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Effect of Warfarin on Outcomes in Septuagenarian Patients with Atrial Fibrillation

Brita Roy, MD, MPH, MS[a], **Ravi V. Desai, MD**[b], **Marjan Mujib, MD, MPH**[a], **Andrew E. Epstein, MD**[c,d], **Yan Zhang, MS, MSPH**[a], **Jason Guichard, MD, PhD**[a], **Linda G. Jones, DNP**[e,a], **Margaret A. Feller, MPH**[a], **Mustafa I. Ahmed, MD**[a], **Inmaculada B. Aban, PhD**[a], **Thomas E. Love, PhD**[f], **Raynald Levesque, M.Sc.**[g], **Michel White, MD**[h], **Wilbert S. Aronow, MD**[i], **Gregg C. Fonarow, MD**[j], and **Ali Ahmed, MD, MPH**[a,e,*]

[a]University of Alabama at Birmingham, Birmingham, AL

[b]Lehigh Valley Hospital, Allentown, PA

[c]Veterans Affairs Medical Center, Philadelphia, PA

[d]University of Pennsylvania, Philadelphia, PA

[e]Veterans Affairs Medical Center, Birmingham, AL

[f]Case Western Reserve University, Cleveland, OH

[g]Montreal, Canada

[h]Montreal Heart Institute, Montreal, Canada

[i]New York Medical College, Valhalla, NY

[j]University of California, Los Angeles, CA

Abstract

Anticoagulation has been shown to reduce ischemic stroke in atrial fibrillation (AF). However, concerns remain regarding their safety and efficacy in those ≥70 years of age who comprise most AF patients. Of the 4060 patients (mean age, 65 years; range, 49–80 years) in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial, 2248 (55% of 4060) were 70–80 years of age, 1901 of whom were receiving warfarin. Propensity score for warfarin use, estimated for each of the 2248 patients, were used to match 227 of the 347 no-warfarin patients (in 1:1, 1:2 or 1:3 sets) with 616 warfarin patients, who were balanced on 45 baseline characteristics. All-cause mortality occurred in 18% and 33% of matched patients receiving and not receiving warfarin, respectively, during up to six (mean, 3.4) years of follow-up (hazard ratio {HR} when warfarin use was compared with its non-use, 0.58; 95% confidence interval {CI}, 0.43–0.77; p<0.001). All-cause hospitalization occurred in 64% and 67% of matched patients receiving and not receiving warfarin, respectively (HR associated with warfarin use, 0.93; 95% CI, 0.77–1.12; p=0.423). Ischemic stroke occurred in 4% and 8% of matched patients receiving and not receiving warfarin, respectively (HR associated with warfarin use, 0.57; 95% CI, 0.31–1.04; p=0.068). Major bleeding occurred in 7% and 10% of matched patients receiving and not receiving warfarin, respectively (HR associated with warfarin use, 0.73; 95% CI, 0.44–1.22;

[*]**Correspondence:** Ali Ahmed, MD, MPH, University of Alabama at Birmingham, 1530 3rd Avenue South, CH-19, Suite 219, Birmingham AL 35294-2041. Telephone: 1-205-934-9632; Fax: 1-205-975-7099; aahmed@uab.edu.

p=0.229). In conclusion, warfarin use was associated with reduced mortality in septuagenarian AF patients but had no association with hospitalization or major bleeding.

Keywords

atrial fibrillation; warfarin; mortality; propensity score; older adults

Anticoagulation has been shown to reduce the risk of ischemic stroke among older adults with atrial fibrillation (AF).[1] Although most high risk patients with AF are over 70 years of age,[2] the safety and efficacy of warfarin in these patients remain unclear.[3] Additionally, there is little data on the effect of long-term anticoagulation on mortality in these patients. Therefore, we conducted a propensity-matched study of the association of warfarin and outcomes in older adults with AF.

Methods

We analyzed a public-use copy of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) data obtained from the National Heart, Lung, and Blood Institute. The design and the primary results of AFFIRM have been previously published.[4, 5] Briefly, AFFIRM was a multicenter randomized clinical trial for rate versus rhythm control treatment strategies for AF conducted in 213 centers in the United States and Canada. Patients with recurrent AF without contraindication to anticoagulant therapy (as determined by their physician) and with high risk for stroke were recruited. Because age was considered a risk factor for stroke in AF, those ≥65 years of age could be enrolled regardless of other risk factors. However, to be eligible for enrollment, those <65 years were required to have at least one other risk factor for stroke, which included prior stroke or transient ischemic attacks, hypertension, heart failure, diabetes mellitus, increased left atrial enlargement, and left ventricular systolic dysfunction. AFFIRM participants had a mean age of 65 years (range, 49 to 80 years) and 76% (3091/4060) of patients were ≥65 years of age.

