatelet therapy there were no episodes of stroke

captured. Multivariable analysis could not be conducted due to the low numbers of thrombotic stroke and a lack of variability in association between risk factors and the primary endpoint leading to convergence issues for the multivariable models. There was only one episode of venous thromboembolism on anticoagulation captured in a patient on full dose rivaroxaban with recurrent unprovoked venous thromboembolism. No difference in rates of stroke was observed between the DOAC types.

Active Malignancy

There were 40 patients with known active malignancy at the time of 'iGuidance' approval generation with a further 2 patients subsequently diagnosed with malignancy. One patient on low dose dabigatran in the context of metastatic prostate cancer had clinically significant gastrointestinal bleeding. There were no thrombotic complications captured.

All-cause Mortality

There were 33 (5%) deaths captured during the follow up period of this study including four (0.6%) due to bleeding complications. These four patients were all over the age of 70 and on low dose anticoagulation. Two had contraindications to DOAC prescription according to AMH guidelines, one due to severe renal impairment and one due to Child Pugh C liver cirrhosis. There was no mortality due to thrombotic stroke.

DISCUSSION

To the best of our knowledge, this study is the first audit of real-world DOAC use in non-valvular AF in Australia. We confirm that DOACs are a safe and effective anticoagulant in the Australian population. Thrombotic (1.34 per 100 person-years) and bleeding (3.13 per 100 person-years) complication rates seen in our institution were similar to the seminal clinical trials [4-7] and consistent with other international real-world data [8-10]. In our population, we did not observe a significant difference in safety profiles between rivaroxaban, apixaban and dabigatran. We were able to analyse the appropriateness of DOAC prescription in 459 patients of whom 36.2 % of patients were not appropriately dosed. This rate appears to be higher than the recent audit by Sato et al who reported 23% of patients in their study receiving an inappropriate dose [20]. Of note, patients who did not meet DOAC prescription criteria had significant bleeding rates (5/10) including two deaths.

The primary challenge for treating clinicians is the difficulty of balancing the thrombosis and bleeding risk in patients, complicated by concurrent medical co-morbidities. This juxtaposition is highlighted in AF by the number of overlapping risk factors seen in both the CHA_2DS_2-VASC score [21] used to estimate annual stroke risk and the HAS-BLED score [22] used to stratify major bleeding risk. This study suggests that the vulnerable patients at highest risk of thrombotic complications are also those at highest risk of bleeding. While the patients with higher CHA_2DS_2-VASC score require anticoagulation due to their incremental annual stroke risk, the bleeding rate was also significantly higher in our patients with CHA_2DS_2-VASC score ≥4 (HR 3.66, CI 1.25-10.73, p=0.018). Hence, careful individual risk assessment is required to balance bleeding and thrombotic complications in these high-risk patients.

To address this delicate balance, low dose anticoagulation is widely used by physicians as a compromise particularly in the elderly and frail populations. Low dose anticoagulation was used in

43.3% of our patients receiving anticoagulation. Contrary to the perception that low dose anticoagulation is a safer option, our data suggests that low dose anticoagulation is associated with both increased bleeding (p=0.023) and thrombotic stroke (p=0.034) when compared to those receiving full dose anticoagulation. One reason for this may be that low dose anticoagulation is more commonly used in high-risk patients with co-morbidities such as older age, renal impairment and higher falls risk. Importantly, this highlights that low dose anticoagulation does not mitigate bleeding risk in these individuals. There remains conflicting evidence in international real-world studies regarding the safety of low dose DOACs [23,24]. Ellis et al reported higher overall bleeding rate in their dabigatran 110mg patients compared to 150mg (2.6 vs 1.5 per 100 patient-years), rivaroxaban 15mg compared to 20mg (4.2 vs 2.5 per 100 patient-years) and apixaban 2.5mg compared to 5mg (6.1 vs 2.5 per 100-patient years) [23] while the Danish observational cohort study by Nielsen et al comparing low dose DOACs with warfarin found similar rates of thrombotic complications with lower bleeding rates in reduced dose dabigatran but not apixaban or rivaroxaban [9]. Other studies have found similar complication rates in both full and low dose DOACs regardless of appropriateness of dosing [20,25]. Ultimately the evaluation of the risk of patient being on or off anticoagulation should be made independent of the dose of anticoagulation prescribed as low dose anticoagulation does not negate the bleeding or thrombotic risks in these patients.

