Guideline-Discordant Periprocedural Interruptions in Warfarin Therapy

Lesli E. Skolarus, MD, MS; Lewis B. Morgenstern, MD; James B. Froehlich, MD, MPH; Lynda D. Lisabeth, PhD; Devin L. Brown, MD, MS

Background—Periprocedural interruptions in warfarin therapy increase thromboembolic risks to patients and are not indicated for all procedures. We sought to determine the frequency and guideline concordance of periprocedural warfarin interruptions to inform a future educational intervention.

Methods and Results—In October and November of 2009, an anonymous postal survey was sent to all patients followed for more than 1 year by the University of Michigan Anticoagulation service. Patients were asked how many times in the prior year they were requested to interrupt warfarin therapy for a medical or dental procedure or test and the specific indication for the requested interruption in warfarin therapy. A total of 1686 of 2133 (79%) subjects responded. The mean age of respondents was 69 years (SD=14 years). The majority were male (56%) and white (93%). Atrial fibrillation was the most common indication for warfarin therapy (n=966, 57%). At least 1 request to interrupt warfarin therapy in the prior year was given by 819 of 1648 (50%) respondents, including 481 of the 947 (51%) respondents taking warfarin for atrial fibrillation. Forty-eight percent of requests to interrupt warfarin among all respondents and 50% of requests to interrupt warfarin, specifically for atrial fibrillation, were for indications not supported by guideline statements.

Conclusions—Periprocedural requests to interrupt warfarin therapy are common and are often discordant with current guidelines. Educational interventions may decrease risk of periprocedural thromboembolic complications. (Circ Cardiovasc Qual Outcomes. 2011;4:00-00.)

Key Words: anticoagulants ■ arrhythmia ■ stroke ■ prevention

More than 30 million warfarin prescriptions are dispensed annually in the United States to prevent thromboembolism. During interruptions in warfarin therapy, many of which occur in the setting of medical procedures, patients are left vulnerable to thromboembolic events. To decrease the risk of periprocedural thromboembolic events, including stroke, it is imperative to understand periprocedural anticoagulation management.

The American College of Chest Physicians (ACCP) in 2008 and the American Society for Gastrointestinal Endoscopy (ASGE) in 2002 recommended continuing anticoagulation for dental procedures, dermatologic procedures, cataract extraction, and colonoscopy (Table 1). These minor procedures comprise up to 30% of procedures among anticoagulated patients. Unfortunately, surveys of physicians and dentists have shown that warfarin is often inappropriately interrupted for procedures, in contradiction to guideline statements.

Previous studies have shown that periprocedural interruptions of warfarin therapy result in up to a 1% risk of thromboembolism. However, the frequency and guideline concordance of warfarin therapy interruptions due to dental and medical procedures are not well known. To inform future interventions aimed at reducing inappropriate periprocedural interruptions in warfarin therapy and their known complications, we conducted a survey of patients cared for by an anticoagulation service. We hypothesized that anticoagulated patients, including those anticoagulated for atrial fibrillation, are frequently asked to discontinue warfarin for dental and medical procedures. We also hypothesized that many of these interruptions in warfarin therapy are for guideline discordant indications, resulting in needless vulnerability to stroke and other thromboembolic events.

Methods

Subjects
Patients from the University of Michigan Anticoagulation Service were queried using a postal survey with a promise of anonymity. The anticoagulation service treats approximately 3400 patients who primarily live in Southeast Michigan. All patients have a University

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of Michigan physician who prescribes warfarin therapy. Currently, the anticoagulation service monitors and adjusts warfarin dosing but does not make decisions regarding the periprocedural management of warfarin therapy. These decisions are made by the prescribing or consulting physician.

**WHAT IS KNOWN**

- Warfarin is commonly prescribed in the United States.
- Current guidelines recommend continuing warfarin in the setting of dental, dermatologic, and cataract procedures.
- Periprocedural interruptions in warfarin result in up to a 1% risk of thromboembolism.
- Proceduralists often require patients to discontinue warfarin for procedures for which guideline statements suggest warfarin continuation.

