Geographic Variation in the Use of Oral Anticoagulation Therapy in Stroke Prevention in Atrial Fibrillation

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Background and Purpose—Underuse of oral anticoagulation in stroke prevention in atrial fibrillation is common; however, it remains unknown how it varies geographically. The objective of this study was to evaluate geographic variation in oral anticoagulation use and in the initiation of new oral anticoagulants (NOACs).

Methods—Using 2013 to 2014 claims data from a 5% random sample of Medicare beneficiaries, we identified patients newly diagnosed with atrial fibrillation who initiated NOACs (n=8659), warfarin (n=11 771) or no oral anticoagulation therapy (n=18 226) in 2013 to 2014. Each patient was assigned to 1 of the 306 Dartmouth hospital-referral regions based on his/her zip code. We constructed logistic regressions to calculate the mean adjusted probability of initiating oral anticoagulation and the mean adjusted probability of initiating an NOAC among patients on oral anticoagulation in each hospital-referral region, after adjustment for demographic, clinical, and provider characteristics and type of insurance. Finally, we computed the correlation between 2 probabilities.

Results—Higher in the Midwest (0.54) and Northeast (0.54) and lowest in the South (0.47), the mean adjusted probability of initiating oral anticoagulation was 0.51, ranging from 0.32 to 0.72. The mean adjusted probability of being prescribed an NOAC among those on oral anticoagulation was 0.42 and was highest in the South (0.50) and lowest in the Midwest (0.36) and Northeast (0.39). In areas with the lower use of oral anticoagulation, patients on any oral anticoagulation therapy had a higher likelihood of being prescribed an NOAC (correlation coefficient, −0.16; P=0.006).

Conclusions—Large geographic variation exists in oral anticoagulation use in atrial fibrillation. The use of oral anticoagulation is lower in the South, where the rates of stroke are unusually high. In the future, it will be important to analyze whether the high rates of stroke in the South can be partially attributed to the underuse of oral anticoagulation in this region. **(*Stroke*. 2017;48:2289-2291. DOI: 10.1161/STROKEAHA.117.017683.)**

Key Words: anticoagulants ■ atrial fibrillation ■ health services research ■ Medicare ■ stroke

Atrial fibrillation (AF) is the most important single cause of ischemic stroke.[1] Oral anticoagulation is highly effective in stroke prevention in AF but underuse is common in the United States, only around half of the patients newly diagnosed with AF who are recommended for oral anticoagulation therapy actually use it.[2] After new oral anticoagulants (NOACs) had entered the market, several studies evaluated the factors associated with the initiation of NOACs, relative to warfarin.[3] However, it remains unclear how the use of oral anticoagulation in AF varies across regions of the United States. To address this question, we used 2013 to 2014 claims data from a 5% random sample of Medicare beneficiaries.

Methods

We identified Medicare beneficiaries newly diagnosed with AF in 2013 to 2014.[4] We excluded those who were not continuously enrolled in Part D or who died before December 31, 2014 (our results are similar after including those who died). For the remainder, we collected oral anticoagulants claims filled between the date of the first AF diagnosis and December 31, 2014. The sample included 8659 NOAC users, 11 771 warfarin users, and 18 226 patients who did not use oral anticoagulation. Each beneficiary was assigned to 1 of the 306 Dartmouth hospital-referral regions (HRRs) using the zip code.[5] This study was approved by the University of Pittsburgh Institutional Review Board as exempt because deidentified data were used.

To estimate geographic variation in oral anticoagulation use that is not explained by patient demographics, type of insurance, and clinical characteristics, we constructed a logistic regression model where the outcome was oral anticoagulant initiation (1 for the NOAC and warfarin groups, 0 for the no oral anticoagulation group). Predictors included indicator variables for HRRs, age, sex, race, eligibility for Medicaid coverage, eligibility for a low-income subsidy, partial enrollment in a Medicare Advantage Part D plan, and clinical characteristics known to affect the initiation of anticoagulation (notes in Figure 1). To examine geographic variation in the probability of being prescribed an NOAC among those on oral anticoagulation that is not attributable to differences in patient demographics, type of insurance, clinical characteristics, or provider factors, we constructed a logistic regression where the outcome was NOAC initiation (1 for the NOAC group, 0 for the warfarin group), and predictors included all variables listed above, as well as several provider-level variables including age, sex, specialty, and number of beneficiaries assigned to the provider that prescribed the first oral anticoagulant after AF

