

# Mortality after ground-level fall in the elderly patient taking oral anticoagulation for atrial fibrillation/flutter: A long-term analysis of risk versus benefit

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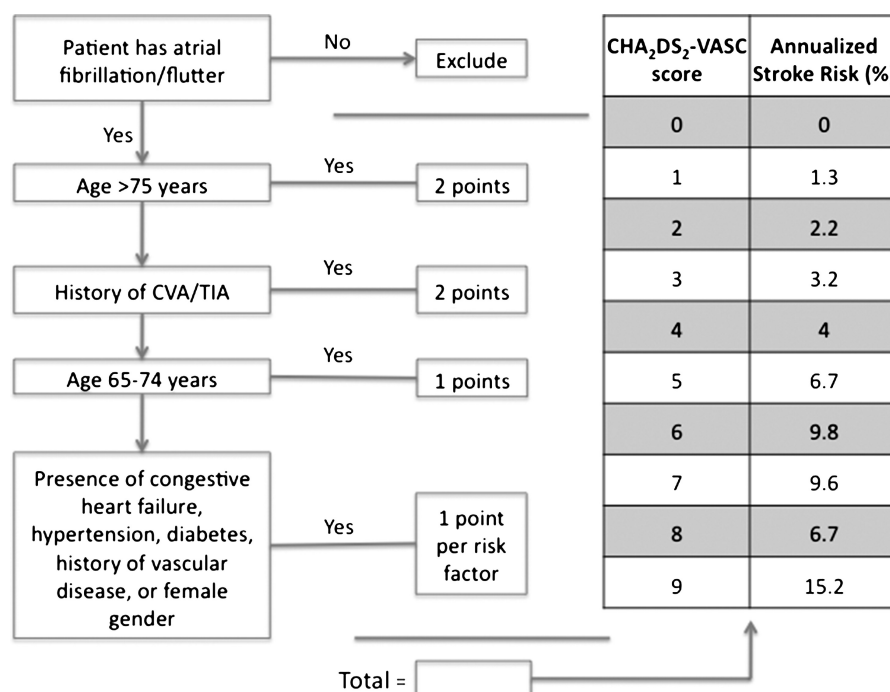
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|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>BACKGROUND:</b>        | Elderly patients with atrial fibrillation or flutter who experience ground-level falls are at risk for lethal head injuries. Patients on oral anticoagulation (OAC) for thromboprophylaxis may be at higher risk for these head injuries. Trauma surgeons treating these patients face a difficult choice: (1) continue OAC to minimize stroke risk while increasing the risk of a lethal head injury or (2) discontinue OAC to avoid intracranial hemorrhage while increasing the risk of stroke. To inform this choice, we conducted a retrospective cohort study to assess long-term outcomes and risk factors for mortality after presentation with a ground-level fall among patients with and without OAC.                                                                |
| <b>METHODS:</b>           | Retrospective analysis of the longitudinal version of the California Office of Statewide Planning and Development database was performed for years 1995 to 2009. Elderly anticoagulated patients (age > 65 years) with known atrial fibrillation or flutter who fell were stratified by CHA <sub>2</sub> DS <sub>2</sub> -VASc score and compared with a nonanticoagulated control cohort. Multivariable logistic regression including patient demographics, stroke risk, injury severity, and hospital type identified risk factors for mortality.                                                                                                                                                                                                                             |
| <b>RESULTS:</b>           | A total of 377,873 patient records met the inclusion criteria, 42,913 on OAC and 334,960 controls. The mean age was 82.4 and 80.6 years, respectively. Most were female, with CHA <sub>2</sub> DS <sub>2</sub> -VASc scores between 3 and 5. Mortality among OAC patients after a first fall was 6%, compared with 3.1% among non-OAC patients. Patients dying with a head injury constituted 31.6% of deaths within OAC patients compared with 23.8% among controls. Risk of eventual death with head injury exceeded annualized stroke risk for patients with CHA <sub>2</sub> DS <sub>2</sub> -VASc scores of 0 to 2. Predictors for mortality with head injury on the first admission included male sex, Asian ethnicity, a history of stroke, and trauma center admission. |
| <b>CONCLUSION:</b>        | Elderly patients on OAC for atrial fibrillation and/or flutter who fall have a greater risk for mortality compared with controls. Patients with low CHA <sub>2</sub> DS <sub>2</sub> -VASc scores (0–3) at high risk for falls with identified risk factors should speak to their prescribing physicians regarding the risk/benefits of continued use of OAC. ( <i>J Trauma Acute Care Surg.</i> 2014;76: 642–650. Copyright © 2014 by Lippincott Williams & Wilkins)                                                                                                                                                                                                                                                                                                           |
| <b>LEVEL OF EVIDENCE:</b> | Epidemiologic/prognostic study, level III.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>KEY WORDS:</b>         | Warfarin; ground-level fall; head injury; mortality; population outcomes.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

