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Research Article

Impact of a Multidisciplinary Care Model with Clinical Pharmacist Involvement on DOAC Dosing Appropriateness in Nonvalvular Atrial Fibrillation

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Abstract

Introduction: Direct oral anticoagulants (DOACs) are the preferred therapy for prevention of thromboembolic events in patients with non-valvular atrial fibrillation (NVAF). Despite their proven efficacy, inappropriate DOAC dosing remains common and has been associated with increased risks of stroke and bleeding. Limited data exist evaluating the impact of interdisciplinary, pharmacist-involved care models on DOAC dosing accuracy. This study evaluated the effect of a multidisciplinary care model on achieving appropriate DOAC dosing in patients with NVAF.

Study Design: This retrospective cohort study compared the frequency of inappropriate DOAC dosing among patients managed under a multidisciplinary care model that included clinical pharmacist involvement versus those managed under a single-provider care model.

Methods: Adult patients (≥ 18 years) with NVAF treated at a university-affiliated ambulatory cardiology clinic and initiated on a DOAC for stroke prevention between June 2019 and June 2023 were included. Patients with valvular atrial fibrillation or a history of venous thromboembolism were excluded. The primary outcome was the occurrence of at least two consecutive inappropriate DOAC doses following treatment initiation. Binary logistic regression was used to assess the association between care model and inappropriate dosing, adjusting for age, body mass index, race, and stroke risk factors.

Results: Over a median follow-up of approximately one year, inappropriate DOAC dosing occurred in 3 patients (2%) in the pharmacist-involved group compared with 36 patients (24%) in the non-pharmacist group ($p < 0.001$). In adjusted analyses, pharmacist involvement was associated with a significantly lower likelihood of inappropriate dosing (adjusted odds ratio [aOR] 0.03; 95% CI, 0.004 - 0.14; $p < 0.001$). Unadjusted analysis demonstrated similar findings (OR 0.06; 95% CI, 0.02 - 0.22; $p < 0.001$).

Conclusion: Incorporation of pharmacists within a multidisciplinary care model was associated with significantly improved DOAC dosing appropriateness in patients with NVAF. These findings highlight the critical role of pharmacist involvement in optimizing anticoagulation therapy and support the integration of interdisciplinary care models in ambulatory cardiology practice.

Keywords: *Multidisciplinary Care Model; Clinical Pharmacist; Direct Oral Anticoagulants (DOACs)' Non-Valvular Atrial Fibrillation (NVAF)*

Background

Direct oral anticoagulants (DOACs) are the preferred agents for stroke prevention in patients with nonvalvular atrial fibrillation (NVAF), offering an effective and convenient alternative to vitamin K antagonists such as warfarin. Dabigatran, rivaroxaban, apixaban, and edoxaban are widely used because of their predictable pharmacokinetics, fewer dietary restrictions, and limited need for routine monitoring. Despite these advantages, appropriate DOAC dosing remains a critical clinical challenge.

DOACs are approved at specific doses, with adjustments based on indication, age, body weight, renal function, and concomitant medications [1]. However, deviations from guideline- and label-recommended dosing are common in real-world practice and may lead to suboptimal clinical outcomes. A 2020 systematic review reported that 25 - 50% of patients receive off-label DOAC dosing inconsistent with FDA-approved labeling [2]. Overdosing has been associated with increased bleeding and all-cause mortality, whereas underdosing may increase the risk of thromboembolic events and hospitalizations. In a prospective observational study of NVAF outpatients, inappropriate dosing rates were 23% for rivaroxaban and 42% for dabigatran etexilate [3]. Ensuring correct DOAC dosing is therefore essential to maximize therapeutic benefit while minimizing harm.

Pharmacists play a key role in optimizing DOAC prescribing. Pharmacist-driven DOAC protocols have been shown to significantly reduce inappropriate dosing, with one study demonstrating a reduction from 32.4% to 13.8% following pharmacist involvement (adjusted odds ratio [OR] 0.42; 95% CI, 0.19 - 0.96; p = 0.039) [4]. Another study found that more than one-third of patients receiving DOAC therapy had potentially inappropriate prescribing or drug-related problems requiring pharmacist intervention [5]. Multidisciplinary collaboration-particularly pharmacist involvement in medication reconciliation, dosing assessment, and monitoring-is critical for improving DOAC safety and effectiveness, especially in patients with NVAF who frequently have multiple comorbidities and complex medication regimens.