Falls risk has been shown to be closely associated with frailty, a contributing factor to higher bleeding risk [26-28]. We note that patients who have a high falls score (score >3) had a higher rate of clinically significant bleeding (HR 2.76, 95% CI: 1.26-6.08, p=0.011). The same cohort of patients also had a significantly higher rate of thrombotic stroke despite anticoagulation (HR 3.60, 95% CI: 1.03-12.61, p=0.046). This again demonstrated the complexity of anticoagulation decisions for high risk

populations and the need for careful patient selection and individualised decision making in discussion with patients.

This study acknowledges the limitations of sample size and potential biases as well as confounders of its retrospective nature including the limitation and quality of information documented on medical records. We note the possibility that some patients may have re-presented elsewhere with complications without being captured by our health service suggesting safety outcomes may be underreported. Our patients are those requiring hospital care which may be skewed towards a sicker population with more co-morbidities, compared to DOAC users in the wider community. Similarly, we note that our patients receiving low dose anticoagulation disproportionally received apixaban and dabigatran, though we note these factors did not influence the result on multivariate analysis. Nevertheless, our study provides an insight into the use of DOACs in real-world patients, not typically prevalent in clinical trials.

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CONCLUSION

In summary, this study provides the first comprehensive overview of DOAC use in non-valvular AF in Australia. While the real-world Australian practice is comparable to international safety data, a number of challenges for clinicians have also been raised. Specifically, we have demonstrated that patients with thromboembolic risk often concurrently have higher bleeding complications. While low dose anticoagulation may be a suitable alternative for some high-risk patients, it should not be considered the default option for all as both bleeding and thrombotic risk are higher. Careful individualised patient risk assessment is required to ensure that the appropriate dose is prescribed.

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Figure 1. Cumulative incidence of key safety outcomes in patients on low dose vs full dose DOAC
a) Cumulative incidence of clinically significant bleed
b) Cumulative incidence of stroke

Table 1. The Northern Hospital modified STRATIFY falls risk assessment[18]

Criteria	Score
Fall during current admission	3
Fall within last 12 months	1
Altered mental state	1
Mobility	1
Impaired balance	1
Age ≥80	1
Requiring frequent toileting	1
Visual impairment affecting everyday function	1
Drug/Alcohol related problems	1

Total Score ≥3 = high falls risk

Table 2. Demographics of study population

	Total study population	Full dose DOAC	Low dose DOAC	p-value †
N (%)	658	373 (56.7%)	285 (43.4%)	
Male	51.5% (n=339)	57.9% (n=216)	43.2% (n=123)	**<0.001***
Age (median, range)	75 (31-96)	69 (31-91)	81 (45-96)	**<0.001***
Rivaroxaban	43.9% (n=289)	61.6% (n=230)	20.7% (n=59)	**<0.001***
Apixaban	39.4% (n=259)	29.0% (n=108)	53.0% (n=151)	**<0.001***
Dabigatran	16.7% (n=110)	9.45 (n=35)	26.3% (n=75)	**<0.001***
CHA_2DS_2-VASc score (median, range)	4 (0-9)	3 (0-9)	5 (1-9)	**<0.001***
Estimated glomerular filtration rate (eGFR) 30-<60 (ml/min/1.73m^2)	32.2% (n=212)	20.4% (n=76)	47.7% (n=136)	**<0.001***
eGFR <30 (ml/min/1.73m^2)	0.6% (n=4)	0% (n=0)	1.4% (n=4)	
High falls risk	24.6% (n=162)	15.5% (n=58)	36.5% (n=104)	**<0.001***
Concurrent antiplatelet	17.3% (n=114)	15.5% (n=58)	19.6% (n=56)	0.168
ALT‡>3x upper limit of normal	1.2% (n=8)	0.5% (n=2)	2.1% (n=6)	0.069

† p-value compares the patients on full dose to low dose anticoagulation

‡ alanine aminotransferase

* clinically significant p-value <0.05

Table 3. Univariant analysis of risk factors for clinically significant bleeding

Variable	Number of patients	Clinically significant bleed	HR (95% CI)	p-value
Overall	658	4.0% (n=26)		
Age:				
<65	121	0.8% (n=1)	1	
65-74	184	3.3% (n=6)	3.86 (0.46-32.02)	0.211
75+	353	5.4% (n=19)	6.89 (0.92-51.74)	0.061
Gender:				
Male	339	4.1% (n=14)	1	
Female	319	3.8% (n=12)	0.89 (0.41-1.93)	0.770
Drug:				
Rivaroxaban	289	3.5% (n=10)	1	
Apixaban	259	4.6% (n=12)	1.43 (0.62-3.32)	0.405
Dabigatran	110	3.6% (n=4)	1.06 (0.34-3.35)	0.919
Low Dose:				
No	373	2.4% (n=9)	1	
Yes	285	**6.0% (n=17)**	**2.59 (1.14-5.85)**	**0.023***
eGFR (ml/min/1.73m^2):				
Normal (90+)	114	1.8% (n=2)	1	
Mild (60-89)	326	2.5% (n=8)	1.42 (0.30-6.76)	0.658

