

POTENTIAL IMPACT OF HOLIDAYS ON INTERNATIONAL NORMALIZED RATIO (INR) IN WARFARIN-USERS AT A MULTIDISCIPLINARY CLINIC



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BACKGROUND

Warfarin is indicated in numerous settings, such as venous thromboembolism (VTE) prophylaxis and treatment, stroke prophylaxis for atrial fibrillation, and embolism prophylaxis for prosthetic cardiac valves. Though warfarin is efficacious, its clinical benefits are dependent on the international normalized range (INR) being in the target range. The INR is determined by the indication for anticoagulation. To measure the effectiveness of warfarin, most clinical studies report the time in therapeutic range (TTR), and warfarin is not presumed to be therapeutic unless the TTR is $\geq 60\%$. Unfortunately, the TTR in the literature ranges from 30-40%. INR is highly variable and affected by multiple factors, such as interacting medications, diet, alcohol intake, acute illness, liver disease, amongst others. We hypothesized that holidays may affect INR values, due to possible changes in diet, medications, and illness during the holiday seasons. At the time of this study, there were no published studies assessing the impact of holidays, travel, and vacation on INR and/or clinical outcomes.

OBJECTIVES

The objective of this study was to characterize potential INR changes before and after each major holiday. Additionally, this study analyzed the frequency of major drug interactions.

METHODS

Participants, Data Collection, and Outcomes

- A retrospective chart review was conducted on all adult patients age 18 years and older managed and followed up at Loma Linda University (LLU) International Heart Institute (IHI) and Faculty Medical Offices (FMO) – Anticoagulation Clinic between 1/1/2018 through 12/31/2018.
- Patients were included if they were taking warfarin at home regardless of indication for anticoagulation.
- Drug-drug interactions were analyzed using IBM Micromedex® 2020 and Lexi-Comp® Online. Major drug interactions were identified.
- Holiday was defined as the ten annual federal holidays recognized by the U.S. Congress.
- Primary outcome was the difference in INR before and after each holiday.

Statistical analysis

- Descriptive statistics are presented for categorical variables in the form of numbers and percentages.
- Mean \pm standard deviation was used to represent the continuous variables.
- Paired t-tests were used to compare continuous data for pre and post INR target data. SPSS version 26 (IBM SPSS, Inc., Armonk, NY) was utilized to analyze the data with the level of significance set at $\alpha = 0.05$.

RESULTS

Table 1. Baseline characteristics

| | | N | % |
|---|-----------------------------------|------|-------|
| Age, mean and SD | | 71.5 | 14.3 |
| Gender | Male | 51 | 55.4% |
| | Female | 41 | 44.6% |
| Race | White | 57 | 62.0% |
| | Hispanic | 24 | 26.1% |
| | Black | 8 | 8.7% |
| | Other | 3 | 3.3% |
| Indication for anticoagulation (INR goal range) | LVAD (1.8-2.5) | 3 | 2% |
| | AF (2-3) | 81 | 88% |
| | Mechanical mitral valve (2.5-3.5) | 8 | 9% |
| Comorbidities | HFpEF | 30 | 32.6% |
| | HFrEF | 5 | 5.4% |
| | HTN | 64 | 70.3% |
| | HLD | 51 | 55.4% |
| | DM | 26 | 28.6% |
| | CAD | 38 | 41.3% |
| | ESRD | 14 | 15.4% |
| | COPD | 6 | 6.5% |
| | Liver disease | 4 | 4.3% |
| | Methamphetamine use (active) | 1 | 1.1% |
| Alcohol use | 0-1 drinks/day | 77 | 86.5% |
| | 1-3 drinks/day | 12 | 13.5% |

SD=standard deviation; INR=international normalized ratio; LVAD=left ventricular assist device; AF=atrial fibrillation; HFpEF=heart failure with preserved ejection fraction; HFrEF=heart failure with reduced ejection fraction; HTN=hypertension; HLD=hyperlipidemia; DM=diabetes mellitus; CAD=coronary artery disease; ESRD=end-stage renal disease; COPD=chronic obstructive pulmonary disease