The role of oral anticoagulation (OAC) for stroke prevention in patients with chronic cardiac arrhythmias (atrial fibrillation or flutter, hereafter AF) has been well established in the cardiology literature. Warfarin is the most common drug in use for maintaining therapeutic anticoagulation.<sup>1,2</sup> Patients with chronic arrhythmias are assessed for a variety of risk factors that have been shown to independently increase their risk for

thromboembolic stroke (or stroke-associated mortality), and based on that risk, they are recommended to begin either an antiplatelet agent or therapeutic anticoagulation (usually with warfarin). The European Society for Cardiology endorsed the CHA<sub>2</sub>DS<sub>2</sub>-VASc scale (Fig. 1) for thromboembolic stroke risk stratification in atrial fibrillation in 2010, citing its improved discrimination for the low-risk AF population as compared



**Figure 1.** Method for calculating CHA<sub>2</sub>DS<sub>2</sub>-VASc score and risk per annum for each possible score.

with the CHADS<sub>2</sub> scale commonly used in the United States.<sup>3</sup> These recommendations were then updated in 2012, with the recommendation that all patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1 or greater be started on OAC.<sup>1,4</sup> Calculations from the literature estimate that for every 1,000 patients treated with OAC for AF, 12 deaths and 25 strokes are prevented.<sup>1</sup>

There has been a relative paucity of literature specifically examining the outcomes of trauma patients who experience a ground-level fall while on OAC. Howard et al.<sup>5</sup> examined single-admission outcomes from two American College of Surgeons (ACS) Level I trauma centers and found a significant increase in mortality among their patients taking warfarin who fell, as did Inamasu et al.<sup>6</sup> in a small cohort in Japan. By contrast, Gangavati et al.<sup>7</sup> found no increased risk with OAC use among patients who experience ground-level falls. Because it is difficult to assemble consistent patient follow-up data for trauma patients, long-term outcome analyses for the trauma patient population have been lacking. Lack of follow-up remains a criticism of trauma center-based studies.<sup>8</sup>

One of the challenges of discharging patients who have fallen while on OAC is not knowing whether to recommend patients to discontinue their OAC for fear that their next fall be fatal. While maintaining therapeutic anticoagulation reduces their stroke risk, continuing OAC incurs an indeterminate risk of intracranial hemorrhage should they fall again. To date, there has not been a study able to assess patients' risk for repeated falls and the associated morbidity/mortality from those falls. In addition, the "apples versus oranges" nature of disparate (and differing) risk profiles for stroke- versus trauma-related morbidity increases the ambiguity of the decision-making process for the discharging provider.

To develop information that might contribute to filling this gap in evidence, we conducted an observational study to assess (1) the immediate and longer-term outcomes of elderly anticoagulated patients with AF who experience a ground-level fall; (2) risk factors for mortality after a fall either on a single admission or after multiple admissions; (3) the characteristics of a patient population with AF who should consider stopping their OAC if they are admitted for a ground-level fall because their risk for fall-related mortality exceeds the stroke prevention benefit they receive.

## PATIENTS AND METHODS

Retrospective analysis of the longitudinal version of the California Office of Statewide Planning and Development Discharge database was performed, which included 100% of California hospitals for years 1995 to 2009. The population of interest was elderly patients (age  $\geq 65$  years) who had been admitted with diagnosis of AF (DRG International Classification of Diseases—9th Rev. [ICD-9] 427.31, 427.32) and who had had a subsequent admission that included a code for chronic OAC use (V58.61). This population was then searched for admission for ground-level falls (ICD-9 E8800, E8801, E8809, E8840, E8842–46, E8849, E8859, E8880, E8881, E8888, E8889). The first fall after satisfying the criteria for age, cardiac arrhythmia, and presence of an anticoagulation code was considered to be the "index fall." Transfers from other inpatient facilities were excluded.

A control non-OAC group was developed in similar fashion by identifying elderly patients, excluding those with codes for cardiac arrhythmia and/or chronic OAC use and then searching for ground-level falls within the available time range. The data for all patients were cross-indexed with the National Death Index to determine the date of death. For each patient, the end of the study period of observation was determined either by death of the patient or the end of the study time frame (December 31, 2009).

A CHA<sub>2</sub>DS<sub>2</sub>-VASc score was calculated for all patients by identifying the presence of ICD-9 codes pertaining to the pertinent risk factors at index admission (Fig. 1). Identified risk factors were assigned a point value, and the points were tabulated. Patients were stratified by their CHA<sub>2</sub>DS<sub>2</sub>-VASc score at the time of their index admission.

Univariate analysis was performed, using Student's *t* test and Pearson's  $\chi^2$  test for continuous and categorical variables. *p* ( $\alpha$ ) values were considered significant at *p* < 0.05. Among OAC patients, multivariable logistic regression was used to identify risk factors associated with death caused by head injury at first admission following a fall. The Bonferroni correction was applied to control for multiple comparisons. Variables were chosen on the basis of being significant in univariate analysis or  $\chi^2$  and being an inherent characteristic of the patient or the treating facility. The variables included age (divided dichotomously at 75 years); a history of diabetes mellitus, hypertension, congestive heart failure, stroke/TIA (transient ischemic attack), or vascular disease; race/ethnicity; admitting facility (divided dichotomously into ACS-verified trauma centers of any level or community hospitals); and injury severity as measured by ICD-9 Injury Severity Score (ICISS). ICISS is an administratively derived scoring system first described by Osler et al.,<sup>9</sup> which has been demonstrated to accurately predict survival in trauma patients using administrative coding data.

