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***Objective*. Anticoagulation quality and record documentation were retrospectively assessed in patients with chronic nonvalvular atrial fibrillation (CNVAF) managed in a routine care setting. *Methods*. Medical record data extraction from physician practices in 4 regions of the United States. *Results*. Of 686 patients, 59% had an electrocardiogram confirming CNVAF, 84% listed at least 1 stroke risk factor, and 60% indicated the goal target international normalized ratio (INR). Two thirds of INRs >3.0 or <2.0 had no recorded dose change, nor did 45% of INRs >5.0. Vitamin K was given (3%) or anticoagulation was temporarily discontinued (9%) for INRs >5.0. The median interval of INR testing was 21 days, which decreased to 7 days for INRs >4.60. Patients spent 58% of the time in therapeutic range. *Conclusion*. Serious deficiencies in quality and documentation of routine medical care of anticoagulation for patients with CNVAF continue to exist. (Am J Med Qual 2007;22:327-333)**

Keywords: routine medical care; health care; anticoagulation; atrial fibrillation; vitamin K antagonists; INR

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Chronic nonvalvular atrial fibrillation (CNVAF) increases the risk of ischemic stroke by 2- to 7-fold,[1] and after the initial stroke, two thirds of patients die or have severe, permanent neurologic deficits.[2] Despite multiple randomized clinical trials[3-5] showing that anticoagulation therapy reduces the risk of ischemic stroke[6-8] and guidelines recommending this intervention,[9] only 42% to 67% of patients with CNVAF and no contraindication are prescribed anticoagulants.[10-13] Multiple explanations have been given to justify why providers do not prescribe anticoagulants, such as fear of hemorrhagic complications, perceived lack of efficacy, difficulties in managing therapy,[14] and the perceived need for expertise to manage anticoagulants.[15] Because the evidence indicates that high-quality anticoagulation management results in better health outcomes,[16] it is important to measure the degree of progress reached in the routine medical management of vitamin K antagonists (VKA), that is, management not overseen by an anticoagulation clinic. Therefore, an International Study of Anticoagulation Management (ISAM) was conducted in the United States and 4 other countries to document the quality of anticoagulation management of CNVAF in routine medical practice.[17] This report addresses the findings from the United States.

METHODS

A multicenter, retrospective cohort study was conducted in 4 geographically dispersed regions in the United States: California, Massachusetts, Indiana, and North Carolina. Each study center had a local principal investigator and study coordinator who were responsible for recruiting affiliated practices that could supply a list of patients meeting the major eligibility criteria. The protocol was approved by Institutional Review Board Services and by the Institutional Review Board of Duke University Medical Center.

Each regional study center enrolled practices that provided long-term anticoagulation management for their patients but did not have staff who dedicated more than 50% of their time to that aspect of patient care (ie, routine medical care [RMC]); maintained a single record for each patient; were able to produce a list of potentially eligible patients that contained, at a minimum, information on age, diagnoses, and anticoagulation use; were operating for at least 12 months prior to the start of the study period; provided prothrombin time results as international normalized ratio (INR); and were not involved in experimental studies or other activities that could have significantly altered the routine management of eligible patients. Patients from California were selected from a computerized list of all patients managed in the network. The other 3 centers approached their own community networks of physicians to recruit practices.

Information about each participating practice collected at the time of enrollment included practice size (ie, total number of patients covered and number whose anticoagulation was managed by the practice during the study period), method of dose management, description of the monitoring process, participation in any research studies or audit activities related to anticoagulation, and details of practice organization and charting. Physicians who contributed patients to the study completed a form at the study's conclusion that documented physician specialty and method of anticoagulation management.