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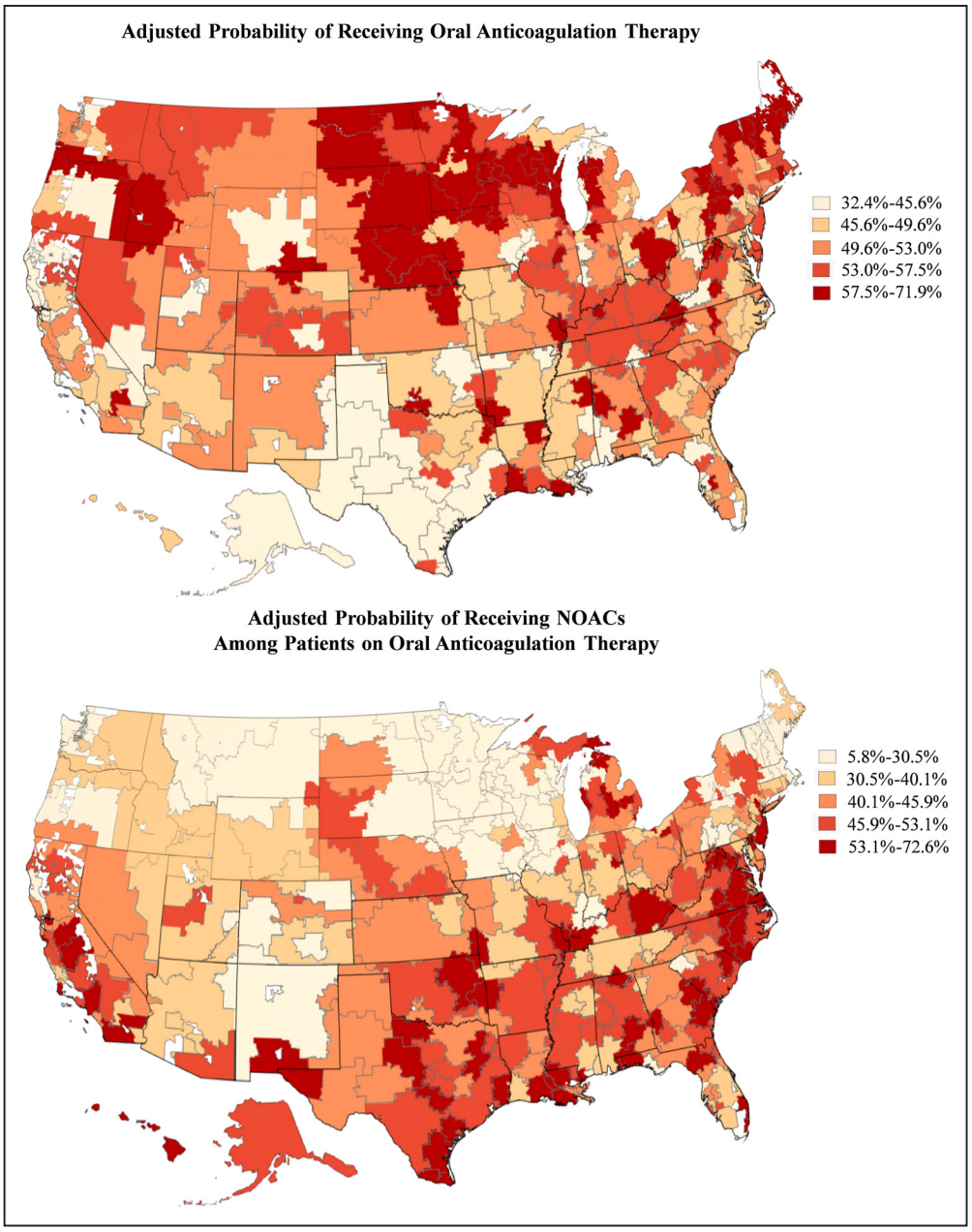

Figure. Quintiles of the adjusted probability of initiating an oral anticoagulation therapy and of the adjusted probability of being prescribed a new oral anticoagulant (NOAC) among patients initiating oral anticoagulant therapy, by hospital-referral region. The **top** map shows quintiles of the adjusted probability of initiating any oral anticoagulation therapy, and the **bottom** map shows quintiles of the adjusted probability of initiating an NOAC among patients who initiated oral anticoagulation. Both probabilities were adjusted for age, sex, race, eligibility for Medicaid coverage, eligibility for low-income subsidy, enrollment in a Medicare Advantage Part D, acute myocardial infarction, chronic heart failure, hypertension, chronic kidney disease, diabetes mellitus, peripheral vascular disease, liver disease, a history of stroke or transient ischemic attack, a history of alcohol or drug use, the number of other Centers for Medicare and Medicaid Services priority comorbidities, a recent history of bleeding, recent use of antiplatelet agents, and recent use of nonsteroidal anti-inflammatory drugs. The probability of initiating an NOAC among those on oral anticoagulation was further adjusted for the age, sex, primary specialty, and number of beneficiaries assigned to the provider that prescribed the first oral anticoagulant agent after the first diagnosis of atrial fibrillation.

