Practice-Level Variation in *Warfarin* Use Among Outpatients With Atrial Fibrillation (from the NCDR PINNACLE Program)

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Warfarin is a complex but highly effective treatment for decreasing thromboembolic risk in atrial fibrillation (AF). We examined contemporary warfarin treatment rates in AF before the expected introduction of newer anticoagulants and extent of practice-level variation in warfarin use. Within the National Cardiovascular Data Registry Practice Innovation and Clinical Excellence program from July 2008 through December 2009, we identified 9,113 outpatients with AF from 20 sites who were at moderate to high risk for stroke (congestive heart failure, hypertension, age, diabetes, stroke score >1) and would be optimally treated with warfarin. Using hierarchical models, the extent of site-level variation was quantified with the median rate ratio, which can be interpreted as the likelihood that 2 random practices would differ in treating "identical" patients with warfarin. Overall rate of warfarin treatment was only 55.1% (5,018 of 9,913). Untreated patients and treated patients had mean congestive heart failure, hypertension, age, diabetes, stroke scores of 2.5 ($p = 0.38$) and similar rates of heart failure, hypertension, diabetes mellitus, and previous stroke, suggesting an almost "random" pattern of treatment. At the practice level, however, there was substantial variation in treatment ranging from 25% to 80% (interquartile range for practices 50 to 65), with a median rate ratio of 1.31 (1.22 to 1.55, $p < 0.001$). In conclusion, within the Practice Innovation and Clinical Excellence registry, we found that warfarin treatment in AF was suboptimal, with large variations in treatment observed across practices. Our findings suggest important opportunities for practice-level improvement in stroke prevention for outpatients with AF and define a benchmark treatment rate before the introduction of newer anticoagulant agents. **(Am J Cardiol 2011;108:1136–1140)**

The emergence of the National Cardiovascular Date Registry (NCDR) Practice Innovation and Clinical Excellence (PINNACLE) program for cardiac outpatients represents a unique data source to evaluate warfarin treatment patterns in a contemporary United States outpatient cohort.[1,2] Results from a contemporary registry can provide important baseline treatment rates with warfarin before the introduction of newer anticoagulants such as dabigatran and rivaroxaban. Accordingly, within the PINNACLE program we examined (1) treatment rates with warfarin in outpatients with nonvalvular atrial fibrillation (AF) who are at moderate to high risk for stroke and (2) extent of patient- and practice-level variations in warfarin use. Presence of significant site-level variation would identify opportunities for quality improvement and our findings will provide important benchmark rates of warfarin treatment before the introduction of newer anticoagulants into routine practice.

Methods

The PINNACLE program has been previously described.[1,2] Briefly, in 2008 the American College of Cardiology Foundation's NCDR launched PINNACLE (formerly known as the Improving Continuous Cardiac Care program [IC^3]), the first national prospective office-based cardiac quality improvement registry in the United States. Academic and private practices were invited to participate in PINNACLE through the American College of Cardiology's Web site, e-mails, brochures, and information Webinars. Physicians or practice representatives (e.g., administrators) in interested practices underwent a series of educational training sessions before data submission.

Within participating practices different patient data were collected at the point of care including patients' symptoms, vital signs, co-morbidities, and medications. In addition,

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Table 1
Baseline characteristics of patients treated and not treated with warfarin

