Inappropriate Warfarin Use in Trauma: Time for a Safety Initiative

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Introduction

• Aging population > 65
  • 2010: 40 million (13.0 %)
  • 2025: 72 million (18.2%)

• 1 million patients take warfarin, majority > 65
Warfarin Risks

- Hemorrhage is the most common complication
  - 6-39% annually
  - Major bleeding 1-3%
  - Fatal bleeding 1%

- Conflicting evidence about anticoagulation specifically warfarin and mortality
Preinjury Warfarin Does Not Impact Outcome in Trauma Patients

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**Objective:** The objective of this study was to determine whether the preinjury condition of anticoagulation had an adverse impact on patients sustaining injury.

**Methods:** A retrospective analysis was performed for prospectively collected registry data from 1995–2000 from all accredited trauma centers in Pennsylvania. The registry was queried for all trauma patients who had anticoagulation therapy as a preinjury condition (PIC). This group served as our experimental cohort. A control cohort (not having warfarin therapy as a PIC) was developed using case-matching techniques for age, sex, Glasgow Coma Scale (GCS), Injury Severity Score (ISS), A Severity Characterization of Trauma (ASCOT) score, and in the head injured patients, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses. Head and non-head injured patients were evaluated separately. The cohorts were examined for 28-day mortality, intensive care unit length of stay (ICU-LOS), hospital length of stay (HOS-LOS), PICs, occurrences, discharge destinations, and functional status at discharge. \( \chi^2 \) and Student’s \( t \) test were used to evaluate the data; \( p \) values < 0.05 were considered significant.

**Results:** Two thousand nine hundred forty-two patients were available for analysis. The prevalence of PICs was significantly greater in the warfarin group for both the head and non-head injured populations \( (p < 0.003 \) and \( p < 0.0001 \) respectively). The incidence of occurrences in the non-head injured population was statistically higher for the warfarin patients \( (p < 0.001) \), but showed no difference in the head injured group regardless of warfarin use \( (p = 0.15) \). Functional status at discharge demonstrated no clinically significant difference between the warfarin and non-warfarin groups in both head and non-head injured populations. There was no difference in discharge destination in the head injured population; however, in the non-head injured population a greater percentage of non-warfarin patients was discharged to home when compared with the warfarin patients.

**Conclusion:** Our data suggest that the PIC of anticoagulation with warfarin does not adversely impact mortality or LOS outcomes in both head and non-head injured patients. In non-head injured patients, however, the occurrence rates and discharge destination were different. More research needs to be done to determine whether this is related to anticoagulation or other reasons (i.e., number of PICs). These data should be used when weighing risk/benefit ratios of prescribing chronic anticoagulation.
Use of Long-Term Anticoagulation is Associated With Traumatic Intracranial Hemorrhage and Subsequent Mortality in Elderly Patients Hospitalized After Falls: Analysis of the New York State Administrative Database

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**Background:** Previous studies addressing the relationship between anticoagulation and risk of traumatic intracranial hemorrhage (ICH) have provided conflicting results, and have examined infrequently elderly patients after falls. We used a statewide hospital discharge database to test the hypothesis that long-term anticoagulation (LTA) increases the likelihood of traumatic ICH and subsequent mortality in this patient population.

**Methods:** Patients aged 65 years or older and hospitalized as the result of a fall were extracted from the New York State Statewide Planning and Cooperative Systems Database for the year 2004. LTA, ICH, and additional injuries including skull fracture, vertebral fracture, rib fracture, lower extremity fracture, thoracic visceral injury, and abdominal visceral injury were defined using corresponding International Classification for Disease, Ninth Edition coding. Covariates included age, gender, and comorbidity. Additional outcomes included length of stay and mortality. Multivariable logistic regression was used to identify independent predictors of traumatic ICH and subsequent mortality.

**Results:** A total of 47,717 patients met the inclusion criteria. Falls were associated with a traumatic ICH in 2,517 patients (5.1%), and the mortality rate of patients with a fall-related, traumatic ICH was 15.5% (n = 394). A total of 1,511 (3.2%) patients hospitalized after a fall used LTA. Based on univariate analysis, ICH was the only injury that occurred more commonly in patients who used LTA, when compared with those who did not (8.0% vs. 5.3%, respectively, \( p < 0.0001 \)). Furthermore, although overall mortality did not differ by use of LTA, mortality after ICH was significantly higher in patients who used LTA when compared with those who did not (21.9% vs. 15.2%, respectively, \( p = 0.04 \)). Controlling for age, gender, and comorbidity, patients on LTA were 50% more likely to sustain a traumatic ICH after a fall (odds ratio = 1.50; 95% confidence interval, 1.23–1.81; \( p < 0.0001 \)). Furthermore, among patients who sustained an ICH, mortality was 1.57-fold greater in patients on LTA (odds ratio = 1.57; 95% confidence interval, 1.02–2.45; \( p = 0.04 \)).