Patients with NVAF are at increased risk for drug duplication, drug-drug interactions, and adverse effects, which may lead to emergency department visits, hospitalizations, and higher healthcare costs. A multicenter study evaluating multidisciplinary atrial fibrillation management in the emergency department demonstrated a 3.7-fold reduction in hospital admissions and a 1.6-fold reduction in length of stay [13]. Despite these findings, limited data exist regarding the impact of team-based care on DOAC dosing appropriateness in ambulatory care settings.

Atrial fibrillation is associated with substantial healthcare utilization and economic burden. Compared with individuals without AF, patients with incident AF have higher rates of inpatient admissions and cardiovascular-related emergency department visits [6,7]. In 2016, AF-related healthcare spending in the United States was estimated at $28.4 billion [8]. Stroke, a major complication of NVAF, further contributes to this burden, with average hospitalization costs of $18,963 for ischemic stroke and $32,035 for hemorrhagic stroke [9]. Annual per-patient stroke-related costs approach $59,900, and total national stroke-related expenditures exceed $34 billion annually [10-12]. With AF prevalence projected to double by 2050 [13-15], inappropriate DOAC dosing represents an increasingly important public health concern.

In this retrospective cohort study, we evaluated differences in the frequency of inappropriate DOAC dosing between an interdisciplinary atrial fibrillation clinic (IAC) and standard single-provider care. We also compared rates of inappropriately high and inappropriately low dosing between these care models to assess the potential benefit of a multidisciplinary approach in optimizing DOAC therapy.

Methods

Study design and patients

This retrospective cohort study was conducted at Loma Linda University Medical Center, a tertiary academic medical center. Patients seen at the Loma Linda University Medical Center International Atrial Fibrillation Clinic between June 1, 2019, and June 20, 2023, were screened for inclusion. Eligible patients were adults aged ≥ 18 years with a diagnosis of NVAF who were prescribed a DOAC. Patients were

excluded if they were prescribed DOACs for indications other than NVAF (e.g. venous thromboembolism or valvular atrial fibrillation), did not receive a DOAC prescription, or lacked follow-up clinic visits after DOAC initiation. This study was reviewed and approved by the Loma Linda University Institutional Review Board, with a waiver of informed consent due to the retrospective nature of the study.

Study groups

After screening, 150 patients receiving care through the interdisciplinary atrial fibrillation clinic were included in the multidisciplinary care group. A comparison group of 150 patients receiving standard care through a single-provider model was also included.

Data collection

Baseline demographic and clinical data-including age, sex, weight, body mass index (BMI), and comorbidities-were collected at the initial visit when DOAC therapy was initiated. DOAC type and dose were recorded at initiation and at follow-up visits occurring at approximately 3, 6, 9, and 12 months. Laboratory values (including serum creatinine), age, weight, and concurrent medications were collected at each visit to assess dose appropriateness.

Creatinine clearance was calculated using the Cockcroft-Gault equation, with actual body weight used for patients with BMI < 30 kg/m^2 and adjusted body weight used for patients with BMI ≥ 30 kg/m^2. DOAC dosing was classified as appropriate if the prescribed dose matched guideline- and label-recommended dosing in at least 50% of clinic visits. Dosing was considered inappropriate if the recommended dose was prescribed in fewer than 50% of visits.

Interdisciplinary clinic workflow and pharmacist role

In this interdisciplinary atrial fibrillation clinic, care is delivered through a shared-visit model in which the physician, clinical pharmacist, and other team members (e.g. nurse practitioner, medical resident, pharmacy resident, and medical assistant) evaluate the patient together during the same clinic encounter. The clinical pharmacist does not see patients independently under a standalone protocol; rather, clinical decisions are made collaboratively in real time through team-based discussion and shared decision-making.

The clinical pharmacist is a Clinical Pharmacy Specialist who has completed a Doctor of Pharmacy (PharmD) degree, postgraduate year 1 (PGY1) residency training, and postgraduate year 2 (PGY2) residency training, followed by advanced clinical practice experience and ongoing self-directed learning. The pharmacist is Board Certified in Cardiology and practices under a physician-pharmacist collaborative practice agreement.