Covariates	Total Cohort (n = 9,113)	Warfarin Therapy		p Value
		Yes (n = 5,018)	No (n = 4,095)	
Mean congestive heart failure/hypertension/age/diabetes/stroke score	2.5 ± 0.8	2.5 ± 0.8	2.5 ± 0.8	0.38
Age ≥75 years	76.5 ± 9.9	76.3 ± 9.5	76.8 ± 10.4	0.45
Age categories (years)				0.07
<70	21.1%	21.4%	20.9%	
70–79	35.9%	36.9%	34.7%	
≥80	43.0%	41.8%	44.4%	
Insurance type				<0.001
Private	61.9%	60.4%	63.8%	
Medicare	33.7%	34.4%	32.9%	
Other public	1.3%	1.5%	1.1%	
None	3.0%	3.6%	2.2%	
Men	51.3%	52.6%	49.7%	0.005
White	87.2%	87.1%	87.3%	0.80
Coronary artery disease*	47.4%	45.6%	49.6%	<0.001
Dyslipidemia†	60.8%	62.9%	58.3%	<0.001
Diabetes mellitus	37.1%	36.8%	37.5%	0.50
Hypertension‡	93.4%	93.8%	93.0%	0.14
Previous stroke/transient ischemic attack	10.3%	9.9%	10.7%	0.18
Congestive heart failure	32.1%	32.5%	31.6%	0.35
Peripheral arterial disease	6.1%	5.1%	7.3%	<0.001
Previous systemic embolism	2.1%	2.8%	1.1%	<0.001
Stable angina pectoris	5.1%	4.9%	5.3%	0.39
Percutaneous coronary intervention with drug-eluting stent in previous 12 months	4.0%	4.0%	4.0%	0.93

* History of coronary artery stenosis ≥70%, percutaneous coronary intervention, or coronary artery bypass surgery.
† Assessed by individual physician most commonly because of low-density lipoprotein cholesterol level >130 mg/dL.
‡ Assessed by individual physician most commonly because of persistently increased systolic blood pressure (>140 mm Hg) or diastolic blood pressure (>90 mm Hg).

data for established performance measurements for coronary artery disease, heart failure, and AF were collected. Data collection was achieved through 1 of 2 mechanisms: (1) paper forms completed at the time of clinic visits or (2) modification of a practice's electronic medical record data-collection system to comprehensively capture requisite PINNACLE data elements. Data from practices are routinely submitted to the NCDR and data quality checks and analyses were performed at Saint Luke's Mid America Heart Institute (Kansas City, Missouri), the primary analytic center for the PINNACLE program.

For the purposes of this study, of 136,796 patients enrolled into PINNACLE from July 1, 2008 through December 31, 2009, we included 18,393 patients with nonvalvular AF. We further restricted the cohort to only those patients at moderate to high risk for stroke (i.e., a congestive heart failure/hypertension/age/diabetes/stroke [$CHADS_2$] score >1) in whom warfarin therapy is considered a performance measurement of high-quality care and included patients from practices with ≥10 eligible patients (total of 9,280 patients excluded).[3,4] The final study sample consisted of 9,113 patients with nonvalvular AF at moderate to high risk for stroke from 20 practices at 51 different office locations.

Coprimary outcomes were (1) rate of warfarin treatment in patients with AF at moderate to high risk for stroke and (2) extent of practice-level variation in warfarin use. To minimize over-representation by patients with multiple visits we included data from only the baseline enrollment visit of each patient.

Baseline characteristics between patients treated and not treated with warfarin were compared using *t* tests for continuous variables and chi-square test for categorical variables. Warfarin treatment rates were determined for each practice and examined with descriptive plots.

To examine extent of practice-level variation in warfarin use multivariable hierarchical regression models were constructed to determine the median rate ratio (RR). These were 2-level hierarchical models with the practice modeled as a random effect and patient covariates as fixed effects.[5] Because treatment rates exceeded 10% we used log-binomial or modified Poisson regression models at all steps, which estimate an RR directly.[6,7] The resulting median RR can be interpreted as the likelihood that 2 random practices would differ in treating "identical" patients with warfarin. Median RR is always ≥1, with a median RR >1.20 suggesting significant practice-level variation.

In addition, we examined in these models whether patient-level predictors were stronger determinants of warfarin treatment than practice-level variation. This is possible because the median RR permits meaningful comparisons with effect sizes of patient factors (e.g., age, gender) included in hierarchical models, thus overcoming interpretational limitations that are inherent with the intraclass correlation coefficient.[8,9] In these models we included as covariates the

Table 2
Rates of antiplatelet therapy for patients treated and not treated with warfarin