Kaplan-Meier survival analysis was performed to estimate the 1-year risk for mortality with a head injury among all survivors of the index hospitalization. Annualized percent mortality was calculated, and two-tailed tests of proportion were performed to assess significant differences between groups. Cox proportional hazard testing was repeated among the population of patient who survived their index admission to assess risk factors for eventual mortality associated with head injury. The Bonferroni correction was applied to control for multiple comparisons. All analyses were performed with STATA 64-bit Special Edition, version 11.2 (Stata Corp, College Station, TX).

## RESULTS

A total of 42,913 patient records met the inclusion criteria for the OAC group and 334,960 for the non-OAC group; their demographics, admitting facilities, and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores are described in Table 1. Both groups were noted to be elderly at index admission (mean ages of 82.4 and 80.6 years, respectively) but a higher percentage of women and nonwhite ethnicities were noted in the non-OAC population.

Patients on OAC admitted after a fall had a 6.0% mortality rate in the first admission (*n* = 2,583) and had a head injury rate of 8.2% (*n* = 3,512, Table 2). The OAC group

**TABLE 1.** Demographics of Elderly Anticoagulated Patients With AF Admitted to Hospitals in California After Experiencing Ground-Level Fall

| Demographics                                 | OAC,<br>n (%) | No OAC,<br>n (%) | <i>p</i>            |
|----------------------------------------------|---------------|------------------|---------------------|
| Total                                        | 42,913        | 334,960          |                     |
| Age at index admission,<br>mean (SD)         | 82.4 (6.8)    | 80.6 (8.1)       | <0.001              |
| Male sex                                     | 17,879 (41.2) | 97,798 (29.1)    | <0.001              |
| Race/ethnicity                               |               |                  |                     |
| White                                        | 37,110 (86.4) | 252,913 (75.8)   | <0.001 ( $\chi^2$ ) |
| Black                                        | 802 (1.9)     | 12,299 (3.7)     |                     |
| Hispanic                                     | 2,860 (6.7)   | 38,355 (11.5)    |                     |
| Asian                                        | 1,564 (3.6)   | 23,392 (7.0)     |                     |
| Hawaiian/American Indian                     | 590 (1.4)     | 6,661 (2.0)      |                     |
| Insurance status                             |               |                  |                     |
| Medicare                                     | 40,070 (93.3) | 299,294 (89.7)   | <0.001 ( $\chi^2$ ) |
| MediCal (Medicaid)                           | 569 (1.3)     | 9,730 (2.9)      |                     |
| Private coverage                             | 2,254 (5.2)   | 23,373 (7.0)     |                     |
| Uninsured                                    | 75 (0.2)      | 1,139 (0.3)      |                     |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc score |               |                  |                     |
| 0                                            | 70 (0.2)      | 1,046 (0.3)      | 0.824               |
| 1                                            | 631 (1.5)     | 12,115 (3.6)     | 0.004               |
| 2                                            | 4,441 (10.3)  | 52,086 (15.5)    | <0.001              |
| 3                                            | 11,309 (26.2) | 107,639 (32)     | <0.001              |
| 4                                            | 14,102 (32.7) | 107,018 (31.9)   | 0.094               |
| 5                                            | 8,072 (18.7)  | 38,443 (11.4)    | <0.001              |
| 6                                            | 3,371 (7.8)   | 13,913 (4.1)     | <0.001              |
| 7                                            | 992 (2.3)     | 3,450 (1)        | 0.001               |
| 8                                            | 176 (0.4)     | 357 (0.1)        | 0.465               |
| 9                                            | 3 (0.01)      | 2 (0)            | 0.989               |
| Accepting facility                           |               |                  |                     |
| Level I trauma center                        | 2,409 (5.6)   | 19,259 (5.7)     | <0.001 ( $\chi^2$ ) |
| Level II trauma center                       | 8,881 (20.6)  | 61,324 (18.2)    |                     |
| Level III trauma center                      | 1,935 (4.5)   | 11,735 (3.5)     |                     |
| Level IV trauma center                       | 381 (0.9)     | 3,177 (0.9)      |                     |
| Nontrauma hospital                           | 29,563 (68.5) | 241,124 (71.7)   |                     |

Comparator group is of nonanticoagulated elderly patients admitted for ground-level fall.

had a significantly greater number of subdural bleeds among head injury subtypes (46.9% vs. 42.6%). Both all-cause mortality and head injury–associated mortality in the OAC group were significantly increased as compared with the rates in the nonanticoagulated comparator group (3.1% and 5.6%, respectively). Death with an associated head injury constituted 31.6% of all deaths (*n* = 818) in the OAC group, significantly higher than the 23.8% found in the non-OAC group (*n* = 2,487).

Both the OAC group and non-OAC group were found to have high all-cause mortality at 1-year (34.6% vs. 22.1%) and 5-year (70.8% vs. 49.6%) intervals. Each group was composed in the majority of patients who only fell once, but both groups had patients who were admitted multiple times for ground-level falls. Incidentally noted in the OAC group was a hip fracture rate of 33.4%, less than the 41.8% noted in the non-OAC group.

