Electronic Decision support for Improvement of Contemporary Therapy for Stroke Prevention

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Background: Despite ample clinical trial data demonstrating that oral anticoagulation (OAC) treatment is highly effective in reducing stroke for patients with atrial fibrillation (AF), OAC treatment remains underutilized in current clinical practice. Targeting hospitalist and emergency department providers with electronic decision support represents a potential quality improvement opportunity in the use of OAC medication in AF patients. *Methods:* We conducted a 3-center study in which 2 sites utilized an electronic alert (EA) embedded in the electronic health record and 1 site provided usual care. The EA calculated the CHA_2DS_2-VASc score for clinicians. Patients were tracked following discharge from either the emergency department or hospital. We hypothesized that the EA would increase the rate of OAC use by 15% compared to usual care, with a study sample size of 360 patients. Study exclusions included severe heart valve disease, advanced renal disease, and severe dementia. The primary endpoint was OAC use at the time of hospital discharge or 30 days after hospital discharge (whichever was the last observation recorded). *Results:* Among 309 patients included for analysis (mean age 70.2 years), the median CHA_2DS_2-VASc score was 3.5. The frequency of OAC use at follow-up at the usual care hospital was 55.9% (95% confidence interval 47.4-67.9). At the 2 EA sites, the rate of OAC use at the last observation point was 43.9% ($P = .06$). Aspirin use at follow-up was similar at the usual care site and the EA sites (53.8% versus 46.3%). The rate of OAC use in patients greater than 75 years was 60.0% in the usual care site and 48.4% ($P = .09$) at the EA sites. *Conclusions:* The EA in our study was not sufficient to ameliorate therapeutic inertia in the use of OAC for stroke prevention in AF.

Key Words: Atrial fibrillation—ischemic stroke—electronic alerts—embolic stroke—cardioembolism

Atrial fibrillation (AF) is a frequent and devastating cause of ischemic stroke.[1] Its prevalence in the United States is 5.1 million and is expected to reach 16 million in 2050.[2] The correct identification of patients with AF at risk of stroke has direct therapeutic implications as oral anticoagulation (OAC) significantly reduces the risk of stroke recurrence.[3-7] Furthermore, OAC use is correlated with reduced stroke severity in patients with AF.[8-9] Unfortunately, fewer than 60% of AF patients with a clear indication for anticoagulation receive OAC treatment.[10-13] In a recent analysis from the Get with the Guidelines Registry, among 91,155 high-risk AF subjects, 83.5% were not receiving therapeutic warfarin or novel oral anticoagulants (NOACs) before the stroke.[14] More than 70% of patients were receiving antiplatelet therapy or no antithrombotic therapy, with the remaining patients on a

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subtherapeutic warfarin regimen. Reducing barriers to anticoagulation remains a challenge to overcome knowledge-to-action gaps in clinical practice.

Recent evidence demonstrates that a program using computerized support systems increased physician's attainment of recommended guidelines for venous thromboembolism prophylaxis, leading to a dramatic reduction in thromboembolic events.[15] A systematic review has shown that computerized diagnostic reminders, disease management, and drug-dosing or prescribing systems are also useful for improving practitioner performance, in conditions including transient ischemic attack.[16-17] We sought to assess whether an electronic alert (EA) system would prove helpful in improving the use of OAC treatment in patients with AF.

Methods

A 3-center study was conducted to assess the utility of an alert within the electronic health record. Two sites utilized the alert and the other site was the control population. The control site was determined using a random number generator. At the intervention sites, the EA included a tool that allowed the clinician to calculate the CHA_2DS_2-VASc score for each patient. CHA_2DS_2-VASc is a risk stratification score that includes clinical elements such as age, prior stroke, and congestive heart failure. A guideline-based treatment recommendation was then provided. If the clinician decided not to prescribe an anticoagulant, they were asked to provide a reason. A depiction of the EA is provided in Supplemental Figure 1.