The current analysis was restricted to 2248 (55% of 4,060) patients who were 70–80 years of age. We chose a cut-off of 70 years because of the high prevalence of AF in this age group.[6] Of the 2,248 patients, 1,901 (85%) were receiving warfarin, with goal International normalized ratio (INR) between 2.0 and 3.0. Patients were followed up for up to 6 years (with mean follow-up time of 3.4 years) with interval follow-up visits every 4 months. All outcomes were blindly adjudicated by the AFFIRM events committee. The primary outcome for the current analysis was all-cause mortality. Secondary outcomes included all-cause hospitalization, ischemic stroke, and major bleeding defined as bleeding requiring transfusion and/or surgery and/or permanent cessation of warfarin.

Considering the significant imbalances in baseline characteristics between the two groups (Table 1), we used propensity scores to assemble a matched cohort.[7, 8] Propensity scores for warfarin use were estimated for each of the 2,248 patients using a non-parsimonious multivariable logistic regression model.[9–11] We were able to match 227 of the 347 patients not receiving warfarin with 616 patients receiving warfarin using a greedy algorithm to match warfarin patients to sets of 1, 2 or 3 patients not receiving warfarin with similar propensity scores.[12–16] The matched cohort of 843 patients was well-balanced between warfarin recipients and non-recipients on the 45 baseline characteristics used in the propensity score model. Absolute standardized differences were estimated to evaluate the pre-match imbalance and post-match balance, and are presented in a Love plot (Figure 1).[17–19] Absolute standardized differences directly quantify biases in the means (or proportions) of covariates across the groups, and are expressed as percentages of the pooled

standard deviations. An absolute standardized difference of 0% indicates no residual bias and differences <10% are considered inconsequential.

For descriptive analyses, we used Pearson's chi-square and Wilcoxon rank-sum tests for the pre-match comparisons, and paired sample t-tests for post-match comparisons of baseline characteristics of patients with and without warfarin use, as appropriate. We used Kaplan-Meier plots and Cox regression analyses to determine associations between warfarin use and outcomes during follow-up. We conducted formal sensitivity analyses to quantify the degree of hidden bias that would need to be present to invalidate our conclusions based on a significant association between use of warfarin and all-cause mortality among matched patients.[20–23] Subgroup analyses were conducted to determine the homogeneity of association between use of warfarin and all-cause mortality. Finally, to assess the generalizability of the findings of the current study based on trial-eligible AFFIRM participants 70–80 years with AF to community-dwelling AF patients in that age group, we compared the baseline characteristics and outcomes of participants included in our study with AF patients 70–80 years in the Cardiovascular Health Study (CHS). All statistical tests were two-tailed with a p-value <0.05 considered significant and all data analyses were performed using SPSS for Windows (Rel. 18; Chicago, IL).

Results

Patients (n=843) had a mean (SD) age of 76 (3) years, 45% were women, and 7% were non-white. Before matching, patients receiving warfarin were more likely to have heart failure and valvular heart disease, have higher CHADS2 scores but similar CHA2DS2VASc scores. These and other baseline imbalances were balanced after matching (Table 1 and Figure 1).

All-cause mortality occurred in 18% and 33% of matched warfarin and no-warfarin patients, respectively during 6 years of follow-up (hazard ratio {HR} when use of warfarin was compared with its non-use, 0.58; 95% confidence interval {CI}, 0.43–0.77; p<0.001; Table 2 and Figure 2). A hidden covariate that is a near-perfect predictor of mortality would need to increase the odds of warfarin use by 48% to explain away this association. The association of warfarin use with mortality in various subgroups of patients are displayed in Figure 3. The associations of warfarin use with various cause-specific mortalities are displayed in Tables 3 and 4.

All-cause hospitalization occurred in 64% and 67% of matched warfarin and no-warfarin patients, respectively (HR associated with warfarin use, 0.93; 95% CI, 0.77–1.12; p=0.423; Table 3). Ischemic stroke occurred in 4% and 8% of matched patients receiving and not receiving warfarin, respectively (HR associated with warfarin use, 0.57; 95% CI, 0.31–1.04; p=0.068; Table 3). Major bleeding occurred in 7% and 10% of matched patients receiving and not receiving warfarin, respectively (HR associated with warfarin use, 0.73; 95% CI, 0.44–1.22; p=0.229; Table 3). Pre-match associations of warfarin use with other outcomes are displayed in Table 4. Baseline characteristics of AF patients 70–80 years enrolled in the AFFIRM trial and community-dwelling AF patients 70–80 years in CHS are displayed in Table 5.

Overall, the 2248 pre-match patients had a mean CHADS2 and CHA2DS2VASc scores of 1.96 (range, 0 to 6) and 3.85 (range, 1 to 9). Unadjusted HR for all-cause mortality associated with every unit increase in CHADS2 score was 1.45 (95% CI, 1.36–1.56; p<0.001), which remained unchanged despite multivariable adjustment for all covariates except those used to estimate CHADS2 score (adjusted HR, 1.32; 95% CI, 1.22–1.43; p<0.001). Similarly, unadjusted HR all-cause mortality associated with every unit increase in CHA2DS2VASc score was 1.38 (95% CI, 1.30–1.46; p<0.001), which remained

unchanged despite multivariable adjustment for all covariates except those used to estimate CHA2DS2VASc score (adjusted HR, 1.26; 95% CI, 1.17–1.35; p<0.001).