Antiplatelet Therapy	Total Cohort (n = 9,113)	Warfarin Therapy		p Value
		Yes (n = 5,018)	No (n = 4,095)	
Aspirin	3,543 (38.9%)	1,461 (29.1%)	2,082 (50.8%)	<0.001
Thienopyridine	294 (3.2%)	114 (2.3%)	180 (4.4%)	<0.001
Aspirin + thienopyridine	589 (6.5%)	175 (3.5%)	414 (10.1%)	<0.001
None	4,687 (51.4%)	3,268 (65.1%)	1,419 (34.7%)	<0.001

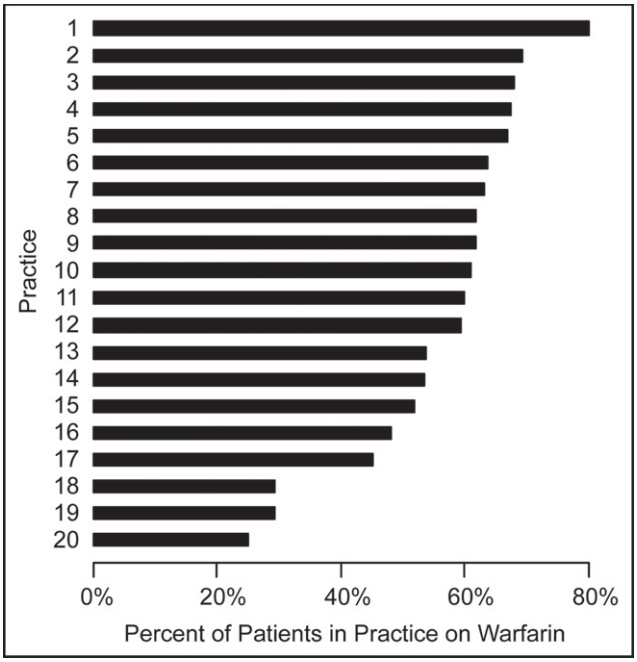

Figure 1. Variation in treatment rates with warfarin across practices showed a median practice treatment rate with warfarin of 61% (range 25 to 80, interquartile range 50 to 65).

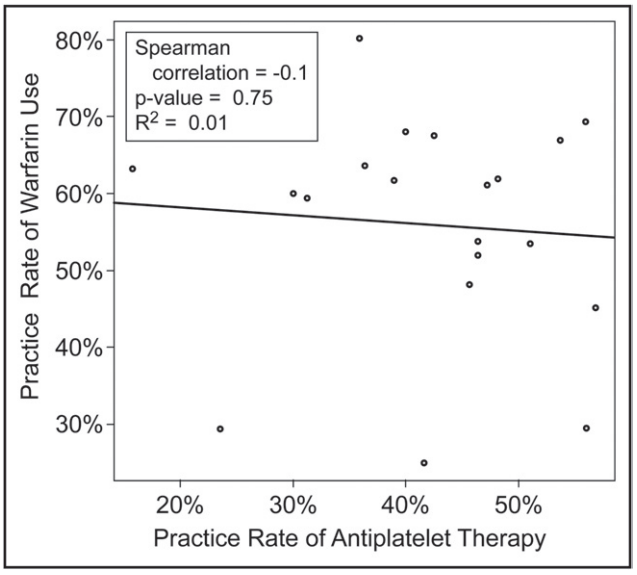

Figure 2. Practice rate of antiplatelet therapy showed little correlation between a practice's rate of warfarin treatment and its rate of antiplatelet (aspirin or thienopyridines) therapy.

following patient characteristics: age (<70, 70 to <80, ≥80 years), gender, insurance type (private, Medicare, public, none), congestive heart failure, hypertension, diabetes mellitus, peripheral arterial disease, concomitant use of thienopyridine therapy, and previous stroke or transient ischemic attack, coronary artery disease, or systemic embolism.