diagnosis.[3] Then, we estimated the average probability of receiving oral anticoagulation and the average probability of being prescribed an NOAC among patients on oral anticoagulation in each HRR, while holding all predictors mentioned above constant.[6] This methodology enabled us to isolate geographic variation that is not explained by the confounders listed above.[6] Finally, we examined the correlation between the adjusted probability of receiving oral anticoagulation and the adjusted probability of being prescribed an NOAC among patients on oral anticoagulation in each HRR.

Results

The mean adjusted probability of initiating oral anticoagulation therapy was 0.51, ranging from 0.32 in Pueblo, Colorado, to 0.72 in Houma, Louisiana, and was highest in the Midwest (0.54) and Northeast (0.54), and lowest in the South region (0.47). The mean adjusted probability of being prescribed an NOAC among those on oral anticoagulation was 0.42, ranging from 0.06 in

Appleton, Wisconsin, to 0.73 in Montgomery, Alabama, and was highest in the South (0.50) and lowest in the Midwest (0.36) and Northeast (0.39; Figure 1). Regional variation in initiating an NOAC among those who initiated any oral anticoagulation (highest to lowest ratio=12.46; coefficient of variation=32.07) was larger than the variation in the oral anticoagulation use (highest to lowest ratio=2.22; coefficient of variation=14.16).

We found an inverse correlation between the probability of initiating oral anticoagulation and the probability of being prescribed an NOAC among those who initiated any oral anticoagulation therapy (correlation coefficient=−0.16; *P*=0.006). In other words, patients living in regions with more use of any oral anticoagulation treatment were less likely to be prescribed an NOAC than patients in regions with less use of oral anticoagulation (Figure).

Discussion

Our study is the first to use the US nationally representative sample of patients with AF to examine geographic variation in the use of oral anticoagulation. We found large geographic variation in the use of oral anticoagulation in stroke prevention in AF, with the likelihood of initiating any oral anticoagulation therapy highest in the Midwest and Northeast and lowest in the South. Furthermore, we observed that patients on oral anticoagulation were less likely to be prescribed NOACs in regions with higher anticoagulation use than in regions with less anticoagulant use. Specifically, the probability of NOAC initiation was highest in the South, where previous studies have observed a greater diffusion of new expensive drugs[7] and lowest in Wisconsin, where, interestingly, warfarin was discovered. Variation in anticoagulation use presented a similar geographic pattern to variation in stroke rates: anticoagulation use was lowest in Texas, Oklahoma, Missouri, Arkansas, Mississippi, and North Carolina, all of which are well known for having unusually high rates of stroke.[8]

Because our sample is mostly representative of stand-alone Medicare Part D plans beneficiaries, who tend to be sicker than Medicare Advantage beneficiaries, one may wonder whether our results are affected by geographic variation in the penetration of Medicare Advantage. To test this hypothesis, we evaluated the correlation between the adjusted probability of using oral anticoagulation and the penetration of Medicare Advantage in each HRR, finding that they were not correlated (correlation coefficient=0.05; *P*=0.428). Nevertheless, our study is subject to 3 limitations: First, Medicare claims data do not capture information on the use of medications that are not submitted for reimbursement. As a result, our results are not adjusted for geographic variation in the penetration of generic programs or anticoagulation clinics that do not bill for prescriptions. Second, there may be unobserved prescriber factors that affect the likelihood of prescribing anticoagulation, such as provider-level risk aversion to the risk of bleeding with anticoagulants or provider education. Third, in our study, we controlled for eligibility for Medicaid or low-income subsidy, but we did not have other indicators of socioeconomic status and education. Nevertheless, our study makes an important contribution to the literature because, the first to use a nationally representative sample, it demonstrated geographic variation in oral anticoagulant use after adjustment for patient and provider characteristics.

In conclusion, oral anticoagulation use in stroke prevention in AF varies substantially by region, with some HRRs more than doubling others. Because oral anticoagulation use was lowest in regions with the highest stroke incidence rates, the implementation of interventions targeted at increasing the use of oral anticoagulation in AF could have high potential to decrease the incidence of stroke in these areas. In future studies, it will be important to analyze whether the unusually high rates of stroke in the stroke belt are partially attributed to the underuse of oral anticoagulation in this region.

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Disclosures

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