Unadjusted HR for incident ischemic stroke associated with every unit increase in CHADS2 score was 1.26 (95% CI, 1.08–1.47; p=0.004), which remained essentially unchanged after multivariable adjustment for all covariates except those used to estimate CHADS2 score (adjusted HR, 1.21; 95% CI, 1.01–1.44; p=0.040). Similarly, unadjusted HR incident ischemic stroke associated with every unit increase in CHA2DS2VASc score was 1.30 (95% CI, 1.14–1.48; p<0.001), and this estimate did not change after multivariable adjustment for all covariates except those used to estimate CHA2DS2VASc score (adjusted HR, 1.30; 95% CI, 1.11–1.52; p=0.001). Similar associations were observed in the matched cohort.

Discussion

Findings from the current study demonstrate that septuagenarian AF patients had high rates of all-cause mortality and that the use of warfarin was associated with a significant reduction in mortality in these patients. These findings are consistent with those based on AFFIRM participants of all age groups.[1] Despite high rates of all-cause and cardiovascular hospitalizations, warfarin use had no association with these events. Warfarin use was associated with a near-significant reduction in incident ischemic stroke but had no association with incident major bleeding. These findings are important, as the incidence of AF increases with age yet warfarin may be underused in this population due to concern for adverse effects and outcomes. This is particularly significant as the incidence of AF is projected to increase with the aging of the population.

The increased mortality without associated increased hospitalization in those not receiving warfarin suggests that these patients had a higher incidence of sudden death that may have precluded hospitalization. However, warfarin use was not associated with a reduction in cardiac death including those due to arrhythmias. Further, warfarin use was also not associated with vascular death including those due to stroke. The observation that warfarin-associated mortality reduction was largely due to reduction in non-cardiovascular mortality is intriguing. However, warfarin has been shown to be associated with reduction in the risk of various cancers including pulmonary neoplasm, and pulmonary embolism and associated deaths.[24–26] Potential explanations for the lack of a significant association of warfarin with major bleeding include selection bias, close monitoring during the trial, lack of power due to small number of events and/or chance. However, the CHADS2 and CHA2DS2VASc scores of trial-eligible older AF patients in AFFIRM were generally similar to those of community-dwelling older AF patients in CHS.

Our results are consistent with the findings from the Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF) in which randomization to warfarin was associated with a significant reduction in mortality over 2 years among 420 AF patients (mean age, 68 years), which was also primarily driven by reduction in non-cardiac mortality.[27] However, in that study, there was also a significant reduction in ischemic stroke. In contrast, patients in our study were older and were receiving contemporary medications such as lipid lowering agents and ACE-inhibitors, which may in part explain the small number of stroke events in AFFIRM.[4]

Current guidelines focus on stroke prevention as the main benefit of warfarin therapy using stroke risk stratification tools such as the CHADS2 score,[28] which recommends warfarin for patients who have a prior history of stroke or have 2 of the following: heart failure, age ≥75, hypertension, or diabetes. However, findings from our subgroup analyses suggest that warfarin-associated mortality reduction may be greater in age 70–75 years and in those

without hypertension. Although warfarin use was not associated with major bleeding in septuagenarian AF patients in our study, warfarin should be used with caution in older adults.[29] In the National Consortium of Anticoagulation Clinics study, although the overall risk of bleeding did not increase with age, among AF patients receiving warfarin, the risk of life-threatening or fatal bleeding was significantly higher among those ≥80 years versus <50 years of age.[29] However, in that study, overall bleeding rates for patients 70–79 years (37%; 157/432) was similar to those ≥80 years of age (30%; 28/93). Corresponding rates for serious (0.9% versus 1.1% among those ≥80 years) and life-threatening (0.1% versus 0.4% among those ≥80 years) bleeding were also comparable.

There were several limitations to our study. Despite balance on a large and diverse set of baseline characteristics, bias due to imbalances on unmeasured baseline characteristics remains possible, as in any observational study. Our sensitivity analysis suggests, however, that the association of warfarin use with mortality reduction observed here was sensitive only to fairly strong confounding from unmeasured variables. Patients in the warfarin group may have discontinued their use during follow-up and vice-versa. The resultant regression dilution may have attenuated the true association between warfarin and mortality in our study.[30] AF patients in the current study were enrolled in clinical trial and excluded those >80 years of age, which may limit generalizability. However, these patients were similar in key baseline characteristics and outcomes to a cohort of community-dwelling AF patients. In conclusion, in a propensity-matched balanced cohort of septuagenarian AF patients, the use of warfarin was associated with reduced mortality but had no association with hospitalization or major bleeding.