**Conclusions:** These data indicate that use of LTA is independently associated with traumatic ICH and subsequent mortality in elderly patients hospitalized after a fall.

**Key Words:** Anticoagulation, Intracranial hemorrhage, Traumatic brain injury, Geriatrics, Falls.

Degree of Anticoagulation, but Not Warfarin Use Itself, Predicts Adverse Outcomes After Traumatic Brain Injury in Elderly Trauma Patients

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**Background:** The relationship between preinjury warfarin use and outcomes after traumatic brain injury in elderly trauma patients remains controversial. We hypothesized that, among elderly warfarin users, the degree of anticoagulation, rather than warfarin therapy itself, would predict the severity of traumatic brain injury.

**Methods:** Retrospective study (2004–2006) of all elderly trauma patients (age ≥65 years) who were evaluated by the trauma service at a Level I trauma center and underwent computed tomography of the head for suspicion of an intracranial injury was performed. Three cohorts were grouped: (1) warfarin users with an admission International Normalized Ratio ≥2 (therapeutic group), (2) warfarin users with an admission International Normalized Ratio <2 (nontherapeutic group), and (3) warfarin nonusers. Main outcome variables were presenting with a Glasgow Coma Scale (GCS) score ≤13 points, intracranial hemorrhage (ICH), overall mortality, and mortality after ICH.

**Results:** A total of 225 trauma patients were studied, including 40 warfarin users (17.3%), of whom 22 (55.0%) were in the therapeutic group. Age, gender, and mechanism of injury were similar among groups. Likelihood of Glasgow Coma Scale score ≤13 (odds ratio [OR] = 5.13, 95% confidence interval [CI] 1.97–13.39, \( p = 0.001 \)), ICH (OR = 2.59, 95% CI 0.92–7.32, \( p = 0.07 \)), overall mortality (OR = 4.48, 95% CI 1.60–12.50, \( p = 0.004 \)), and mortality after ICH (OR = 3.42, 95% CI 1.09–10.76, \( p = 0.03 \)) was increased in the therapeutic as compared with the nonuser group. There was no difference in any measured outcome between the nonuser and nontherapeutic groups.

**Conclusions:** Therapeutic anticoagulation with warfarin, rather than warfarin use itself, is associated with adverse outcomes after traumatic brain injury in elderly patients.

**Key Words:** Warfarin, Intracranial hemorrhage, Traumatic brain injury, Geriatrics, Anticoagulation.

Hypotheses

• Significant number of trauma patients are on pre-injury warfarin for inappropriate indications

• Significant number of trauma patients on pre-injury warfarin are subtherapeutic & supratherapeutic

• Increased overall mortality in those patients on preinjury warfarin
ACCP Guidelines
Warfarin Indications

- Indications for Warfarin:
  - Atrial fibrillation
  - Venous thromboembolism
  - Prosthetic heart valve
  - Ischemic cardiomyopathy
Methods

• 10 year retrospective study
• Patient population: blunt trauma patients on warfarin
  • Appropriate vs. inappropriate indication
  • Appropriate level of anticoagulation
  • Mortality
• Statistical analysis
  • Multivariable logistic regression
  • Mann Whitney rank sums tests
    • Continuous data
  • Chi square tests
    • Categorical data
Results

• 21,136 patients evaluated
  • 1,481 (7%) were on pre-injury warfarin
    • Mean age $\rightarrow$ 81
    • Mean ISS $\rightarrow$ 9
  • 263 (18%) were on warfarin for inappropriate indications
Indications for Warfarin Use

- Atrial fibrillation (60%)
- VTE (20%)
- Prosthetic valve (10%)
- Multiple indications (10%)
- Other (50%)

Legend:
- Green: Atrial fibrillation
- Red: VTE
- Light blue: Prosthetic valve
- Orange: Multiple indications
- Yellow: Other
## Results: Clinical Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Warfarin</th>
<th>No Warfarin</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6.1%</td>
<td>2.6%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Mortality Max AIS of Head ≥ 4</td>
<td></td>
<td>14.9%</td>
<td>0.009</td>
</tr>
<tr>
<td>HLOS</td>
<td>4 (1-49)</td>
<td>2 (0-87)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Limitations

- Retrospective study
- Reviewer bias
- Single institution bias
- Lack of consensus on warfarin indications
Summary/Conclusions

- **17.7%** of patients on warfarin for inappropriate indications, based on ACCP guidelines

- **53.3%** of patients not within therapeutic range

- Increased mortality and hospital length of stay
Recommendations

- Re-evaluation of pre-injury warfarin use and duration of therapy
- Need stricter surveillance for therapeutic ranges
- Time for a national safety initiative
Questions?