**WHAT THE STUDY ADDS**

- Fifty percent of patients receiving chronic anticoagulation were asked to interrupt warfarin for a medical or dental procedure in a year.
- Nearly half (48%) of the periprocedural requests to interrupt warfarin were discordant with the prevailing guidelines.
- Models that included demographics and stroke risk did not predict requests for periprocedural warfarin interruptions.

Surveys were mailed to all living anticoagulation service patients who had been followed by the service for a minimum of 1 year (n=2133). A follow-up postcard was mailed approximately 1 week after the first survey mailing and a second round of surveys was mailed 1 month after the initial mailing. The mailings took place in October and November of 2009. Anticoagulation service staff members were permitted to remind patients to complete the survey during routine clinical telephone conversations. No incentives were provided. The study was approved by the University of Michigan Institutional Review Board, using a waiver of documentation of informed consent. All elements of informed consent were provided. The survey queried information on demographics, vascular risk factors, and indications for taking warfarin. Atrial fibrillation as a vascular risk factor and atrial fibrillation as an indication for warfarin administration were queried separately. Patients were asked how many times in the prior 12 months they were asked to interrupt warfarin therapy for a medical or dental procedure or test. Patients were also asked to recall the specific reason(s) for the requested interruption in warfarin therapy.

**Survey**

An introductory letter that accompanied the surveys outlined the elements of informed consent. The survey queried information on demographics, vascular risk factors, and indications for taking warfarin. Atrial fibrillation as a vascular risk factor and atrial fibrillation as an indication for warfarin administration were queried separately. Patients were asked how many times in the prior 12 months they were asked to interrupt warfarin therapy for a medical or dental procedure or test. Patients were also asked to recall the specific reason(s) for the requested interruption in warfarin therapy. Response options were colonoscopy, dental cleaning, other dental, and “other” with a write-in option. The “other” responses were grouped into 9 general categories (Table 2).

**Statistical Analysis**

Descriptive statistics were used to assess patient demographics, presence of vascular risk factors (yes versus no and missing), and indications for warfarin use among respondents and the subset whose warfarin therapy was prescribed for atrial fibrillation. Models that included demographics and stroke risk did not predict requests for periprocedural warfarin interruptions.

**Table 1. Guidelines Recommending Periprocedural Continuation of Warfarin Therapy**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Guideline Recommendation</th>
<th>Level of Evidence</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor dental procedure2 (single or multooth extract, endodontic procedure)</td>
<td>Continue warfarin</td>
<td>Grade 1B</td>
<td>Grade 1 recommendations are considered strong and indicate that the benefits do (or do not) outweigh risks, burden, and costs.</td>
</tr>
<tr>
<td>Minor dermatologic procedures2 (excisions of basal and squamous cell carcinomas, actinic keratoses, and malignant or premalignant nevi)</td>
<td>Continue warfarin</td>
<td>Grade 1C</td>
<td>Grade 1 recommendations are considered strong and indicate that the benefits do (or do not) outweigh risks, burden, and costs.</td>
</tr>
<tr>
<td>Minor ophthalmologic procedures2 (cataract extraction)</td>
<td>Continue warfarin</td>
<td>Grade 1C</td>
<td>Grade 1 recommendations are considered strong and indicate that the benefits do (or do not) outweigh risks, burden, and costs.</td>
</tr>
<tr>
<td>Low-risk endoscopy procedures2 (diagnostic EGD, flexible sigmoidoscopy and colonoscopy with or without biopsy, diagnostic ERCP, and biliary stent insertion without endoscopic sphincter)</td>
<td>Continue warfarin</td>
<td>Not included in the guideline</td>
<td></td>
</tr>
</tbody>
</table>