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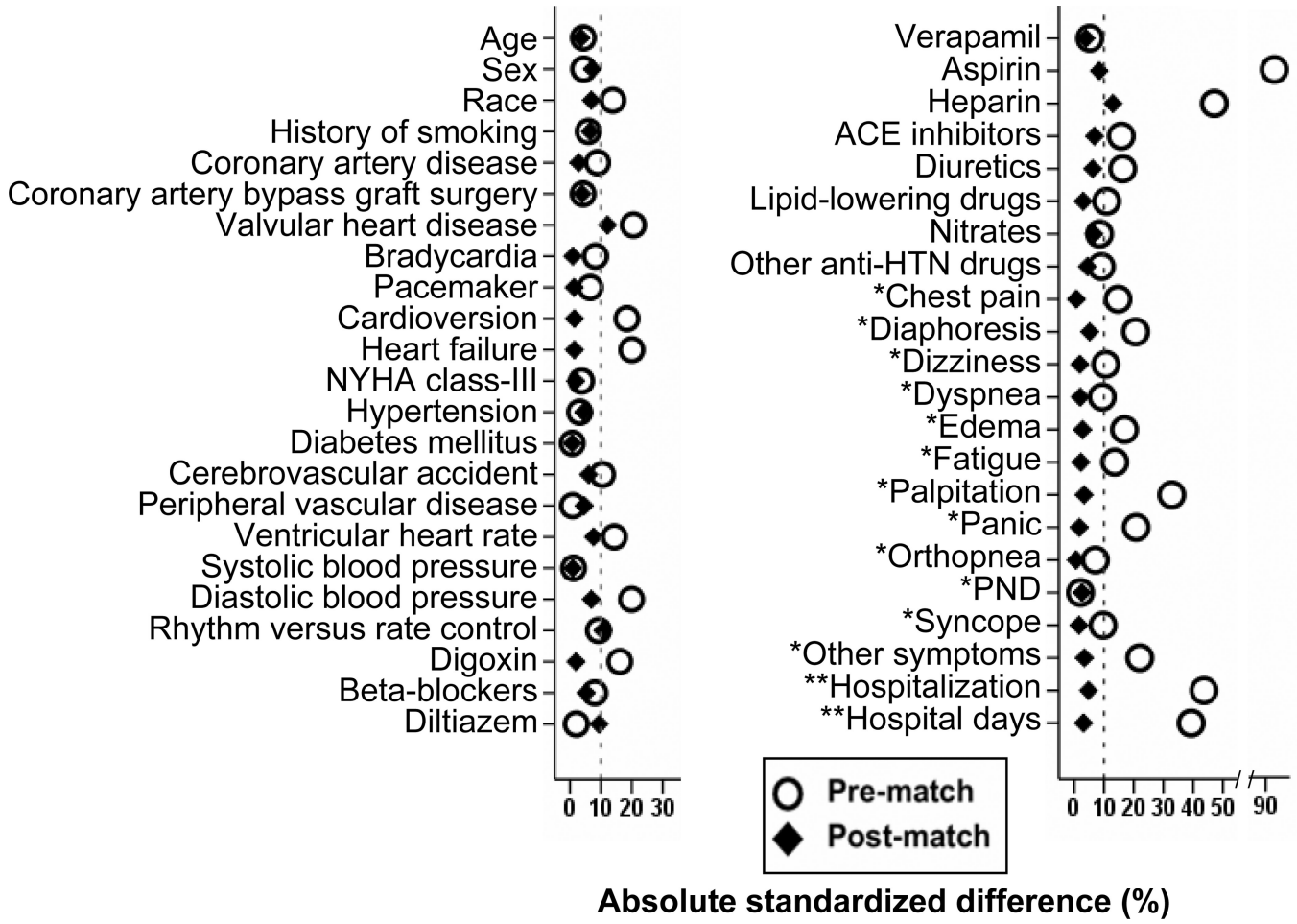
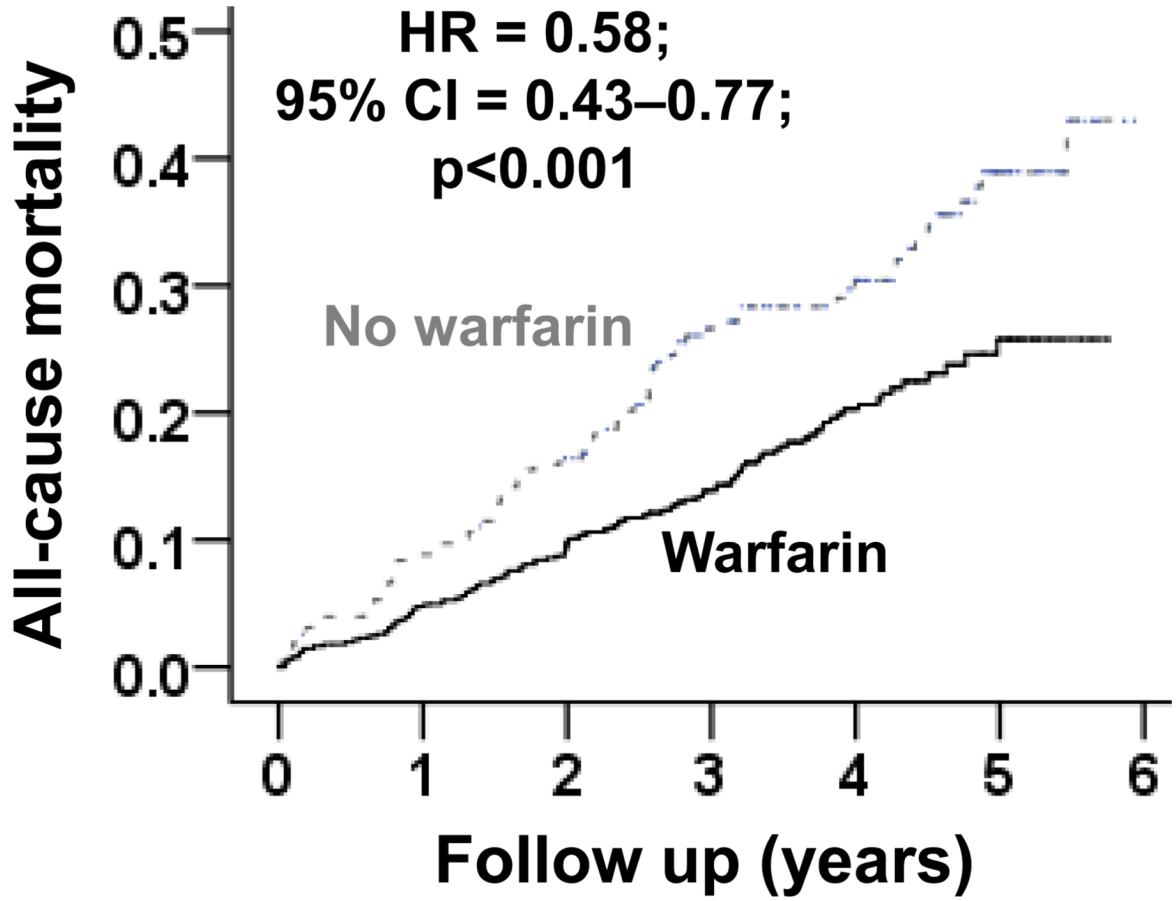