There were 2 populations of interest in the study. First, patients in the emergency department (ED) with a diagnosis of AF and no current documentation of warfarin or NOAC use were identified. For these patients, the ED physician had the option of prescribing OAC treatment for the patient if the patient was to be discharged directly from the ED. In these cases, an expedited appointment (within 10 days) with the anticoagulation clinic was offered. For patients admitted to the hospital from the ED, it was customary to delegate the treatment decision to the inpatient team.

The second population of interest was patients seen by internal medicine hospitalists. This group of patients was selected due to the surge in hospitalist programs over the past two decades and the responsibility incumbent upon hospitalists to initiate OAC treatment in appropriate patients. For these patients, the EA was triggered on the morning following admission if it was identified that there was AF and no current use of warfarin or a NOAC (criteria for the alert in supplemental Table 1). At the 2 intervention sites, the EA was supplemented by the local principal investigator (PI) having discussions with the ED physicians or the hospitalists regarding the treatment rationale for OAC use and the study goals.

At the control site, an experienced stroke coordinator extracted data from the EMR of patients seen in the ED or by the internal medicine hospitalist service. No education was provided by the local PI to the ED or hospitalist physicians regarding AF or the study goals. Inclusion and exclusion criteria for the study are found in Table 1.

Patient visits to the study hospital or outpatient offices affiliated with the health system were followed for up to 6 months after discharge. The last follow-up was recorded for each subject and for patients with no documented follow-up visits, the treatment at the time of hospital discharge was recorded. Data on medication use was collected by the study coordinator at each site.

The primary outcome measure is a comparison of OAC utilization in the active intervention sites versus the usual care site. We aimed to achieve a 15% absolute increase in the number of patients at risk (CHA_2DS_2-VASc score ≥ 2) receiving OAC at the time of the last follow-up. The 15% increase in the rate of OAC medication was chosen since some high-performing hospitals report a 70% rate of OAC use for AF patients. The primary endpoint was determined either at hospital discharge or 30 days after hospital discharge, using the last recorded observation. To demonstrate a 15% difference in OAC use, power calculations showed that a sample size of 360 patients provides greater than 85% power to detect a treatment difference. A group sample size of 120 patients in the usual care group and 240 patients in the active intervention site was initially selected. A 2-sided Z test with pooled variance at the significance level of .05 was used.

After the study was initiated, a study amendment was approved to allow each site to extract data on up to 150 patients. This was done to account for subjects that were lost to follow-up or died within 6 months of hospital discharge. The institutional research board at all participating sites approved this study, with a waiver for patient consent.

Statistical Analysis

Chi-square testing was done in order to assess OAC use at the active intervention and control sites. Similar testing

Table 1. *Study Criteria*

Inclusion criteria
1. Age 40-90 years
2. Willing to follow-up as an outpatient
3. CHADS-VASC score of greater than or equal to 1
Exclusion criteria
1. Already on anticoagulation with warfarin or NOAC
2. Alcohol or drug abuse which would interfere with outpatient follow-up
3. Dementia severe enough to interfere with outpatient follow-up
4. Life expectancy estimated to be less than 2 years
5. Cr is greater than 3.0
6. Known bleeding disorder or prothrombin time greater than 15 seconds
7. Platelet count less than 100,000
8. Previous cerebral hemorrhage
9. Moderate to severe mitral stenosis or mitral regurgitation

was done to evaluate the likelihood of OAC use according to key characteristics (prior stroke, CHA_2DS_2-VASc category, etc.). For comparisons that required multivariable analysis with the binary outcome of OAC use, we utilized a logistic regression and reported the odds ratio and 95% confidence intervals (CI). Statistical analysis was performed using the computing environment R (version 3.3.1, The R Foundation for Statistical Computing).

Results

Data was extracted from the 3 study sites over a 16-month period (September 2016-December 2017). The study was terminated early due to slow enrollment at 1 of the intervention sites, with only 164 of the target 240 patients enrolled. At the control site, records of 145 subjects were reviewed, providing a total of 309 subjects.