EGD indicates esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography.
indications for warfarin use. Median and interquartile ranges (IQR) were calculated for the number of requests for warfarin therapy interruptions. The indications for temporary interruption of warfarin therapy were assessed using frequencies and percents. Because atrial fibrillation is a common indication for warfarin and the risks and benefits of withholding warfarin can be more clearly estimated for a single indication, the analyses were therefore repeated in the subset of respondents prescribed warfarin for atrial fibrillation. Colonoscopy, cataract removal, dental, and dermatologic procedures were designated as guideline-discard indications. In model 1, multivariable logistic regression was used to explore the association between demographics (age treated continuously, sex) and vascular risk factors (hypertension, diabetes, coronary disease, hyperlipidemia, atrial fibrillation, stroke/transient ischemic attack, sleep apnea) and requests for periprocedural warfarin interruption (dichotomous). In model 2, a multivariable logistic regression model was used to test the association between periprocedural requests for warfarin interruption (dichotomous) and the indication for warfarin, adjusting for demographics (age treated continuously, sex). The indications for warfarin were dichotomized into high thrombotic risk (atrial fibrillation with a history of stroke/transient ischemic attack or mechanical heart valve), and all other indications. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. The predictive validity of the models was evaluated using the c statistic. A c statistic of 0.5 indicates that the model’s prediction was no better than chance, whereas a c statistic of 1 indicates perfect model discrimination. Analyses were performed using TIBCO Spotfire S +8.1 for Windows.

Results
Baseline demographics and vascular risk factors of the 1686 respondents (79% response rate) are summarized in Table 3. The mean age of the respondents was 69 years (SD=14 years), and more than half (56%) were male. Ninety-three percent of the survey respondents were white. The majority of respondents had a history of hypertension (63%). Nearly two-thirds of respondents (63%) reported a history of atrial fibrillation, and 57% identified it as the indication for anticoagulation therapy. As shown in Table 4, the other

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Respondents (n=1686) n (%)</th>
<th>Respondents Anticoagulated for Atrial Fibrillation (n=966) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69 (14)</td>
<td>74 (11)</td>
</tr>
<tr>
<td>Male</td>
<td>927 (56)</td>
<td>587 (62)</td>
</tr>
<tr>
<td>Race</td>
<td>White 1555 (93)</td>
<td>909 (96)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Non-Hispanic 1535 (98)</td>
<td>892 (99)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1069 (63)</td>
<td>674 (70)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>354 (21)</td>
<td>217 (22)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>782 (46)</td>
<td>522 (54)</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>733 (43)</td>
<td>414 (43)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1060 (63)</td>
<td>N/A</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>383 (23)</td>
<td>228 (24)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>370 (22)</td>
<td>219 (23)</td>
</tr>
</tbody>
</table>

TIA indicates transient ischemic attack.

common indications for warfarin therapy included pulmonary embolism, deep venous thrombosis, and stroke. A total of 819 of 1648 (50%) respondents had at least 1 request for a periprocedural interruption in warfarin therapy during the prior 12 months. There were a total of 1401 periprocedural requests to interrupt warfarin therapy among the 1648 respondents. On average, each respondent had 0.85 (SD=1.2) (median; 0; IQR, 0 to 1) periprocedural requests to interrupt warfarin.

Among those respondents reporting atrial fibrillation as their indication for warfarin therapy, 481 of 947 (51%) had at least 1 request to interrupt warfarin therapy. There were 798 requests to interrupt warfarin among the 947 respondents. On average, each respondent had 0.84 (SD=1.1) (median; 1; IQR, 0 to 1) periprocedural requests to interrupt warfarin.

Among all requests for interruption of warfarin therapy, those for dental procedures (a combination of dental cleaning and other dental procedures) were the most common (26%, n=368), followed by surgery (20%, n=286) and colonoscopy (18%, n=259) (Table 2). Nearly half (48%, n=694) of all requests to interrupt warfarin therapy were for guideline-discordant indications. A similar proportion (50%, n=417) of requests to interrupt warfarin therapy for respondents anticoagulated for atrial fibrillation were also discordant with current guidelines.