Within the clinic, the pharmacist's responsibilities include comprehensive medication reconciliation; anticoagulation management for patients with nonvalvular atrial fibrillation, including verification of DOAC dosing appropriateness based on patient-specific factors (e.g. renal function, age, and body weight); assessment of drug selection, dosing, safety, and drug-drug interactions; and optimization of cardiovascular pharmacotherapy in alignment with contemporary guideline-directed medical therapy. The pharmacist provides specific expertise in ensuring appropriate dosing and safety monitoring of Class III antiarrhythmic agents and participates actively in clinical decision-making related to stroke prevention, rhythm and rate control strategies, and comorbidity management.

Pharmacist recommendations are guided by evidence-based clinical practice guidelines, including those from the American College of Cardiology (ACC), American Heart Association (AHA), and Heart Rhythm Society (HRS), as well as institutional standards of care. All treatment decisions are finalized collaboratively by the interdisciplinary team, ensuring consistency with guideline recommendations while incorporating patient-specific factors and preferences. The pharmacist also provides education to both patients and providers to support medication adherence, safety, and informed shared decision-making.

Outcomes

The primary outcome was the difference in the proportion of appropriately dosed DOAC prescriptions between the multidisciplinary care model and the single-provider care model. The secondary outcome was the distribution of inappropriate dosing, categorized as inappropriately low or inappropriately high.

Statistical analysis

Data were analyzed using SPSS version 25 (IBM SPSS, Inc., Armonk, NY), with statistical significance set at $\alpha = 0.05$. Continuous variables were summarized using means and standard deviations and compared using independent t-tests. Categorical variables were reported as frequencies and percentages and compared using chi-square or Fisher's exact tests, as appropriate. Unadjusted and adjusted binary logistic regression analyses were performed to evaluate the association between care model (multidisciplinary vs single-provider) and appropriate DOAC dosing.

Results

Primary outcome

A total of 300 patients were included in the analysis, with 150 patients in the multidisciplinary care group and 150 patients in the single-provider care group. Baseline characteristics were similar between groups (Table 1). The mean age was 68 years, 60% of patients were Caucasian, the mean BMI was 30 kg/m^2, and 9 - 18% of patients had chronic kidney disease at baseline.

Characteristic	Multidisciplinary Group (n = 150)	Single Provider Group (n = 150)
Age group (years)	66.4 ± 14.6	69.7 ± 12.0
18 - 64	61 (40.6%)	48 (32.0%)
65 - 74	41 (27.3%)	51 (34.0%)
75+	48 (32.0%)	51 (34.6%)
Gender (Female)	59 (39.3%)	66 (44.0%)
Average BMI (kg/m^2)	30.49 ± 28.36	29.97 ± 29.93
Ethnicity		
White	90 (60.0%)	89 (59.3%)
African American	11 (7.3%)	27 (18.0%)
Asian	1 (0.6%)	2 (1.3%)
Hispanic	41 (27.3%)	30 (20.0%)
Other	2 (1.3%)	2 (1.3%)
Smoking Status		
Non-Smoker	96 (64%)	50 (33.3%)
Former Smoker	53 (35.3%)	100 (66.7%)
Current Smoker	1 (0.6%)	0 (0%)
DOACs		
Apixaban	114 (76.0%)	103 (68.6%)
Rivaroxaban	34 (22.6%)	43 (28.6%)
Dabigatran	2 (1.3%)	4 (2.7%)
Edoxaban	0 (0%)	0 (0%)
CHA2DS2-VASc Score	3.13 ± 1.5	3.3 ± 1.8
0	2 (1.3%)	4 (2.7)
1	20 (13.3%)	20 (13.3)
≥ 2	128 (85.3%)	126 (84.0)