Patient characteristics are provided in Table 2. The mean age was 70.2 years (SD 12.2), with 56% women. At the intervention sites, 91% of patients were hospitalist patients, compared to 87% inpatients at the control site. Across all 3 sites, the median CHA_2DS_2-VASc score was 3.5. The overall rate of OAC use across all sites was 45.5%. When the CHA_2DS_2-VASc score was broken down according to the following categories, the rate of OAC was as follows: score 1: 32.7%, score 2-3: 52.5%, score greater than or equal to 4: 53.2% (P = .03). After controlling for age and site, there was a significant difference in OAC use with higher CHA_2DS_2-VASc score relative to a score of 1 at the control site only (Table 3). For patients with a prior stroke compared to those without such an event, rates of OAC use were 40.0% versus 50.2% (P = .52).

The rate of OAC use at the active sites was 43.9% (95% CI 36.0%-51.8%) and the rate was 55.9% at the control site (P = .06, CI 47.4%-64.9%). Among patients receiving OAC medication, 66% were placed on a NOAC and 34% on warfarin. Aspirin use at follow-up was 46.4% at the active sites (CI 38.4-54.3) and 53.8% at the control site (CI 45.3-62.2). In 33% of patients, aspirin use was concomitant therapy with an OAC medication. The rate of OAC use in patients greater than 75 years was 60.0% (CI 46.1-73.9) in the usual care site and 48.4% (P = .09, CI 35.1-61.6) at the

Table 2. *Patient characteristics*

Variable	Intervention sites (n = 164)	Control site (n = 145)	*P* value
Sex*			
Male	93 (56.7%)	81 (55.9%)	.97
Female	71 (43.3%)	64 (44.1%)	
Mean age (years) (SD)†	69.85 (12.53)	70.57 (11.89)	.61
Age >75 years*	62 (37.8%)	XX 55 (37.9%)	1
History of stroke *	11 (6.7%)	9 (6.2%)	1
History of TIA*	8 (4.9%)	4 (2.8%)	.50
Vascular disease*	94 (57.3%)	53 (36.6%)	.0004
Congestive heart failure*	68 (41.5%)	21 (14.5%)	<.001
Diabetes mellitus*	57 (34.8%)	39 (26.9%)	.17
Hypertension*	132 (80.5%)	101 (69.7%)	.04
Mean CHA_2DS_2-VASc†	3.78 (1.87)	3.10 (1.59)	.0006
Median CHA_2DS_2-VASc [Interquartile range)]	4 [2,5]	3 [2,4]	
Obstructive sleep apnea*	23 (14.0%)	19 (13.1%)	.94
Previous major bleed†	3 (1.8%)	2 (1.4%)	1

***Fisher's Extract test
*Chi-squared test
†T-test

Table 3. *Likelihood of OAC use*

CHADS VASC 1 (reference level)	Odds ratio	*P* value	95% CI
Control site			
CHADS VASC 2-3	1.250574	.064440	(.9885073, 1.582118)
CHADS VASC 4+	1.322194	.022504	(1.0429033, 1.676279)
Active EA sites			
CHADS VASC 2-3	1.142211	.264449	(.9050608, 1.441502)
CHADS VASC 4+	1.095065	.382032	(.8938270, 1.341609)

EA sites. The 3 most common reasons identified for lack of OAC prescription were perceived low stroke risk, patient refusal, and history of prior bleeding.

Discussion

The management of AF with OAC is one of the most effective treatments for stroke prevention.[18] Our study aimed to determine whether an automated EA would increase the use of OAC for AF compared to usual care. Although the study did not find an increase in anticoagulant use, we were able to demonstrate the practicality of implementing the alert in different centers and in varied patient care settings (ED, internal medicine hospitalist service).