Practices in California and Indiana used a computerized billing system, whereas Massachusetts and North Carolina used a paper list to identify patients who had a diagnosis of atrial fibrillation, and who filled a prescription for a VKA during the study period of July 1, 2001, through June 30, 2002. The records of all patients who met these screening criteria were reviewed by data abstractors to establish whether the patient met the eligibility criteria, which were age 18 years or older, recorded diagnosis of CNVAF documented by at least 1 electrocardiogram with a written interpretation of atrial fibrillation or by a physician's note specifying the diagnosis, and VKA prescriptions covering at least 60 consecutive days during the study period and managed at the participating practice during the entire study period. Breaks in treatment or follow-up during the qualifying

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period were allowed provided that they lasted fewer than 14 days and were due to a documented inpatient admission or invasive procedure(s). Individuals were ineligible if they had recorded rheumatic heart disease, prior heart valve surgery, or a prosthetic heart valve at any time; if during the study period they were monitored in a specialized anticoagulation clinic; if they were involved in a prospective clinical study related to anticoagulation care; or if they were successfully cardioverted during the qualifying 60-day period.

Nursing staff from each site were trained in a 1-day session focusing on the data abstraction process and the use of the interactive voice response system (IVRS). For each potentially eligible patient who met all the criteria, the abstractor completed a paper form covering data on patient characteristics, medical history, anticoagulation use, other medications, monitoring visits, and INR test results. Particular attention was given to collecting data to estimate the quality of anticoagulation control (eg, INR values) and to explicitly registering missing information in each of the sections. Information related to VKA was obtained from prescriptions, notes in the chart, and dispensing information.

To improve data recording accuracy and efficiency, the IVRS was used to record all data. For quality control purposes, the coordinating center conducted an audit of a randomly selected 10% of the enrolled patients per center.

The coordinating center was responsible for the training of abstractors, data collection process, supervision of staff activities, supervision of quality assurance, and data analyses according to a predefined plan. The database was reviewed to verify codes and identify errors. Follow-up, for the purpose of analyzing data, started with the first day of the qualifying period of VKA use (ie, the first 60-day period of continuous use) and extended to the conclusion of the study period, death, permanent departure from the study practice, permanent transfer of anticoagulation management, or permanent discontinuation of anticoagulation. "Permanent" meant that there was no resumption within the study period.

Univariate analyses were carried out to summarize baseline patient characteristics, duration of treatment at start of follow-up, physician and practice characteristics, and monitoring system. Bivariate analyses included cross-tabulations and correlations of stroke risk factors and anticoagulant use with baseline characteristics. The primary outcome was the overall mean INR and percentages of time above, within, and below the target INR range. For INRs, the denominator was analyzable days of follow-up. Days between 2 INR tests were considered "nonanalyzable" if there was a temporary discontinuation of treatment for 14 days or more, a hospitalization lasting 14 days or more, or if the patient was monitored elsewhere for 14 days or more. The events (numerators) included the number of INR tests, number leading to change in dose, and number where treatment was temporarily discontinued. For each patient, INR values for days between tests were imputed using linear interpolation.[18] This allowed derivation of the time spent at given INR levels and the proportion of follow-up time in a given INR range. In case of missing INR values, INRs were interpolated using the adjacent nonmissing INR value. All analyses were done with SAS software, version 8.0 (SAS Institute Inc, Cary, NC).

RESULTS

Patients were drawn from 28 out of 116 practices invited to participate in 4 regions of the United States representing 100 physicians. Two thousand and 10 medical records of patients who received anticoagulation care during the study period were screened; 690 met criteria to be fully reviewed. Upon full review, 3 did not meet the eligibility criteria and 1 was a duplicate. The final sample consisted of 686 patients from 28 practices with 100 practitioners (Table 1). Sixty-seven percent of the physicians characterized their practice as internal medicine, 25% as family medicine, 10% as cardiology, 9% as other, 4% as geriatrics, and 1% as general practice (more than 100% because some practices listed dual characterization).

Fifty-three percent of patients were male; mean age was 75 years. The result of an electrocardiogram confirming CNVAF was recorded in 59% of cases; 40% did not document the type of CNVAF. Most patients (84%) were followed for more than 9 months during the study period.

The presence or absence of risk factors for stroke was not recorded in 8% to 30% of medical records (Table 2). Fifty-three percent of patients older than 65 years had more than 1 risk factor for stroke, whereas 23% of those younger than 65 years had more than 1 risk factor for stroke.