Moderate (30-59)	212	**7.5% (n=16)**	**4.75 (1.06-21.31)**	**0.042***
Severe (<30)	4	0.0% (n=0)	-	-
Unknown	2	0.0% (n=0)	-	-
Previous stroke:				
No	511	3.7% (n=19)	1	
Yes	147	4.8% (n=7)	1.23 (0.51-2.97)	0.648
Previous bleeding history:				
No	625	3.5% (n=22)	1	
Yes	33	**12.1% (n=4)**	**3.69 (1.26-10.79)**	**0.017***
Falls risk:				
No	496	3.0% (n=15)	1	
Yes	162	**6.8% (n=11)**	**2.36 (1.08-5.18)**	**0.032***
CHA_2DS_2-VASC				
<4	255	1.6% (n=4)	1	
4+	403	**5.55 (n=22)**	**3.66 (1.25-10.73)**	**0.018***
Concurrent antiplatelet:				
No	543	3.3% (n=18)	1	
Yes	114	7.0% (n=8)	2.29 (1.00-5.25)	0.050

* clinically significant p-value <0.05

Table 4. Univariant analysis of risk factors for thrombotic stroke

Variable	Number of patients	Thrombotic Stroke	HR (95% CI)	p-value
Overall	658	1.7% (n=11)		
Age:				
<65	121	1.7% (n=2)	3.56 (0.37-34.41)	0.273
65-74	184	0.5% (n=1)	1	-
75+	353	2.3% (n=8)	6.05 (0.88-41.67)	0.067
Gender:				
Male	339	1.8% (n=6)	1	
Female	319	1.6% (n=5)	1.03 (0.30-3.54)	0.967
Drug:				
Rivaroxaban	289	1.7% (n=5)	1	
Apixaban	259	1.5% (n=4)	1.21 (0.31-4.73)	0.786
Dabigatran	110	1.8% (n=2)	1.09 (0.21-5.61)	0.916
Low Dose:				
No	373	0.8% (n=3)	1	
Yes	285	**2.8% (n=8)**	**4.03 (1.11-14.66)**	**0.034***
eGFR (ml/min/1.73m^2):				
Normal (90+)	114	1.8% (n=2)	1	
Mild (60-89)	326	1.8% (n=6)	1.18 90.25-5.66)	0.833
Moderate (30-59)	212	1.4% (n=3)	1.33 (0.25-7.21)	0.738

Severe (<30)	4	0.0% (n=0)	-	-
Unknown	2	0.0% (n=0)	-	-
Previous stroke:				
No	511	1.0% (n=5)	1	
Yes	147	4.1% (n=6)	3.69 (1.15-11.78)	0.543
Previous bleeding history:				
No	625	1.6% (n=10)	1	
Yes	33	3.0% (n=1)	2.08 (0.26-16.53)	0.489
Falls risk:				
No	496	1.2% (n=6)	1	
Yes	**162**	**3.1% (n=5)**	**3.60 (1.03-12.61)**	**0.046***
CHA_2DS_2-VASC				
<5	397	0.8% (n=3)	1	
5+	261	**3.1% (n=8)**	**5.15 (1.32-20.06)**	**0.018***
Concurrent antiplatelet:				
No	543	2.0% (n=11)	1	
Yes	114	0.0% (n=0)	-	-

* clinically significant p-value <0.05

Real-World Direct Oral Anticoagulants Experience in Atrial Fibrillation: Falls Risk and Low Dose Anticoagulation are Predictive of both Bleeding and Stroke Risk

Running Head: Real-World Experience of DOAC in AF

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Abstract

Background: Clinical trials have demonstrated that direct oral anticoagulants (DOAC) are non-inferior to vitamin K antagonist for stroke prevention in non-valvular atrial fibrillation (AF) with comparable safety outcomes; however real-world Australian data is limited.