Figure 1.

Absolute standardized differences of 45 baseline characteristics between patients receiving and not receiving warfarin, before and after propensity score matching (*Symptoms experienced during atrial fibrillation in the last six months; **Hospitalization for qualifying episodes of atrial fibrillation; ACE = angiotensin-converting enzyme; HTN = hypertension; NYHA = New York Heart Association; PND = paroxysmal nocturnal dyspnea)



Number at risk

No warfarin	227	206	185	132	99	39
Warfarin	616	577	537	372	216	61

Figure 2.
Kaplan-Meier plots for (a) all-cause mortality, and (b) all-cause hospitalization by warfarin use (HR=hazard ratio; CI=confidence interval)

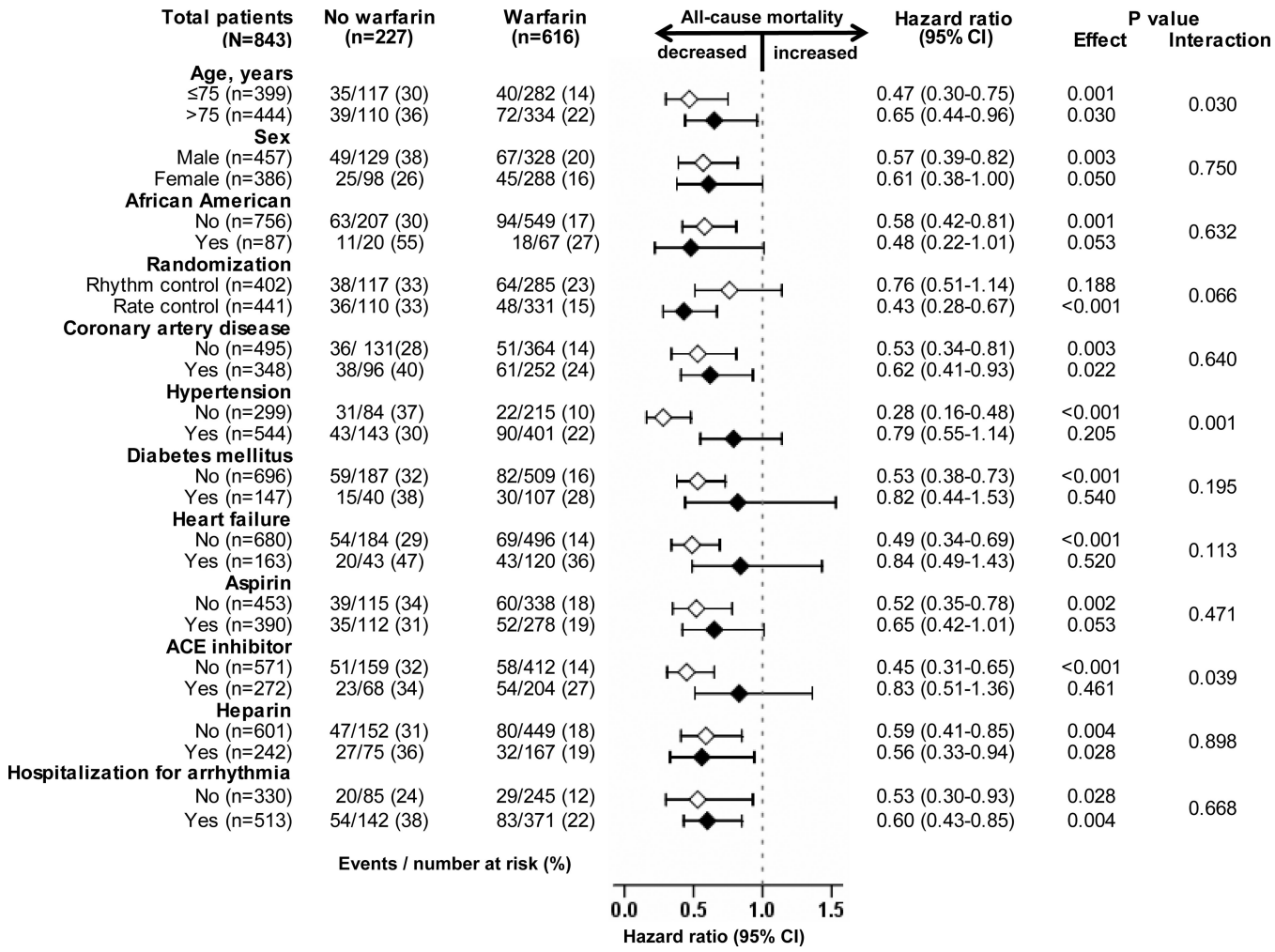


Figure 3.

Association of warfarin use with all-cause mortality in subgroups of propensity-matched atrial fibrillation patients 70 years of age (CI=confidence interval)

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Table 1

Baseline characteristics of atrial fibrillation (AF) patients ≥70 years by warfarin use, before and after propensity matching

	Before matching			After matching		
n (%) or mean (±SD)	**No warfarin (n=347)**	**Warfarin (n=1901)**	**P value**	**No warfarin (n=227)**	**Warfarin (n=616)**	**P value**
Age (years)	76 (±3)	75 (±3)	0.458	76 (±3)	76 (±3)	0.655
Female	164 (47%)	857 (45%)	0.453	98 (43%)	288 (47%)	0.355
African American	37 (11%)	129 (7%)	0.011	20 (9%)	67 (11%)	0.382
Current smoker	28 (8%)	124 (7%)	0.291	19 (8%)	41 (7%)	0.391
Systolic blood pressure (mm Hg)	136 (±20)	136 (±19)	0.847	136 (±19)	136 (±19)	0.909