When stratified by CHA<sub>2</sub>DS<sub>2</sub>-VASc score, percent mortality of patients sustaining a head injury during the index fall ranged from 1.4% to 3.1% and was significantly different from

their nonanticoagulated peers (Table 2). Multivariable logistic regression analysis identified the following risk factors for mortality associated with head injury at index fall: male sex, Asian ethnicity, a history of stroke or TIA, admission to any level trauma center, and ICISS (Table 3).

Kaplan-Meier survival analysis of mortality with a head injury across all CHA<sub>2</sub>DS<sub>2</sub>-VASc score categories after the index admission demonstrated the annualized risk to range from 0.5% to 4.6%. The risk for OAC patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores 2 to 7 were significantly higher than the risk for their nonanticoagulated peers (Table 4). When Cox proportional hazard analysis was performed to identify risk factors for eventual mortality with a head injury, age of 75 years or greater was identified as a risk factor in addition to male sex, Asian ethnicity, a history of stroke/TIA, and trauma center admission (Table 5).

## DISCUSSION

It has been well established that increasing age brings a concomitant increase in the risk of ground-level falls.<sup>10–13</sup> While previous trauma literature has demonstrated across a variety of settings that the use of OAC for stroke prevention in patients with cardiac arrhythmias may increase risk of mortality, these studies have largely been performed examining blunt trauma as a heterogeneous group of injuries.<sup>14–17</sup> Furthermore, findings in the published literature have not always been coherent when looking at large populations. Wojcik et al.<sup>18</sup> examined the state trauma registry data from Pennsylvania in 2001 and did not find an increase in either mortality or length of stay among patients admitted with head injury on OAC. Brewer et al.<sup>19</sup> found loss of consciousness to be predictive of mortality but not anticoagulant use. Others have found a specific international normalized ratio (INR) value or degree of INR elevation to be a risk factor for mortality but the binary presence or absence of OAC to be unrelated to mortality.<sup>15,20,21</sup>

Therapeutic anticoagulation carries a concomitant risk of adverse bleeding events, including life-threatening intracerebral and gastrointestinal hemorrhage. Weighing the risk of bleed-related mortality against the ongoing risk of stroke and/or thromboembolism is difficult. Scoring systems have been developed to stratify patients who undergo bleeding events and stop their therapy if they are deemed high risk (e.g., the HEMORR<sub>2</sub>HAGES, HAS-BLED, and/or ATRIA trials).<sup>22–24</sup> Unfortunately, using these strategies requires patients to be diligent in the follow-up with their providers and their providers to be equally diligent in monitoring their patients as they age.

We conducted an observational study to determine the long-term outcomes of elderly anticoagulated patients with AF who experience a ground-level fall and to assess risk factors for mortality related to falls both for short- and long-term time frames. Our data confirm on a large population level that patients who have been prescribed OAC and experience low-velocity falls have outcomes worse than those of their nonanticoagulated peers. Where are the opportunities to decrease the risk to this population?

First, we recognize that any fall for this elderly population is fraught with risk for long-term morbidity and/or mortality. The population of elderly patients who fall (on or

**TABLE 2.** Outcomes From Index Fall Admission for Both Anticoagulated Elderly Patient With AF and Nonanticoagulated Elderly Patients Without AF

| Outcome                                                                                      | OAC, n (%)        | No OAC, n (%)        | p                   |
|----------------------------------------------------------------------------------------------|-------------------|----------------------|---------------------|
| Total                                                                                        | 42,913            | 334,960              |                     |
| Head injury                                                                                  | 3,512 (8.2)       | 18,870 (5.6)         | <0.001 ( $\chi^2$ ) |
| Intracerebral bleed                                                                          | 267 (7.6)         | 1,213 (6.4)          |                     |
| Contusion                                                                                    | 528 (15)          | 3,599 (19.1)         |                     |
| Subarachnoid                                                                                 | 551 (15.7)        | 3,055 (16.2)         |                     |
| Subdural                                                                                     | 1,648 (46.9)      | 8,051 (42.6)         |                     |
| Extradural                                                                                   | 42 (1.2)          | 260 (1.4)            |                     |
| Mixed (subarachnoid/subdural/extradural)                                                     | 161 (4.6)         | 1,431 (7.6)          |                     |
| Unspecified                                                                                  | 637 (18.1)        | 2,806 (14.9)         |                     |
| Craniotomy                                                                                   | 74 (2.1)          | 413 (2.2)            | 0.761               |
| Death                                                                                        | 2,583 (6)         | 10,409 (3.1%)        | <0.001              |
| Death with head injury                                                                       | 818 (31.6)        | 2,487 (23.8)         |                     |
| Percent mortality among head-injured patients                                                | 23.30%            | 15.60%               |                     |
| <b>Mortality With Head Injury at Index Fall, by CHA<sub>2</sub>DS<sub>2</sub>-VASc Score</b> | <b>OAC, n (%)</b> | <b>No OAC, n (%)</b> | <b>p</b>            |
| 0                                                                                            | 1 (1.4)           | 10 (0.9)             | 0.707               |
| 1                                                                                            | 8 (1.4)           | 116 (1)              | 0.441               |
| 2                                                                                            | 90 (2.2)          | 421 (0.8)            | <0.001              |
| 3                                                                                            | 221 (2.2)         | 702 (0.6)            | <0.001              |
| 4                                                                                            | 222 (1.6)         | 615 (0.6)            | <0.001              |
| 5                                                                                            | 148 (1.8)         | 358 (0.9)            | <0.001              |
| 6                                                                                            | 93 (2.8)          | 202 (1.5)            | <0.001              |
| 7                                                                                            | 31 (3.1)          | 55 (1.6)             | 0.002               |
| 8                                                                                            | 4 (2.3)           | 8 (2.2)              | 0.981               |
| 9                                                                                            | 0 (0)             | 0 (0)                | n/m                 |
| Hip/pelvic fracture                                                                          | 14,437 (33.4)     | 140,581 (41.8)       | <0.001              |
| All-cause mortality                                                                          |                   |                      |                     |
| 1-y all-cause mortality                                                                      | 34.6%*            | 22.1%*               | <0.001              |
| 5-y all-cause mortality                                                                      | 70.8%*            | 49.6%*               | <0.001              |
| No. falls                                                                                    |                   |                      |                     |
| 1                                                                                            | 25,575 (82.9)     | 288,101 (85.7)       | <0.001 ( $\chi^2$ ) |
| 2                                                                                            | 5,955 (13.8)      | 39,294 (11.7)        |                     |
| 3+                                                                                           | 1,383 (3.3)       | 8,665 (2.6)          |                     |