Among patients who were receiving anticoagulation treatment at the start of the follow-up, 88% were prescribed warfarin, fewer than 12% (11.84%)

Table 1

Distribution of Practices, Physicians, and Patients in the 4 Regions

Site	# of Practices Accepted	# Physicians Invited	# Physicians Accepted	# of Physicians Participating	# of Records Screened	# of Records Meeting Criteria	# of Records Excluded
Massachusetts	5	30	18	16	300	200	3
California	15	54	49	48	695	156	1
Indiana	2	15	5	4	276	134	0
North Carolina	6	44	44	32	739	200	0
Total	28	143	116	100	2010	690	4

Table 2

Patient Characteristics and Recorded Risk Factors for Stroke

Patient Characteristics	N (%)
Age	
<65	102 (15)
65-74	208 (30)
75-84	284 (41)
>84	92 (14)
Sex	
Male/Female	364 (53)/320 (47)
Race	
White	396 (58)
Black	21 (3)
Other	7 (1)
Unknown	262 (38)
Type of atrial fibrillation	
Paroxysmal	175 (26)
Persistent	241 (35)
Unknown	270 (39)
Risk Factors	**Patient Records**
Hypertension	68%
Diabetes	22%
Previous ischemic stroke or transient ischemic attack	11%
Prior systemic embolism	1%
Coronary artery disease	38%
Congestive heart failure	26%
Cancer	20%
No recorded risk factors	16%

Table 3

Responses by Physicians to Selected Survey Questions Focusing on Processes of Care (67 of 100 physicians responded)

INR test associated with a face-to-face encounter >50% of the time	30%
Use of point-of-care testing >85% of the time	27%
Use of point-of-care testing never	72%
Patient informed of result by MD >85% of the time	3%
Patient informed of result by RN >85% of the time	63%
Patient informed of result by lab tech >85% of the time	16%
Patient informed of result by pharmacist	0%
Result conveyed by face-to-face encounter (>85% of the time)	19%
Result conveyed by telephone (>85% of the time)	64%
Result conveyed by mail	1%
Dose change conveyed by face-to-face encounter (>85% of the time)	19%
Dose change conveyed by telephone (>85% of the time)	66%
Dose change conveyed by mail	0%
Dose changes provided in writing	34%
Dose adjustment guided by clinical judgment	75%
Dose adjustment guided by guideline, algorithm, computer	19%
Mean (SD) interval for monitoring stable, uncomplicated patients	27 (±5)

INR = international normalized ratio.

received an anticoagulant that was unspecified, and fewer than 1% received anisindione (0.16%). Most records (99%) did not have a goal target INR documented, and 40% did not specify a goal target therapeutic range.

Sixty-seven of the 100 physicians (67%) responded to the practitioner survey. Table 3 summarizes responses to several questions related to processes of care. Twenty-seven percent used point-of-care testing to measure the INR most of the time. Most INR results and dose changes were conveyed by telephone. Clinical judgment was most often used to adjust doses. The median interval for INR testing in stable patients was 28 days.

The mean and median interval between all INR tests was 25 and 21 days, respectively. The median interval decreased as the INR increased from 3.01 to 3.59 (17 days), 3.60 to 4.59 (14 days), and >4.60 (7 days); for INRs between 1.50 and 1.99 (18 days); and <1.50 (14 days).

Table 4

Dose Management

	INR			
	<2.00	3.01-5.00	5.01-9.00	>9.01
VKA change in dose N (%):				
Yes	777 (32.4)	414 (34.9)	58 (55.2)	3 (50.0)
No	1592 (66.4)	771 (65.1)	47 (44.8)	3 (50.0)
Unknown	30 (1.2)	0	0	0
VKA temporarily discontinued N (%):				
Yes	14 (0.6)	15 (1.3)	9 (8.6)	1 (16.7)
No	2337 (97.4)	1168 (98.5)	96 (91.4)	5 (83.3)
Unknown	48 (2.0)	2 (0.2)	0	0
Vitamin K given N (%)				
Yes	3 (0.1)	2 (0.2)	1 (1.0)	2 (33.3)
No	1936 (80.7)	994 (83.9)	79 (75.2)	3 (50.0)
Unknown	460 (19.1)	189 (15.9)	25 (23.8)	1 (16.7)

INR = international normalized ratio; VKA = vitamin K agonist.