Diastolic blood pressure (mm Hg)	73 (±10)	75 (±10)	0.001	74 (±10)	74 (±10)	0.379
Ventricular rate, bpm	71 (±13)	73 (±14)	0.016	71 (±13)	72 (±14)	0.332
Maximum ventricular rate during AF, bpm	122 (±30)	104 (±31)	<0.001	120 (±30)	109 (±33)	<0.001
Duration of AF ≥2 days	118 (34%)	1446 (76%)	<0.001	78 (34%)	392 (64%)	<0.001
$CHADS_2$ score	1.8 (±1.1)	2.0 (±1.2)	0.020	1.8 (±1.1)	1.9 (±1.2)	0.343
CHA2DS2VASc score	3.8 (±1.5)	3.9 (±1.4)	0.232	3.7 (±1.5)	3.8 (±1.4)	0.332
Hospitalization due to AF	227 (65%)	841 (44%)	<0.001	142 (63%)	371 (60%)	0.539
Hospitalizations duration (days)	4 (±4)	2 (±3)	<0.001	4 (±4)	3 (±4)	0.686
Critical care duration (days)	0.4 (±1.2)	0.2 (±0.8)	<0.001	0.4 (±1.2)	0.3 (±1.0)	0.053
Non-critical care duration (days)	3.3 (±4.0)	2.1 (±3.2)	<0.001	3.1 (±3.8)	3.1 (±3.8)	0.956
Past medical history						
Coronary artery disease	151 (44%)	744 (39%)	0.125	96 (42%)	252 (41%)	0.718
Acute myocardial infarction	64 (18%)	359 (19%)	0.847	40 (18%)	122 (20%)	0.475
Vulvular heart disease	32 (9%)	304 (16%)	0.001	14 (6%)	58 (9%)	0.134
Stroke or transient ischemic attack	40 (12%)	287 (15%)	0.083	24 (11%)	77 (13%)	0.445
Heart failure	58 (17%)	471 (25%)	0.001	43 (19%)	120 (20%)	0.861
Bradycardia	38 (11%)	162 (9%)	0.144	22 (10%)	58 (9%)	0.903
Diabetes mellitus	59 (17%)	328 (17%)	0.909	40 (18%)	107 (17%)	0.932
Hypertension	234 (67%)	1309 (69%)	0.599	143 (63%)	401 (65%)	0.572
Peripheral arterial disease	27 (8%)	152 (8%)	0.892	21 (9%)	49 (8%)	0.545
Pacemaker	34 (10%)	151 (8%)	0.248	23 (10%)	60 (10%)	0.865