Results of the multivariable logistic regression models to explore predictors of requests to interrupt warfarin are shown in Table 5. In model 1, age (OR, 0.99; 95% CI, 0.98, 1.0), heart disease (OR, 1.29; 95% CI, 1.05, 1.59), and high cholesterol (OR, 1.32; 95% CI, 1.07, 1.63) were significantly associated with a request for warfarin interruption. However, this demographic and vascular risk factor model performed poorly (c=0.58). In model 2, after adjustment for demographics, a high-risk indication for warfarin was not associated with a request to interrupt warfarin (OR, 0.96; 95% CI, 0.76, 1.21). This model also performed poorly (c=0.54).

Discussion
This survey of patients cared for by an academic anticoagulation service reveals that medical and dental providers’ requests to interrupt warfarin are often discordant with current guidelines. In our study, nearly 50% of the requests to
Warfarin markedly reduces the risk of stroke among patients with atrial fibrillation. Because atrial fibrillation is so common and such an important risk factor for stroke, educational interventions addressing the patient, proceduralist, and anticoagulation manager targeting guideline-discordant periprocedural warfarin interruptions would have significant public health impact.

One strength of this study is the high survey response rate. However, several limitations warrant discussion. This survey relied on self-report, which may have been inaccurate. Because all study participants were from a single academic anticoagulation service, the results of the survey may not reflect the medical practice in the community. In addition, few ethnic or racial minorities were surveyed; thus, results may not be applicable to minorities. Furthermore, to keep the survey brief and clear, we did not seek information about aspirin use, duration of requested warfarin interruption, bridging anticoagulation with low-molecular-weight heparin, whether warfarin therapy was actually interrupted for the procedure, whether the requested interruptions were reported to the anticoagulation service in real time, or the occurrence of procedures without requests to interrupt warfarin. We did not ask about any medical consequences of warfarin interruption. Because we did not query duration of warfarin use, previous warfarin interruptions and their outcomes, or information about congestive heart failure to calculate a CHADS2 score, we were unable to explore these as predictors of warfarin interruptions.

Information regarding practices of individual respondents’ providers and additional respondent level data that may have improved our models’ ability to predict interruptions in warfarin therapy were not available. Finally, guideline statements are subject to change, as with the 2009 update of the ASGE guidelines that postdated this survey. Nonetheless, our results speak to the application of guidelines prevailing during the time period of the survey.

Requests for periprocedural warfarin interruptions are common and frequently guideline discordant. Educational interventions that target practitioners likely to request guideline-discordant interruptions of warfarin for commonly performed procedures may help limit patient risk. Additionally, strategies that improve patient reporting of requests for warfarin therapy interruption to the anticoagulation service may be helpful.

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**Disclosures**
Dr Froehlich received grants from Sanofi-Aventis and honoraria from Sanofi-Aventis, Pfizer, and Merck/Shering-Plough. He is on the Speakers’ Bureau for Sanofi-Aventis, Pfizer, and Merck/Shering-Plough and is a consultant for Sanofi-Aventis and Pfizer.

**References**

### Table 5. Results of Multivariable Logistic Regression Model to Identify Factors Associated With Warfarin Interruption

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95% CI) Model 1: Adjusted for Demographics and Comorbidities</th>
<th>OR (95% CI) Model 2: Adjusted for Demographics and Warfarin Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.99 (0.98, 1.0)</td>
<td>0.99 (0.98, 1.0)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.95 (0.78, 1.17)</td>
<td>0.90 (0.74, 1.10)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.83 (0.66, 1.03)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.90 (0.70, 1.16)</td>
<td></td>
</tr>
<tr>
<td>Heart disease</td>
<td>1.29 (1.05, 1.59)</td>
<td></td>
</tr>
<tr>
<td>High cholesterol</td>
<td>1.32 (1.07, 1.63)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.25 (0.99, 1.58)</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0.83 (0.65, 1.05)</td>
<td></td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>1.27 (1.0, 1.63)</td>
<td></td>
</tr>
</tbody>
</table>

TIA indicates transient ischemic attack.


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