Figure 1. INR before and after each major holiday

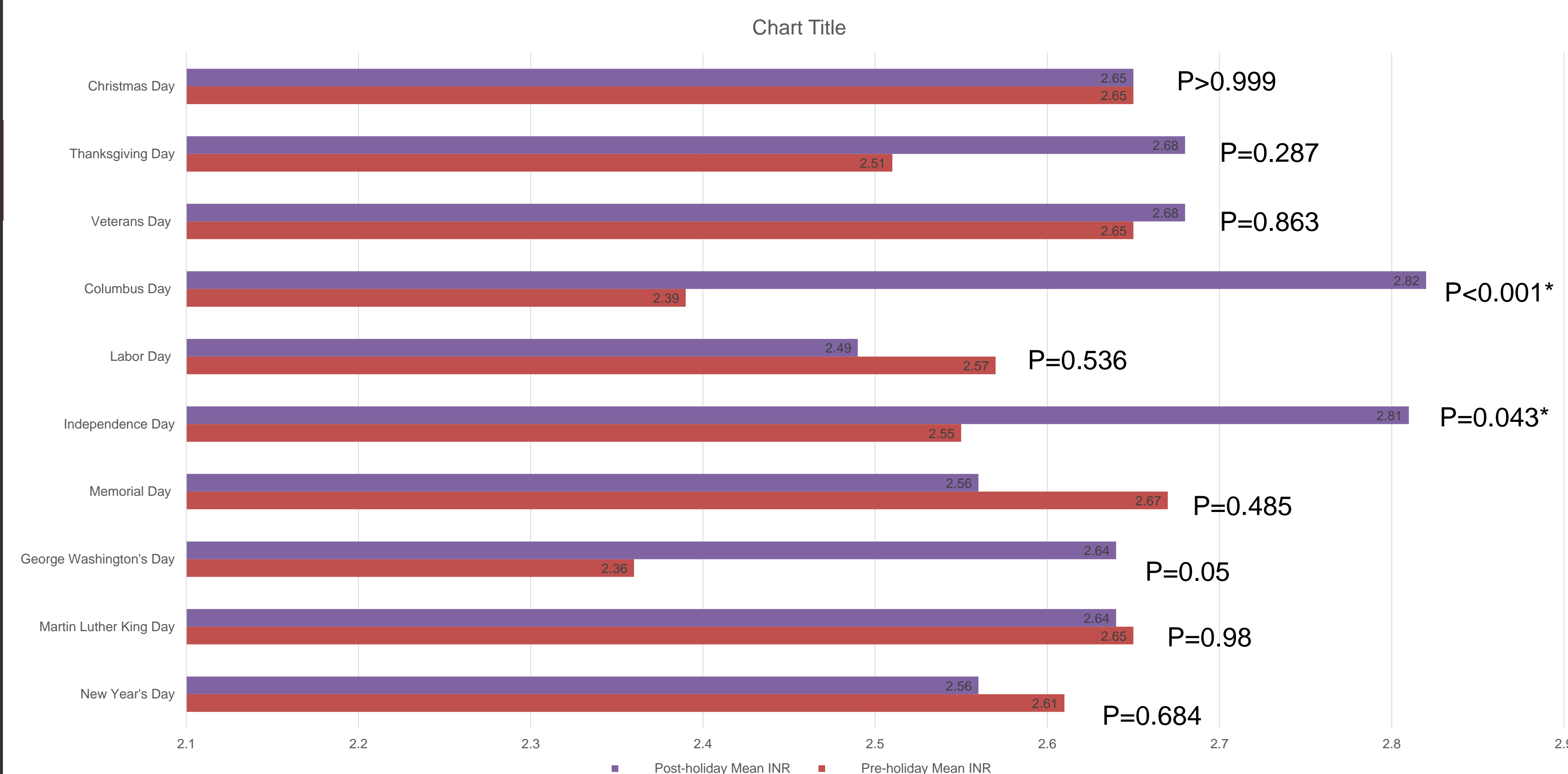
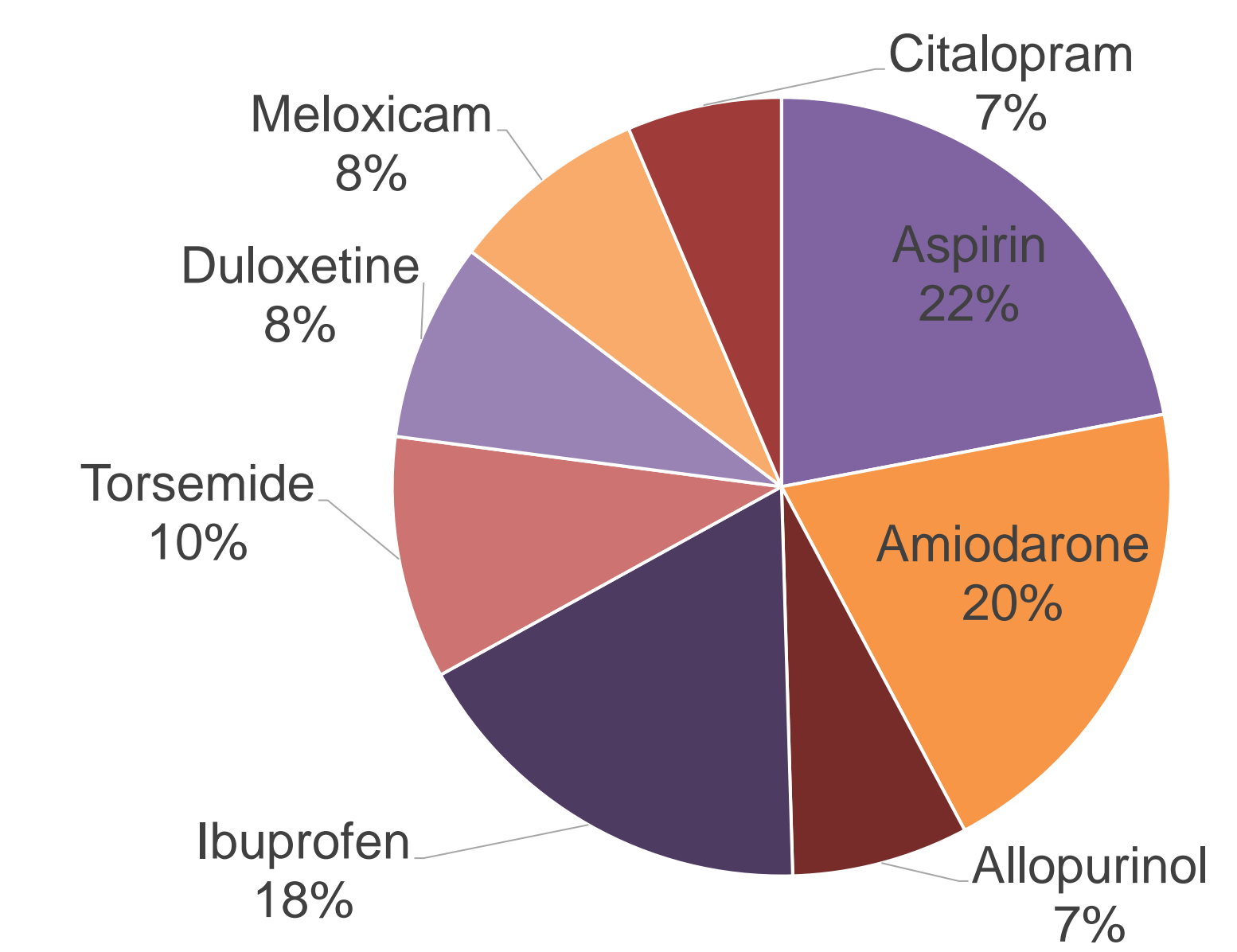