For each analysis the null hypothesis was evaluated at a 2-sided significance level of 0.05 with 95% confidence intervals calculated. All analyses were performed with SAS 9.2 (SAS Institute, Cary, North Carolina) and R 2.7.0 (Foundation for Statistical Computing, Vienna, Austria).[10]

Results

Of 9,113 patients with nonvalvular AF at moderate to high risk for stroke and eligible for warfarin treatment, 5,018 (55.1%) were treated with warfarin and 4,095 (44.9%) were not. Baseline characteristics of those treated and not treated with warfarin are listed in Table 1. Compared to untreated patients, patients treated with warfarin were similar in $CHADS_2$ score, age, and rates of congestive heart failure, hypertension, diabetes mellitus, and previous stroke. However, patients treated with warfarin were more frequently men and were more likely to have dyslipidemia, peripheral arterial disease, and previous systemic embolism. In contrast, patients not treated with warfarin were more likely to have private health insurance and previous coronary artery disease. Notably, rates of percutaneous coronary intervention with a drug-eluting stent within the previous year, for which thienopyridine therapy would be warranted, were similar for the 2 groups.

There was no relation between $CHADS_2$ score and treatment rates. Of 5,612 patients with a $CHADS_2$ score of 2, 3,086 (55.0%) were treated with warfarin. For the 2,510 patients with a $CHADS_2$ score of 3, 1,399 (55.7%) were treated with warfarin. For the 991 patients with a $CHADS_2$ score of ≥4, 533 (53.8%) were treated with warfarin. Table 2 lists use of antiplatelet therapies for patients treated and not treated with warfarin. Notably, of the 4,095 patients not treated with warfarin, 2,082 (50.8%) were treated with aspirin alone, 180 (4.4%) with a thienopyridine alone, 414 (10.1%) with aspirin and a thienopyridine, and 1,419 (34.7%) with neither aspirin nor thienopyridine therapy.

At the practice level the median practice rate for warfarin treatment was 61%. There was significant variation in warfarin treatment, with a range of 25% to 80% and an interquartile range of 50% to 65% (Figure 1). Median RR was

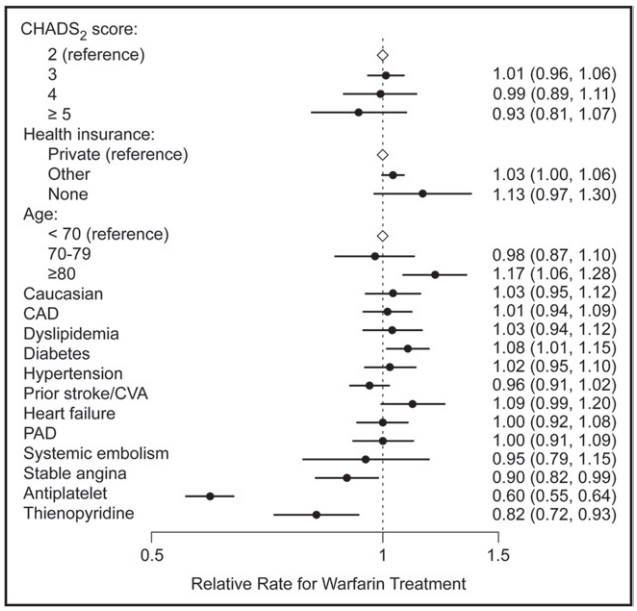

Figure 3. Patient characteristics were not strong predictors of warfarin treatment including components of the congestive heart failure/hypertension/age/diabetes/stroke score. Median rate ratio for site-level variation of 1.31 was larger than estimates of effect for any patient factor, suggesting that practice-level variation explained a larger proportion of variance in warfarin treatment than individual patient factors. CAD = coronary artery disease; CVA = cerebrovascular accident; PAD = peripheral artery disease.

1.31 (95% confidence interval 1.22 to 1.55, $p < 0.001$), suggesting moderate site-level variation in warfarin treatment across practices in PINNACLE. There was no correlation between number of patients with AF at a practice and a practice's rate of warfarin treatment (Spearman correlation −0.14, $p = 0.20$). Moreover, practices with low warfarin treatment rates were not more likely to prescribe antiplatelet therapy than practices with high warfarin treatment rates (Spearman correlation −0.10, $p = 0.75$; Figure 2).