\*p-values marked "n/m" were not calculated due to lack of data. Percentage calculation from Kaplan-Meier survival analysis.

off anticoagulation) is a group at the "end of actuarial tables:" at first admission, the mean ages were 82 and 80 years, respectively. Although the median follow-up was relatively short (<2.5 years), 1-year all-cause mortality was substantial. Furthermore, octogenarians on OAC for AF are a highly comorbid population, with concomitant diagnoses of cardiovascular disease. The vast majority of patients (82.9%) only fall once, but at least one third of the patient population admitted with a ground-level fall in either group additionally experienced a hip fracture. A significant portion of these patients will likely become nonambulatory and thereby decrease their risk for falls in the future.

However, patients who survive their first fall are not guaranteed to survive future falls. Patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater remain at significantly higher risk for mortality from a subsequent fall. Which of the survivors should stop OAC? Similar to how brief alcohol interventions have been shown to be feasible on trauma services,<sup>25,26</sup> we

propose that trauma providers are ethically required to discuss this question with their patients at the time of discharge to allow patients to weigh the risks and benefits of their own choices.

Based on the results of our study, it is clear that there are patients who have been placed on OAC in violation of current guidelines: patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 0 do not need anticoagulation. Patients whose annual mortality risk slightly exceeds or is slightly less than their annualized stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc 1–3) must make a difficult assessment—perhaps in concert with their prescribing cardiologist—of their likelihood of falling again and whether they might prefer to trade a small risk for stroke for a small risk of death. Some patients might choose an antiplatelet agent such as aspirin over OAC. Literature from a recent review of 11,414 patient-years of follow-up in low-risk AF patients on antiplatelet therapy demonstrated a 0.9% risk of stroke in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1; the authors deemed the risk to be sufficiently low to not warrant OAC.<sup>27</sup> Antiplatelet therapy



**TABLE 3.** Multivariable Logistic Regression for Risk Factors Associated With Mortality With Head Injury at Index Fall

| Variable                     | Odds Ratio | 95% Confidence Interval | p       |
|------------------------------|------------|-------------------------|---------|
| Age 65–74 y                  | Default    | Default                 | Default |
| Age > 75 y                   | 1.1        | 0.8 to 1.4              | 0.585   |
| Any trauma center admission* | 2.3        | 1.6 to 3.2              | <0.001  |
| White                        | Default    | Default                 | Default |
| Black                        | 1          | 0.5 to 2.2              | 0.922   |
| Hispanic                     | 1.2        | 0.9 to 1.7              | 0.221   |
| Asian*                       | 2.3        | 1.6 to 3.2              | <0.001  |
| Hawaiian/American Indian     | 0.9        | 0.4 to 1.9              | 0.768   |
| Male sex*                    | 1.9        | 1.6 to 2.3              | <0.001  |
| Congestive heart failure     | 1.1        | 0.9 to 1.3              | 0.249   |
| Hypertension                 | 1.1        | 0.9 to 1.4              | 0.106   |
| Diabetes mellitus            | 1          | 0.8 to 1.3              | 0.774   |
| History of vascular disease  | 1          | 0.5 to 1.7              | 0.949   |
| History of stroke/TIA*       | 4.2        | 3.3 to 5.3              | <0.001  |
| ICISS*                       | 0.0001     | <0.001 to <0.001        | <0.001  |

\*p < 0.0035 and 95% confidence interval does not cross 1.0.