Table 2. Prevalence of major drug interactions

| | N | % |
|-----------------------------------|---|-------|
| Number of major drug interactions | 1 | 70.7% |
| | 2 | 21.7% |
| | 3 | 6.5% |
| | 4 | 1.1% |
| | 5 | 0% |

Figure 2. Major Drug Interactions with Warfarin



DISCUSSION

- Significant differences in pre- and post-holiday were found for Columbus Day and Independence Day. We did not find significant differences for other major holidays, such as Christmas or Thanksgiving. The latter 2 tend to be family-oriented holidays that may be more reflective of one's diet, compared to the first 2 which may involve outdoor events with friends/acquaintances.
- Additionally, we found major drug interactions with warfarin, though most patients only had 1 such interaction (figure 2). Almost half of the patients had coronary artery disease, so concomitant aspirin therapy may be reasonable with adequate monitoring. Most patients had atrial fibrillation as their primary indication for anticoagulation, and amiodarone can be continued as long as the warfarin dose is adjusted according to routine INR values. Lastly, patients were on non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or meloxicam.
- Limitations include those related to the retrospective, observational nature of the study; the inability to address medication adherence; that TTR was not assessed; and that clinical implications were not assessed. This study should be hypothesis-generating for larger, randomized-controlled studies in the future.

CONCLUSIONS

- Patients on warfarin therapy should be counseled to maintain a consistent diet during the holidays, especially Columbus Day and Independence Day. Patients should be advised to avoid NSAIDs for pain and be recommended alternatives such as acetaminophen, as long as there are no contraindications.

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This study has been approved by the Loma Linda University Institutional Review Board.