HAS-Bled Score	1.05 ± 0.8	1.6 ± 1.1
0	37 (24.6%)	27 (18.0%)
1	74 (49.3%)	86 (57.3%)
2	33 (22.0%)	24 (16.0%)
3	6 (4.0%)	10 (6.7%)
≥ 4	0 (0%)	3 (2.0%)
Comorbid Conditions		
Hypertension	101 (67.3%)	111 (74.0%)
Diabetes	34 (22.7%)	37 (24.7%)
Stroke History	13 (8.7%)	20 (13.3%)
Heart Failure	69 (46.0%)	62 (41.3%)
Vascular Disease	32 (21.3%)	36 (24.0%)
Chronic Kidney Disease	14 (9.3%)	27 (18.0%)
Pertinent Concurrent Drugs		
Amiodarone	31 (20.7%)	24 (16.0%)
Diltiazem	12 (8.0%)	20 (13.3%)
Dronedarone	5 (3.3%)	0 (0%)

Table 1: *Baseline characteristics.*

Inappropriate DOAC dosing occurred in 36 patients (24%) in the single-provider care group compared with 3 patients (2%) in the multidisciplinary care group ($p < 0.001$) (Table 2). The number needed to treat to prevent one instance of inappropriate dosing was five.

		Inappropriate (n = 39)	Appropriate (n = 261)	P-value
Group	Single Care Provider	36 (24%)	114 (76%)	<0.001*
	Multidisciplinary Model	3 (2%)	147 (98%)	
Gender	Female	19 (15%)	106 (85%)	0.338
	Male	20 (11%)	155 (89%)	
Race	White	6 (6%)	93 (94%)	0.012*
	Black	6 (16%)	32 (84%)	0.584
	Hispanic	5 (9%)	48 (91%)	0.395
	Asian	2 (18%)	9 (82%)	0.603
	Non-specified	12 (20%)	49 (80%)	0.699
Smoker	Never	17 (12%)	129 (88%)	0.725
	Former	22 (14%)	131 (86%)	
	Current	0 (0%)	1 (100%)	
Age (with mean standard deviation)		76.3 ± 10.9	66.9 ± 13.4	<0.001*[a]
BMI (with mean standard deviation)		27.3 ± 7.2	30.9 ± 7.5	0.005*[a]
Stroke (Ischemic/Hemorrhagic)		8 (24%)	25 (76%)	0.042*

Table 2: *Univariate results.*

Univariate analysis identified age, BMI, race, and history of ischemic or hemorrhagic stroke as potential confounders. After adjustment for these variables, patients receiving multidisciplinary care remained significantly more likely to be appropriately dosed (adjusted OR 39.3; 95% CI, 6.9 - 225.5; $p < 0.001$) (Table 3).

	Adjusted Odds Ratio	Lower 95% CI	Upper 95% CI	P-value
Group (Multidisciplinary vs Single care provider)	39.345	6.863	225.546	<0.001*
Age	0.935	0.897	0.975	0.002*
BMI	1.052	0.982	1.127	0.148
Race (Whites vs Non-whites)	0.261	0.059	1.164	0.078
History of stroke (Yes vs No)	0.695	0.249	1.938	0.484

Table 3: *Multivariate logistic regression (Adjusted odds ratio).*

Secondary outcome

Among the 39 patients receiving inappropriate doses, 15 (38%) were prescribed inappropriately low doses and 24 (62%) were prescribed inappropriately high doses (Table 4).

	Inappropriately low	Inappropriately high
Number of patients (%)	15 (38%)	24 (62%)

Table 4: *Secondary outcome.*

Discussion

In this study, we evaluated the impact of a multidisciplinary care approach incorporating pharmacist involvement compared with a single-provider care model on the appropriateness of DOAC dosing in patients with nonvalvular atrial fibrillation. Our findings demonstrate a marked and clinically meaningful improvement in DOAC dosing appropriateness among patients managed within the multidisciplinary model. Specifically, inappropriate dosing occurred in only 2% of patients in the multidisciplinary group compared with 24% in the single-provider care model (Table 2). Importantly, this benefit was observed within a concurrent, co-managed care model, in which pharmacists functioned as embedded medication experts participating in real-time clinical decision-making rather than operating under independent prescribing protocols.