has clearly demonstrated a benefit in stroke risk reduction (albeit less than OAC).<sup>2,28</sup> However, it is important for patients and providers to recognize that choosing an antiplatelet agent in place of OAC does not necessarily absolve patients of the risk of head injury.<sup>29–31</sup>

The inherent difficulty of a medical decision (to take a medication or not) is made more challenging yet because the patient and provider are forced to make an “apples versus oranges” selection, affirmatively choosing between qualitative risks of differing types, each of which may result in death or disability. Based on our data, however, patients at CHA<sub>2</sub>DS<sub>2</sub>-VASc scores 1 to 3 who are deemed high fall risk and have

**TABLE 4.** Calculated Annual Mortality With Associated Head Injury Compared With the Literature-Based Annual Risk for Stroke

| CHA <sub>2</sub> DS <sub>2</sub> -VASc Score | Annualized Mortality With Head Injury if Patients Survive Their First Fall, % |        |        | Literature-Based Annual Stroke Risk, % |
|----------------------------------------------|-------------------------------------------------------------------------------|--------|--------|----------------------------------------|
|                                              | OAC                                                                           | No OAC | p      |                                        |
| 0                                            | 2.0                                                                           | 1.0    | 0.589  | 0.0                                    |
| 1                                            | 0.5                                                                           | 0.9    | 0.450  | 1.3                                    |
| 2                                            | 2.3                                                                           | 1.1    | <0.001 | 2.2                                    |
| 3                                            | 2.2                                                                           | 1.0    | <0.001 | 3.2                                    |
| 4                                            | 2.1                                                                           | 1.0    | <0.001 | 4.0                                    |
| 5                                            | 2.1                                                                           | 1.6    | <0.001 | 6.7                                    |
| 6                                            | 2.5                                                                           | 2.1    | 0.014  | 9.8                                    |
| 7                                            | 4.6                                                                           | 2.2    | <0.001 | 9.6                                    |
| 8                                            | 2.1                                                                           | 2.4    | 0.881  | 6.7                                    |
| 9                                            | n/m                                                                           | n/m    | n/a    | 15.2                                   |

**TABLE 5.** Cox Proportional Hazard Analysis for Risk Factors Associated With Eventual Mortality With Head Injury After Discharge From Index Fall Admission

| Variable                     | Hazard Ratio | 95% Confidence Interval | p       |
|------------------------------|--------------|-------------------------|---------|
| Age 65–74 y                  | Default      | Default                 | Default |
| Age > 75 y*                  | 1.4          | 1.2–1.6                 | <0.001  |
| Any trauma center admission* | 1.3          | 1.2–1.5                 | <0.001  |
| White                        | Default      | Default                 | Default |
| Black                        | 1.5          | 1–2.3                   | 0.047   |
| Hispanic                     | 1            | 0.7–1.2                 | 0.838   |
| Asian*                       | 1.7          | 1.4–2.2                 | <0.001  |
| Hawaiian/American Indian     | 1.2          | 0.8–2                   | 0.513   |
| Male sex*                    | 1.4          | 1.3–1.6                 | <0.001  |
| Congestive heart failure     | 1.1          | 0.8–1.2                 | 0.319   |
| Hypertension                 | 1            | 0.9–1.1                 | 0.567   |
| Diabetes mellitus            | 1            | 0.8–1.1                 | 0.796   |
| History of vascular disease  | 0.7          | 0.5–1.3                 | 0.392   |
| History of stroke/TIA*       | 3.1          | 2.6–3.6                 | <0.001  |

\*p < 0.0035 and 95% confidence interval does not cross 1.0.

risk factors for eventual mortality on OAC as identified by our logistic regression (age > 75 years, male sex, Asian ethnicity, history of stroke, or admission to a trauma center) should more strongly consider discontinuation of OAC, at least OAC with warfarin. Are there alternatives to warfarin with less of a potential for hemorrhagic complications? Perhaps not. While novel compounds (direct thrombin inhibitors, etc.) may have lesser risk for hemorrhage, they also present distinct treatment challenges because their anticoagulant effects are not readily reversible, and their safety profile is still evolving.<sup>32,33</sup>

An intriguing finding from the data is the ethnic disparity seen between the OAC and non-OAC groups at index fall: a greater percentage of patients in the OAC group are white. Although whites are more likely to develop AF, the difference in proportion between OAC and non-OAC patients who fall suggests provocatively that ethnic minorities with AF are less likely to be prescribed OAC and therefore contribute a smaller percentage of patients who fall while taking OAC. Racial disparity in the treatment for AF has been reported before, notably in the REGARDS study.<sup>34</sup> We do not think that this affects our recommendations. In our results, only Asians were shown to be at higher risk for mortality, and this is most likely caused by the known increase in expression of the VKORC1AA allelic variant in Asians.<sup>35</sup> This variant increases sensitivity to warfarin, and as a result, Asian patients are generally treated with lower doses of warfarin to achieve similar therapeutic effect.<sup>36–38</sup> In fact, consensus guidelines for treatment of AF in the elderly Asian population recommend a target INR of 1.6 to 2.6 instead of 2 to 3, arguing that the higher INR carries too high a risk of bleeding complications.<sup>39</sup>