n (%) or mean (±SD)	Before matching			After matching		
	No warfarin (n=347)	Warfarin (n=1901)	P value	No warfarin (n=227)	Warfarin (n=616)	P value
Cardioversion	117 (34%)	810 (43%)	0.002	80 (35%)	213 (35%)	0.857
Randomization to rhythm treatment	161 (46%)	969 (51%)	0.117	117 (52%)	285 (46%)	0.174
Anti-arrhythmic drug failures	49 (14%)	309 (16%)	0.318	34 (15%)	92 (15%)	0.988
Symptoms during AF						
Chest pain	97 (28%)	411 (22%)	0.009	60 (26%)	161 (26%)	0.931
Diaphoresis	84 (24%)	304 (16%)	<0.001	46 (20%)	138 (22%)	0.505
Dizziness	135 (39%)	643 (34%)	0.067	88 (39%)	233 (38%)	0.803
Dyspnea	172 (50%)	1031 (54%)	0.109	118 (52%)	314 (51%)	0.795
Edema	54 (16%)	421 (22%)	0.006	43 (19%)	110 (18%)	0.717
Fatigue	176 (51%)	1093 (58%)	0.019	120 (53%)	319 (52%)	0.781
Palpitation	209 (60%)	838 (44%)	<0.001	129 (57%)	360 (58%)	0.674
Panic	53 (15%)	163 (9%)	<0.001	26 (12%)	74 (12%)	0.824
Syncope	21 (6%)	75 (4%)	0.074	13 (6%)	33 (5%)	0.834
Flutter	71 (21%)	841 (44%)	<0.001	47 (21%)	250 (41%)	<0.001
Other symptoms	56 (16%)	169 (9%)	<0.001	28 (12%)	83 (14%)	0.664
Medications						
Digoxin	162 (47%)	1040 (55%)	0.006	116 (51%)	309 (50%)	0.809
Beta-blockers	132 (38%)	798 (42%)	0.171	89 (39%)	226 (37%)	0.503
Diltiazem	108 (31%)	574 (30%)	0.729	77 (34%)	182 (30%)	0.222
Verapamil	30 (9%)	193 (10%)	0.388	24 (11%)	58 (9%)	0.615
Aspirin	213 (61%)	380 (20%)	<0.001	112 (49%)	278 (45%)	0.277
Heparin	118 (34%)	273 (14%)	<0.001	75 (33%)	167 (27%)	0.091
ACE inhibitors	106 (31%)	723 (38%)	0.008	68 (30%)	204 (33%)	0.384
Diuretics	134 (39%)	887 (47%)	0.006	98 (43%)	247 (40%)	0.421
Lipid lowering agents	57 (16%)	393 (21%)	0.069	34 (15%)	99 (16%)	0.699

*CHADS2 scoring system for risk of stroke in atrial fibrillation is based on the presence of each of the following conditions (with points assigned to each of them are indicated in the parenthesis): Congestive heart failure (1), Hypertension (1), Age >75 years (1), Diabetes mellitus (1), history of Stroke (2).

**CHA2DS2VASc scoring system for risk of stroke in atrial fibrillation is based on the presence of each of the following conditions (with points assigned to each of them are indicated in the parenthesis): Congestive heart failure or left ventricular dysfunction (1), Hypertension (1), Age >75 years (2), Diabetes mellitus (1), a history of Stroke (2), Vascular disease (1), Age 65–74 years (1), Sex category (1 for Female)

Table 2

Association of warfarin use with all-cause mortality

	Events (%)		Absolute risk difference*	Hazard ratio (95% confidence interval)	P value
	No warfarin	Warfarin			
All-cause mortality					
Before matching (N=2248)	n=347	n=1901			
Unadjusted	97 (28%)	365 (19%)	− 9%	0.71 (0.57–0.89)	0.003
Multivariable-adjusted[a]	---	---		0.70 (0.54–0.91)	0.007
Propensity-adjusted[b]	---	---		0.67 (0.52–0.87)	0.003
After matching (N=843)	n=227	n=616			
Propensity-matched	74 (33%)	112 (18%)	− 14%	0.58 (0.43–0.77)	<0.001

*Absolute risk difference was calculated by subtracting the percentage of events in the warfarin group from that of the no-warfarin group (before values were rounded)

[a]Adjusted for all 45 baseline characteristics

[b]Adjusted for propensity score.

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Table 3

Associations of warfarin use with other outcomes among 843 propensity-matched atrial fibrillation patients 70 years of age or older