There were few patient-level predictors associated with warfarin treatment. Overall $CHADS_2$ score, age, hypertension, diabetes mellitus, heart failure, coronary artery disease, and previous stroke or transient ischemic attack were not associated with warfarin treatment. Treatment with aspirin or thienopyridine therapy was associated with not receiving warfarin treatment, but whether use of antiplatelet therapy was the result or cause for not initiating warfarin treatment is unclear. Notably, in the multivariable hierarchical model the effect size of median RR was greater than those of any patient-level predictor for warfarin use (Figure 3), suggesting that site-level variation explained a larger proportion of variance in warfarin treatment than patient factors.

We examined what proportion of untreated patients was initiated on warfarin during the subsequent visit. We found that only 232 of the 4,095 untreated patients (5.7%) were initiated on warfarin after the first visit and our study findings were similar when analyses were repeated with these patients reclassified as warfarin-treated patients (results not shown).

Discussion

In this prospective multisite cohort of 9,113 cardiac outpatients with nonvalvular AF, we found that warfarin use in patients at moderate to high risk for stroke was only 55%. There was substantial variation across practices in warfarin treatment rates, with a median rate of 61% and a range from 25% to 80%. In fully adjusted models, practice-level variation explained a larger amount of the observed variance in warfarin treatment than any patient characteristic. Our findings therefore suggest that warfarin treatment will remain suboptimal unless characteristics of high-performing practices can be identified and generalized to those practices with the lowest rates.

Despite being a performance measurement for AF significant barriers exist in initiating warfarin therapy compared to medications for other cardiac conditions such as β blockers or statins. These barriers include patient refusal because of concerns about bleeding risk, need for routine monitoring, and physician factors (e.g., time allotted for outpatient clinic visits).[11,12] Because it is unlikely that differences in practice rates of patient contraindications to warfarin therapy or refusal to take warfarin could account for the wide range of practice treatment rates (from 25% to 80%), presence of substantial site-level variation in this cohort likely reflects actual differences in quality of care across practices. Of equal concern, this variation was not explained by higher rates of antiplatelet therapy in practices with low warfarin treatment rates. However, reasons for why some practices are able to achieve high warfarin treatment rates remain unclear. Because our cohort included patients from only 20 practices, our study would be severely underpowered in analyses of the relation between specific practice characteristics and practice rates of warfarin treatment. Future studies are therefore needed to clarify which provider or practice factors—such as presence of an anticoagulation clinic or anticoagulation protocols, collaborative office practices with anticoagulation pharmacists and/or nurses, average clinic time for outpatient visits at a practice, and physician views about warfarin use—may be responsible for the large observed variations in warfarin use across practices.

With the introduction of newer anticoagulants such as dabigatran and likely rivaroxaban in clinical practice, our findings also provide an important benchmark rate for anticoagulant use in contemporary outpatient practice in the United States. If barriers to initiating warfarin treatment indeed include lack of office clinician time in a busy outpatient clinic and low levels of reimbursement for patient education and monitoring of anticoagulation levels, it is likely that treatment rates with effective anticoagulants in patients with AF at moderate to high risk of stroke will increase after the introduction of these newer agents, which do not require monitoring of drug levels or adjusting of doses. Future studies within PINNACLE will need to examine whether treatment rates increase overall at the patient level and whether practice-level variation narrows after the introduction of these novel anticoagulants into clinical practice.

Our study findings should be interpreted in light of the following limitations. First, although our study enrolled >9,113 patients

with AF, PINNACLE practices may be highly motivated for quality improvement; therefore, warfarin treatment rates may be even lower in practices not participating in PINNACLE. Second, although practices were asked to submit data on all patients with AF, the PINNACLE program has no way of determining whether data on some patients were excluded from the program. However, to the extent that participating practices depend on the PINNACLE program to report for their pay-for-performance measurements, it is in the practices' economic interests to submit complete data on all their cardiac patients. Third, the PINNACLE registry did not systematically collect information on potential contraindications to anticoagulant or antiplatelet therapy. However, rates of contraindications have been reported to be about only 6% in other registries.[13] Moreover, rates of contraindications to anticoagulant therapy are not expected to vary widely across practices and therefore would be unlikely to account for the significant variation observed across practices. Fourth, although treatment with warfarin is viewed as a metric of quality care, the present study was not designed to examine clinical outcomes, which also may vary substantially with treatment patterns.

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