Finally, there is the initially counterintuitive result that patients treated at a trauma center have an increased risk for mortality. Any emergency provider recognizes that not all ground-level falls are equivalent: the location of the fall and

the first body part to hit a surface can dramatically alter the end result of a fall. We suspect the finding that patients who are admitted to a trauma center after fall have increased mortality represents a selection bias by emergency medical service (EMS) providers in the field. EMS guidelines allow some latitude by providers to direct patients to a higher-level trauma facility if they feel it warranted. The field triage guidelines were recently updated to reflect the growing recognition by the ACS Committee on Trauma that patients on OAC are a special population at risk for delayed injury and that EMS crews responding to these patients need to be mindful of that risk.<sup>40</sup>

The limitations of our study are several, primarily around the limitations of our data. Administrative data can only give us the certainty that a patient did have a cardiac arrhythmia at one time and that an OAC was being managed at least at one point thereafter. We cannot account for patients who may have stopped their OAC between the initial proof of it being taken and their fall or the potentially confounding use of antiplatelet regimens in addition to OAC. In addition, we cannot assess the state of anticoagulation at the time of admission to the hospital, which would be a very useful means of stratifying which patients were overanticoagulated and therefore at higher risk for hemorrhagic complication.

However, there are particular strengths to the use of this database. First, it provides a means of “virtual follow-up” for trauma patients who are a classically difficult patient group in which to obtain longitudinal outcomes. We are able to provide a descriptive history of the elderly patient on OAC, which has been done to some extent in the cardiology literature but usually in the context of patients who are good “study patients” (i.e., deemed more likely to be compliant with regimens and follow-up). In contrast to the low incidence of intracranial hemorrhage in the anticoagulation literature, patients in the “real world” are at significant risk for head injury upon falling. Furthermore, greater than one in six patients on OAC will fall again and be at similar risk for head injury and head-injury associated mortality.

## CONCLUSION

The use of OAC preceding a ground-level fall is a potentially harmful and sometimes lethal combination in the elderly population and should be taken seriously by trauma care providers. The majority of these patients go to community hospitals that may frequently be unprepared to rapidly evaluate them with imaging and coagulation tests and provide immediate reversal of drug-induced coagulopathy (steps critical to managing these injuries).<sup>41,42</sup> Future trauma system policy should deliberate whether these patients should be triaged to trauma centers to receive higher-level care on a routine basis. Patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 0 have no indication to take OAC or antiplatelet therapy, and patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores 1 to 3 should give strong consideration to discontinuing their OAC if they are deemed high risk for falls. Although the mortality rates from ground-level falls are not overwhelmingly high in patients on OAC, they are sufficiently high that physicians should engage patients in a thorough discussion of the risks of remaining on OAC after a trauma admission for a fall.

## AUTHORSHIP

Ta.S.I. (of University of California San Diego [UCSD] Department of Surgery) performed the literature search for this study, which Ta.S.I. (UCSD), Th.S.I. (of Indiana University [IU]), D.C., and R.C. designed. Ta.S.I. (UCSD), R.P., and D.C. contributed to the data collection. Ta.S.I. (UCSD) and D.C. analyzed the data, which Ta.S.I. (UCSD), Th.S.I. (IU), D.C., and R.C. interpreted. Ta.S.I. (UCSD) wrote the manuscript, which Th.S.I. (IU) and R.C. critically revised.

## DISCLOSURE

The authors declare no conflicts of interest.

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## DISCUSSION

**Dr. Nicholas Namias** (Miami, Florida): The authors have tackled the difficult question of the risk of stroke from atrial arrhythmia off of oral anticoagulation versus the risk of mortality from falling on oral anticoagulation in patients with atrial arrhythmias.

They culled their patients from a state database that included all hospital discharges and they defined the risk of stroke off anticoagulation using the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, a validated score for the risk of stroke from atrial fibrillation.

They were able to analyze nearly 43,000 patients who were on anticoagulation and compared them to 334,000 patients not on oral anticoagulation. They found that the risk of eventual death with head injury exceeded annualized stroke injury rate for patients at low risk of stroke, as defined by CHA<sub>2</sub>DS<sub>2</sub>-VASc score.

Patients on anticoagulation had more head injuries, more deaths, and more deaths with head injuries. The implication, of course, is that elderly patients with atrial arrhythmias and a low CHA<sub>2</sub>DS<sub>2</sub>-VASc score in whom the risk of mortality from a fall exceeds or approximates the risk of stroke should not be on oral anticoagulation or at least on some lesser thromboprophylaxis such as a low dose aspirin. I have three questions.

First, should the advice to people with a low score be simply, “Don’t fall”? While the mortality from falling approaches or exceeds the risk of stroke off oral anticoagulation, if they just don’t fall they won’t get a head injury.

From a public health perspective, isn’t it better to prevent stroke in the set of all patients with scores of 1, 2, and 3 than to prevent death in the few of those who will fall?

Second, why do you recommend that patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 3 consider stopping anticoagulation? Your table shows that the risk of stroke is 3.2% and the risk of death from fall with head injury is 2.2%. Should your recommendations stop at a score of zero to 2?