Previous efforts to modify physician behavior with regard to OAC use in AF have had mixed results. The Automated Risk Assessment for Stroke in Atrial Fibrillation study was a cluster randomized trial involving 47 outpatient practices in England.[19] If a patient with AF presented to the practice and was not on an OAC medication, a screen reminder message would appear. Overall, there was not a significant difference in OAC use with the electronic reminders, with a mean proportion of OAC prescription of 66.3% in the intervention practices, compared to 63.9% in the control practices.

Investigators from the Mayo Clinic instituted a clinical alert system for inpatients with AF.[20] With newly diagnosed AF, providers were automatically notified and referred to evidence-based guidelines. Within 30 days of notification, the use of warfarin was 27% in high-risk patients, compared to 36% among historical control patients in the year prior to the implementation of the alert system.

A study that had positive results with use of an EA system focused on inpatients with AF who were naïve to OAC treatment.[21] The alert included a tool, similar to our study that allowed calculation of the CHA_2DS_2-VASc score and provided recommendations for treatment. Among 889 patients who were guideline-eligible for anticoagulants, OAC medication was prescribed in 22.0% of the alert patients versus 15.9% of the control group ($P = .02$). OAC or antiplatelet therapy was administered to 71.4% of the alert group, compared to 62.4% of the control group ($P = .004$).

The large treatment gap with regard to appropriate stroke prophylaxis in AF was illustrated once again in our study. In the intervention sites, less than half of patients received an OAC prescription at the last follow-up time point. At the control site, slightly more than one half of patients received OAC treatment. Based on the American Heart Association/American Stroke Association primary stroke prevention guidelines,[22] at 1 of the sites, the alert was used in the ED since this represents a novel area to initiate appropriate stroke prophylaxis. Despite extra efforts to support ED physicians, such as with an expedited appointment in the anticoagulation clinic, relatively few ED physicians felt comfortable prescribing an OAC medication for AF. This may have been since this was viewed as outside their scope of practice, especially if AF was not the primary diagnosis. Even among internal medicine hospitalists, the rate of anticoagulant use was disappointing and identification of barriers for OAC use by this physician group is needed[23,24]. Very few patients (<2%) had major bleeds in the past so this did not appear to be an obstacle to OAC utilization. Therapeutic inertia has been found previously in AF management among both cardiologists and general practitioners.

Several logistical issues may have affected clinician acceptance of the alert and the overall study results. First, at 1 of the sites, the alert would trigger on the morning after admission. Therefore, if a patient was admitted the previous day and the clinical team decided that the patient was a "good" anticoagulation candidate, treatment may have started with intravenous heparin or low molecular weight heparin. These patients would have been "harvested" out of the study population, leaving only suboptimal anticoagulation candidates as subjects of the alert. In the ED, timing of the alert was challenging. If the alert was triggered at the time of the first electrocardiogram performance, some ED clinicians may not have been prepared to decide on OAC use at the point of care. If the alert was triggered at the time of discharge, it may have been too late to alter physician behavior.

This trial has several limitations. Although efforts were made to perform the study at 3 academic, high volume stroke centers, there may have been undocumented confounding variables that made the control site different from the 2 intervention sites. In addition, the control site may have had a pre-existing higher rate of OAC use due to engrained community practices or perhaps stronger integration with primary care practices. We did not assess baseline use of OAC treatment at the 3 sites, which is a study limitation. The primary outcome of OAC use was determined based on an active prescription in the chart of a study subject; whether subjects were actually taking an OAC as prescribed cannot be determined through this method of outcome ascertainment. The early termination of the study reduced the study power but since the observed medication use was in the opposite direction of our study hypothesis, it is very unlikely that we would have been able to demonstrate a treatment difference favoring the active sites if the original sample size was recruited.

In summary, we did not find that an automated alert with calculation of an AF risk stratification tool improved the rate of OAC use in patients with AF. We found a stubbornly persisting treatment gap, demonstrating the ongoing challenge of overcoming therapeutic inertia in the AF population.

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Supplementary Materials

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2018.10.041.

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