Aims: We aim to evaluate local real-world DOAC use focusing on safety, particularly in high-risk patients.

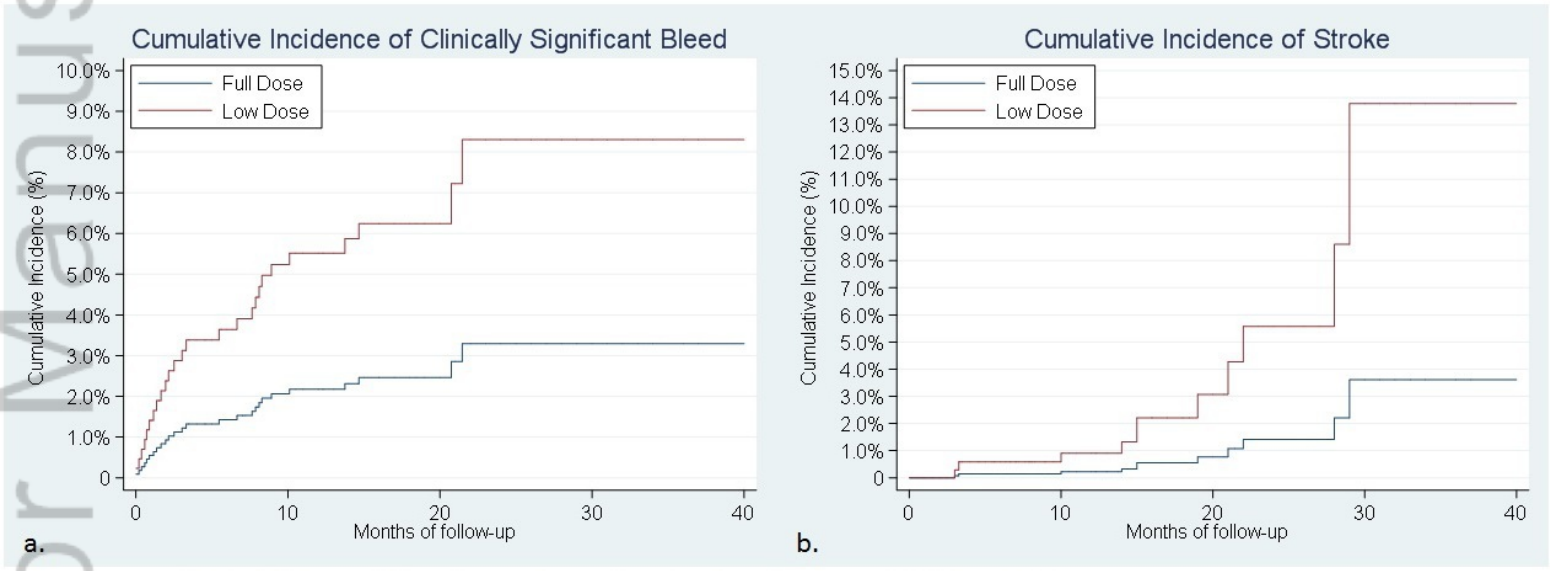
Methods: A retrospective evaluation of 658 patients commenced or continued on DOAC between September 2013-September 2016 for non-valvular AF at Northern Hospital, a tertiary hospital in Victoria, Australia was performed.

Results: Factor Xa inhibitors were more commonly prescribed than direct thrombin inhibitor (83.3% vs 16.7%) for AF management. The median patient age was 75 years. The rate of clinically significant bleeding on anticoagulation was 3.13 per 100 person-years (including four deaths) with risk factors including history of bleeding (HR 3.52, 95% CI 1.22-10.17), concurrent antiplatelet therapy (HR 2.62, 95% CI: 1.11-6.20) and high falls risk (HR 2.76, 95% CI: 1.26-6.08). Patients on low dose DOAC had significantly higher bleeding risk compared to those on full dose (5.05 vs 1.82 per 100 person-years). The rate of thrombotic stroke despite anticoagulation was 1.34 per 100 person-years with risk factors including low dose anticoagulation (p=0.034), high falls risk (p=0.046) and previous stroke (p=0.028).

Conclusions: DOAC use in real-world Australian practice is safe and effective, consistent with international data. Low dose anticoagulation and falls risk are associated with increased bleeding and thrombotic risk demonstrating overlapping risk factors. Careful individualised patient risk assessment is still required as low dose anticoagulation is not without risks.

Key Words

Anticoagulants; Atrial fibrillation; Thrombosis; Haemorrhage; Frailty



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