Several patient characteristics-including race, age, BMI, and history of stroke-were identified as potential confounding factors. After adjusting for these variables, multidisciplinary care remained strongly associated with appropriate DOAC dosing, with an adjusted odds ratio of 39.3 (95% CI 6.9 - 225), indicating a robust association between pharmacist-involved multidisciplinary care and appropriate DOAC dosing, despite the wide confidence interval. The wide confidence interval likely reflects the low number of inappropriate dosing events in the multidisciplinary group, rather than model instability. While the magnitude of this association is notable, it underscores the substantial impact that structured pharmacist involvement can have on anticoagulation management, particularly in complex outpatient populations. Age emerged as a statistically significant variable after adjustment; however, this study was not designed to isolate the independent effect of age on dosing appropriateness. Future studies should further explore age-related prescribing considerations within multidisciplinary care frameworks.

Our findings align with prior studies demonstrating the benefits of pharmacist involvement in anticoagulation management. A 2017 study evaluating a pharmacist-driven DOAC protocol reported a significant reduction in inappropriate dosing following implementation (32.4% vs. 13.8%; OR 0.34; 95% CI, 0.16 - 0.73; p = 0.005) [4]. Similarly, a 2019 study identified potentially inappropriate DOAC prescribing or drug-related problems in more than one-third of patients, necessitating pharmacist intervention [5]. Notably, these studies were conducted in inpatient settings, whereas our study extends this evidence to the outpatient ambulatory care setting, where patients are exposed to longer-term risks associated with suboptimal dosing and where medication regimens frequently evolve over time.

In our secondary analysis, among patients receiving inappropriate DOAC doses, 62% were prescribed inappropriately high doses and 38% inappropriately low doses. This trend toward overdosing is clinically concerning, as excessive anticoagulation increases bleeding risk without improving thromboembolic protection. Conversely, underdosing places patients at increased risk for ischemic stroke and systemic embolism. These findings reinforce the need for ongoing medication assessment, dose adjustment, and monitoring-functions well suited to pharmacist-led or pharmacist-integrated care models.

Beyond clinical outcomes, our findings carry important economic implications. Inappropriate DOAC dosing has been consistently associated with costly adverse events, including stroke and major bleeding. The average hospitalization cost for ischemic stroke is estimated at $18,963 and rises to $32,035 for hemorrhagic stroke [9]. Collectively, stroke-related care contributes approximately $34 billion annually to U.S. healthcare expenditures, a burden expected to increase as atrial fibrillation prevalence rises [11,13-15]. Major bleeding events further contribute to healthcare costs; one analysis reported an average acute incremental cost of $15,699 per major bleeding episode among patients with NVAF [18].

Although this study did not directly measure healthcare costs, the substantial reduction in inappropriate DOAC dosing observed in the multidisciplinary group suggests meaningful potential for cost avoidance. By preventing dosing-related adverse events and reducing avoidable hospitalizations, pharmacist-integrated care models may offer a high-value strategy for optimizing both clinical outcomes and resource utilization. Importantly, this economic value is achieved through improved medication management rather than additional diagnostic testing or therapeutic escalation, making pharmacist involvement a scalable and sustainable intervention.

Taken together, our results support the integration of pharmacists as essential members of multidisciplinary atrial fibrillation care teams in outpatient settings. Pharmacists are uniquely positioned to evaluate renal function trends, assess drug-drug interactions, reconcile evolving medication regimens, and ensure guideline-concordant DOAC dosing over time. The observed improvements in dosing appropriateness, coupled with the potential for downstream cost avoidance, reinforce the clinical and economic justification for pharmacist involvement in chronic anticoagulation management.

Limitations and Future Directions

This study has several limitations. Its retrospective design precludes causal inference, and the single-center setting may limit generalizability. Additionally, the study was not designed to evaluate clinical outcomes such as stroke or bleeding events. Although this clinic did not employ a standardized pharmacist-driven dosing protocol, the concurrent interdisciplinary model reflects real-world ambulatory cardiology practice and may enhance the external validity of these findings.

Future prospective, multicenter studies are needed to confirm these findings and assess the long-term impact of multidisciplinary care on clinical outcomes and healthcare utilization. Further evaluation of the specific roles of individual team members may also help refine optimal care models for patients with atrial fibrillation.

Conclusion

A multidisciplinary atrial fibrillation care model that includes pharmacist involvement significantly improves the appropriateness of DOAC dosing in patients with NVAF in the outpatient setting. This approach has the potential to enhance patient safety, improve clinical outcomes, and reduce the economic burden associated with inappropriate anticoagulant use.

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