And, finally, why do you think there were more hip fractures in patients not on oral anticoagulation (OAC)? This was in your manuscript, although not presented from the podium today. Those patients ought to be healthier, the ones that are not on OAC. OAC clearly doesn't prevent fractures so maybe your comparative group was just too healthy and too active so they broke hips.

Your comparative group was elderly patients without atrial fibrillation who fell. Maybe the comparator should have been elderly patients with atrial fibrillation not on oral anticoagulation as a marker of just being sick and frail. Please comment.

**Dr. Deborah A. Kuhls** (Las Vegas, Nevada): I would say that this is one of the most important issues that we need to tease out and help our primary care physicians who not only start anticoagulation but perhaps advise their patients who might have had some other traumatic event when to resume them or if to resume them.

So the question that I have is whether your data is really skewed by the fact that perhaps patients who have atrial fibrillation who are on, who are not on anticoagulation perhaps are already screened for the risk of falls or some other event and if that would skew your data.

And the second question I have and I just don't know the answer to it, is this scoring system commonly used in the United States since it's a European scoring system?

**Dr. Slate Wilson** (Portland, Oregon): For those lower grade CHA<sub>2</sub>DS<sub>2</sub>-VASC scores, it's very interesting because the internists are now switching over to novel oral anticoagulants, and all those nasty things which can't be reversed when they fall. And I'm interested to see what you would advise these low-grade people to use.

**Dr. Patricia Byers** (Miami, Florida): I want to applaud the authors for attacking a very important public health issue and something that we struggle with in trauma systems every day in deciding what to do with these patients and pointing out that most of them don't go to trauma centers, rightly or wrongly.

But my question for you has to do with your recommendations. I was just wondering what your hypothesis was about Asians—I don't know, maybe perhaps diet-related Omega 3 fatty acids that, you know, give a propensity for bleeding versus thrombosis.

**Dr. Tazo S. Inui** (San Diego, California): I thank you very much for all the questions. With regard to Dr. Namias' question, with regard to the question of should we just tell these patients, "Don't fall," I think the answer is yes.

But until we get much better at predicting falls in the elderly patients or unless Medicare starts paying for medical grade bubble wrap, we have to help people make informed decisions about whether they want to make a bad choice risking strokes or make a bad choice risking death. So we're stuck with it, I'm afraid.

As regards the second question of the CHA<sub>2</sub>DS<sub>2</sub>-VASC 3 group, yes, their stroke risk outweighs their mortality as we

found it. But we thought it was appropriate to include these patients as we're asking them to make a difficult informed decision.

It's possible that somebody in that CHA<sub>2</sub>DS<sub>2</sub>-VASC 3 group, an Asian male, for example, with a CHA<sub>2</sub>DS<sub>2</sub>-VASC score of 3 who is a high fall risk should come off their oral anticoagulation because they are at more risk than everybody else.

Unfortunately, the limitations of this data are that we can't slice it down tight enough to know really what their personal risk is. But, again, this is a personal decision, making hard choices.

As regards the difference in hip fracture rate, one potential reason is that there is a higher percentage of men in the oral anticoagulation group, which may alter the combined osteoporosis risk. Additionally, they are more likely to have cardiovascular disease, and it's been shown that increased beta blocker utilization may be protective against hip fractures, but this is purely speculative.

As regards to Dr. Kuhls' questions, certainly there is a selection bias in that patients who are very high risk for falls are pre-screened from the Coumadin group. But that doesn't change the risks for any patient currently on Coumadin for atrial fibrillation. If anything, the risk is artificially low as the patients at highest risk for falls are excluded.

The CHA<sub>2</sub>DS<sub>2</sub>-VASC scoring system is being used inconsistently in the United States. This is in part because the last update to atrial fibrillation guidelines from the AHA was in 2006, years before CHA<sub>2</sub>DS<sub>2</sub>-VASC was developed, and at that time the AHA recommended the CHADS-2 scoring system. The next AHA set of guidelines will likely incorporate the CHA<sub>2</sub>DS<sub>2</sub>-VASC calculator, as it has been shown to have much better discrimination for patients deemed low-risk on the CHADS-2 scale, and a significant minority of ischemic strokes come from the low-risk group.

In regards to Dr. Wilson's question about novel oral anticoagulants, the cardiology literature says we don't know what the risks are. And they are right. They don't. Any trauma system will tell you that direct thrombin inhibitors are a problem. I think that when it comes to low-risk patients, they just need to be aware that should they fall, they have real risks that are higher than the problems of the folks that are just on warfarin alone.

Finally, with regard to Dr. Byers' question about Asian patients—there is probably a biochemical basis with a genetic answer. And this is probably a genetic answer. Asians tend to have a high percentage of a particular polymorphism of Vitamin K epoxide reductase which means that they are more sensitive to warfarin. In fact, in Japan the recommendations for atrial fibrillation are that patients be anticoagulated with, from an INR of 1.6 to 2.6 and that's particularly because they are at higher risk of intracranial hemorrhage.

So this is a particular genetic problem that is well recognized in the cardiology literature, however, not necessarily recognized by our primary care providers in the U.S.