CHEST

Original Research

ANTITHROMBOTIC THERAPY

Gaps in Monitoring During Oral Anticoagulation

Insights Into Care Transitions, Monitoring Barriers, and Medication Nonadherence

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Background: **Among patients receiving oral anticoagulation, a gap of > 56 days between international normalized ratio tests suggests loss to follow-up that could lead to poor anticoagulation control and serious adverse events.**
Methods: **We studied long-term oral anticoagulation care for 56,490 patients aged 65 years and older at 100 sites of care in the Veterans Health Administration. We used the rate of gaps in monitoring per patient-year to predict percentage time in therapeutic range (TTR) at the 100 sites.**
Results: **Many patients (45%) had at least one gap in monitoring during an average of 1.6 years of observation; 5% had two or more gaps per year. The median gap duration was 74 days (interquartile range, 62-107). The average TTR for patients with two or more gaps per year was 10 percentage points lower than for patients without gaps ($P < .001$). Patient-level predictors of gaps included nonwhite race, area poverty, greater distance from care, dementia, and major depression. Site-level gaps per patient-year varied from 0.19 to 1.78; each one-unit increase was associated with a 9.2 percentage point decrease in site-level TTR ($P < .001$).**
Conclusions: **Site-level gap rates varied widely within an integrated care system. Sites with more gaps per patient-year had worse anticoagulation control. Strategies to address and reduce gaps in monitoring may improve anticoagulation control.** ***CHEST 2013; 143(3):751–757***

Abbreviations: ACC = anticoagulation clinic; INR = international normalized ratio; IQR = interquartile range; TTR = time in therapeutic range; VA = Veterans Health Administration

Like any anticoagulant, warfarin is hazardous; correct use is imperative to avoid thromboembolic or hemorrhagic complications. The narrow therapeutic window and variable dose response of warfarin mandate frequent monitoring of the international normalized ratio (INR) to ensure that the patient remains within the therapeutic range. During our study period, prominent guidelines recommended INR testing at least every 28 days[1] or every 42 days,[2] although the latest American College of Chest Physicians guidelines allow an interval of up to 90 days for selected patients with extremely stable control.[3] The Anticoagulation Forum states that "A tracking system (e.g. an electronic

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database) should be implemented to minimize the possibility that a patient on anticoagulation therapy could be lost to follow-up, even for a brief period."[4]

Despite our sense that preventing gaps in INR monitoring is important, relatively little is known about gaps, including how often they occur and their relationship to anticoagulation control. However, our previous work has suggested that sites with excellent anticoagulation control have systems in place to minimize gaps, whereas sites with poor control do not.[5] This raises the possibility that intervening to help sites develop such systems could improve anticoagulation control and outcomes for patients.

We, therefore, used a large database of patients receiving warfarin from the Veterans Health Administration (VA) to examine the prevalence of gaps in INR monitoring and their patient-level and site-level correlates. We sought to answer the following questions: (1) How frequent are gaps in INR monitoring among patients receiving long-term warfarin therapy? (2) How do gaps impact patient-level anticoagulation control, as measured by time in therapeutic range (TTR)? (3) What patient-level characteristics predict gaps in monitoring? (4) Do sites of care differ in the rate of gaps per patient-year? (5) Does the rate of gaps predict site-level anticoagulation control? The overarching goal of our study was to examine the suitability of the site-level rate of gaps in INR monitoring as a performance measure in anticoagulation care and a target for quality improvement efforts.

Materials and Methods

Data

The database for this study also been described elsewhere.[6,7] The Veterans Affairs Study to Improve Anticoagulation (VARIA) included all patients receiving oral anticoagulation from the VA between October 1, 2006, and September 30, 2008, as described later. The study was approved by the institutional review board of the Bedford VA Medical Center (Protocol Number: Rose 0001).

Patients

We included all patients aged 65 years and older who received warfarin from the VA during the 2-year study period. We limited this study to patients aged 65 years and older because of the availability of Medicare data. We excluded patients enrolled in Medicare Advantage during any part of the study period (15,905 or 22%), because Medicare use data for such patients are incomplete. The combined VA and Medicare database ensured essentially complete capture of all INR testing for these patients.[8] Although we were aware of all dates when the INR was tested (which allowed us to measure gaps in monitoring), we had access to INR results only in the VA data, and all TTR calculations came from this source.

We excluded patients whose primary indication to receive warfarin was valvular heart disease. Many such patients have a target INR range of 2.5 to 3.5, rather than the more standard 2 to 3, and because we could not identify which patients had the higher target range, we could not calculate TTR.

Laboratory Values and Calculation of Percentage TTR

We calculated TTR using Rosendaal's method,[9] which uses linear interpolation to assign an INR value to each day between successive observed INR values. Gaps of >56 days between INR values were not interpolated. After interpolation, the percentage of time during which the interpolated INR values lay between 2.0 and 3.0 (from 0% to 100%) was calculated.[9]

We excluded INR tests measured during hospitalizations, because hospitalized patients may receive temporary parenteral anticoagulation or no anticoagulation. For this study, we also excluded INR data from each patient's first 6 months of therapy with warfarin (the "inception period"), when treatment may have differed from that received by experienced warfarin patients.

Sites of Care

We included 100 VA sites of care, each of which has a specialized anticoagulation clinic (ACC) run by clinical pharmacists.[10] By policy, all patients whose anticoagulation is managed in the VA are treated by specialized ACCs.[10] Most patients visited only one site of care; for the remainder (3% of patients), we partitioned their data by site.

Risk-Adjustment Model

We have previously described our risk-adjustment model for TTR.[6,7] We considered many variables that might have affected TTR, including demographics, area-level poverty, driving distance to care, physical health conditions, mental health conditions, number of medications, and number of hospitalizations. We used a simple, rather than a hierarchical, approach to derive our risk-adjustment model, because the exact *P* values were not important in this context, and the point estimates were unchanged regardless of the approach taken. Table 1 lists the variables that compose the risk-adjustment model for TTR. We calculated risk-adjusted TTR as follows. First, we calculated each patient's observed TTR and applied the risk-adjustment model to calculate the expected TTR. Second, an observed minus expected score was calculated for each patient; we also computed the mean observed, expected, and observed minus expected score for each site of care. Therefore, site-level risk-adjusted TTR was based on the mean observed TTR and the mean expected TTR at each site.

Rate of Gaps in Monitoring

We defined a gap in monitoring as any period >56 days between two successive INR tests. This interval was chosen because a gap of 56 days is traditionally understood to indicate a lack of monitoring, and a period across which TTR is not interpolated.[9] We considered both VA and Medicare INR values when calculating gaps; that is, any outpatient INR test in either system caused the clock to be reset, and the patient was given another 56 days to obtain the next INR. However, in INR tests obtained during an inpatient stay, we did not reset the clock for calculating gaps. We calculated gaps per year for each patient, as well as gaps per patient-year for each site of care.

We also conducted sensitivity analyses, exploring what our findings would have been had we counted only gaps that did not contain a hospital stay. Applying this alternative definition of "gap" reduced the calculated rate of gaps for some patients, but otherwise the results obtained were quite similar to those presented here.

Possession of Warfarin

We characterized warfarin possession during gaps to better understand their context. We considered patients to be in possession