Documentation of INRs was limited. VKA dose was changed for 36% of INRs above therapeutic range and 32% of those below. VKA was temporarily discontinued for 2% of elevated INRs. Vitamin K was given in 0.5% of elevated INRs, although in 17% of cases, it was unknown whether or not vitamin K was given. Table 4 summarizes the dose response to out-of-range INRs as documented in the patient records.

Based on Rosendaal's method of interpolation,[18] INRs were within the INR therapeutic range of 2.0 to 3.0 58% of the time, below range 28% of the time, and above range 14% of the time. Using the frequency of INRs in or out of range, we found that 51% of the INRs were within range, 31% below range, and 17% above range. The time-in-therapeutic range was slightly shorter for females and for patients <65 years old compared with older patients. An analysis by risk factors showed variation of the percentage of time for therapeutic INRs without any specific pattern: on average, patients without stroke risk factors were in range 54% of the time, those with 1 risk factor were in range 59% of the time, those with 2 risk factors were in range 55% of the time, and those with 3 or more stroke risk factors were in range 59% of the time. Independent of the method of dosing, patients were in therapeutic range more than half of the time (51% when computer dosing was used, 57% with algorithm/guidelines, and 57% with clinical judgment).

All sites were audited, and discrepancy rates between the first and second data extraction ranged from 0.4% to 4.6%.

DISCUSSION

Although the process of care and related outcomes have been well documented for anticoagulation clinics or patient self-management using point-of-care prothrombin time monitoring devices at home,[19-21] there is limited information about the outcomes of care[21] and even less about the processes of care in the RMC of oral anticoagulation. Using CNVAF as a uniform indication for oral anticoagulation, this study characterizes the processes of care of oral anticoagulation management in an RMC setting and assesses quality of management by using surrogate end points, such as time in therapeutic range and response to a nontherapeutic INR. We found a substantial fraction of INRs or percentage of time out of therapeutic range, with more below range than above range, as has been found by others.[22] Surveys suggest that physicians remain reluctant to incur the risk of severe bleeding, preferring instead to err on the side of subtherapeutic levels.[23,24] Overall, the time-in-therapeutic range in this study was in the upper range compared with reports from other studies of RMC where time or percent INRs in range are reported to be from a low of 33% up to 64%.[22] These results may be better because anticoagulation management has improved over the years. Alternatively, these practices may not be typical because many were associated with academic medical centers.

The physicians' response to an out-of-range INR was also used as a measure of high-quality dose management. In all cases, more frequent monitoring would be indicated. These responses to out-of-range INRs indicate major deficiencies in VKA management. The median INR interval for retesting after an out-of-range value did decrease, but guidelines suggest even more frequent monitoring for markedly nontherapeutic INRs is in order.[22]

We found that many of the charts lacked a confirmatory electrocardiogram or documentation of the type of atrial fibrillation or risk factors justifying anticoagulation.[25] Forty percent of charts did not specify a target INR. We also found insufficient information related to anticoagulation supervision, particularly in those patients who were out of control.

Poor documentation of patient data, laboratory test results, drug dose changes, and other resulting medical decisions may have an impact on outcomes[26] and might be a factor in malpractice litigations.

A major limitation of this study is that the potential management lapses may, in part, be related to documentation of care rather than to the actual practice, given that the information we collected came from the written medical record and not from physician or patient interviews or other sources of information. However, this study was designed to assess documentation and the quality of care based upon that documentation, and we cannot unequivocally confirm the quality of anticoagulation provided to these patients. There also is a potential for selection bias because the abstractors needed to review preselected charts to determine study eligibility. Although we have no reason to believe it happened, it is possible that incomplete medical records or those of patients with poor outcomes were excluded.

Despite several decades of evidence regarding the benefits of proper anticoagulation in patients with CNVAF and consistent recommendations in this regard, there remains a substantial gap in ensuring optimal prophylaxis in RMC. In contrast to anticoagulation clinics, individual physician practices may lack the robust systems needed to monitor and adjust warfarin therapy and to communicate with patients. Perhaps we have reached the limit of what can reasonably be achieved in RMC and only the advent of new anticoagulants with a broader therapeutic range and less onerous management will allow practices to finally meet these requirements.

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