	Events (%)		Absolute risk difference*	Hazard ratio (95% confidence interval)	P value
	No warfarin (n=227)	Warfarin (n=616)			
Cardiovascular mortality	27 (12%)	56 (9%)	− 3%	0.80 (0.51–1.27)	0.346
Due to cardiac causes	20 (9%)	43 (7%)	− 2%	0.84 (0.49–1.43)	0.516
Arrhythmic	12 (5%)	24 (4%)	− 1%	0.76 (0.38–1.52)	0.432
Non-arrhythmic	8 (4%)	19 (3%)	− 1%	0.96 (0.42–2.20)	0.931
Due to vascular causes	7 (3%)	13 (2%)	− 1%	0.70 (0.28–1.75)	0.442
Non-cardiovascular mortality	40 (18%)	48 (8%)	− 10%	0.45 (0.30–0.70)	<0.001
Cancer	14 (6%)	24 (4%)	− 2%	0.61 (0.31–1.19)	0.609
Pulmonary	8 (4%)	10 (2%)	− 2%	0.43 (0.18–1.07)	0.068
Others	17 (8%)	15 (2%)	− 6%	0.33 (0.17–0.67)	0.002
All-cause hospitalization	152 (67%)	394 (64%)	− 3%	0.93 (0.77–1.12)	0.423
Due to cardiovascular causes	103 (44%)	252 (41%)	− 3%	0.90 (0.72–1.14)	0.386
Due to non-cardiovascular causes	104 (46%)	258 (42%)	− 4%	0.90 (0.71–1.13)	0.355
Ischemic stroke	17 (8%)	26 (4%)	− 4%	0.57 (0.31–1.04)	0.068
Major bleeding**	22 (10%)	44 (7%)	−3%	0.73 (0.44–1.22)	0.229

*Absolute risk difference was calculated by subtracting the percentage of events in the warfarin group from that of the no-warfarin group (before values were rounded)

**Major bleeding was defined as bleeding requiring transfusion and/or surgery and/or permanent cessation of warfarin

Table 4

Adjusted associations of warfarin use with other outcomes among 2248 atrial fibrillation patients 70 years of age or older

	Unadjusted events (%)		Absolute risk difference**	Hazard ratio* (95% confidence interval)	P value
	No warfarin (n=347)	Warfarin (n=1901)			
Cardiovascular mortality	36 (10%)	182 (10%)	− 0%	0.92 (0.66–1.39)	0.700
Due to cardiac causes	28 (8%)	143 (8%)	− 0%	0.92 (0.58–1.45)	0.708
Arrhythmic	15 (4%)	82 (4%)	− 0%	0.96 (0.51–1.78)	0.888
Non-arrhythmic	13 (4%)	61 (3%)	− 1%	0.87 (0.44–1.72)	0.684
Due to vascular causes	8 (2%)	39 (2%)	− 0%	0.95 (0.40–2.25)	0.904
Non-cardiovascular mortality	52 (15%)	154 (8%)	− 7%	0.51 (0.35–0.73)	<0.001
Cancer	20 (6%)	64 (3%)	− 3%	0.56 (0.31–1.01)	0.053
Pulmonary	13 (4%)	40 (2%)	− 2%	0.54 (0.26–1.12)	0.096
Others	19 (6%)	50 (3%)	− 3%	0.43 (0.23–0.80)	0.008
All-cause hospitalization	227 (65%)	1218 (64%)	− 1%	0.96 (0.82–1.12)	0.600
Due to cardiovascular causes	154 (44%)	779 (41%)	− 3%	1.12 (0.93–1.36)	0.235
Due to non-cardiovascular causes	152 (44%)	780 (41%)	− 3%	1.04 (0.85–1.27)	0.701
Ischemic stroke	21 (6%)	77 (4%)	− 2%	0.79 (0.45–1.38)	0.400
Major bleeding***	35 (10%)	140 (7%)	− 3%	0.76 (0.50–1.15)	0.195

*Adjusted for propensity score for warfarin use

**Absolute risk difference was calculated by subtracting the percentage of events in the warfarin group from that of the no-warfarin group (before values were rounded)

***Major bleeding was defined as bleeding requiring transfusion and/or surgery and/or permanent cessation of warfarin

Table 5

Characteristics of atrial fibrillation (AF) patients 70–80 years in AFFIRM and CHS

n (%) or mean (±SD)	CHS (n=102)	AFFIRM (n=2248)	P value
Age, years	74.6 (±3.5)	75.4 (±3.4)	0.019
Female	46 (45%)	1021 (45%)	0.949
African American	10 (10%)	166 (7%)	0.364
Current smoker	9 (9%)	152 (7%)	0.343
Systolic blood pressure, mm Hg	137 (±21)	136 (±19)	0.438
Diastolic blood pressure, mm Hg	72 (±12)	75 (±10)	0.003
Ventricular rate, bpm	71 (±13)	73 (±14)	0.144
$CHADS_2$ score	1.8 (±1.2)	2.0 (±1.2)	0.351
CHA2DS2VASc score	3.6 (±1.5)	3.8 (±1.4)	0.176
Past medical history			
Coronary artery disease	23 (23%)	895 (40%)	<0.001
Acute myocardial infarction	12 (12%)	423 (19%)	0.073
Hypertension	62 (61%)	1543 (69%)	0.095
Diabetes mellitus	28 (28%)	387 (17%)	0.008
Heart failure	24 (24%)	529 (24%)	1.000
Stroke or transient ischemic attack	19 (19%)	327 (15%)	0.255
Medications			
Warfarin	50 (49%)	1901 (85%)	<0.001
Heparin	10 (10%)	391 (17%)	0.046
Aspirin	13 (13%)	593 (26%)	0.002
Digoxin	79 (78%)	1202 (54%)	<0.001
Beta-blockers	16 (16%)	930 (41%)	<0.001
ACE inhibitors	8 (8%)	829 (37%)	<0.001
Diuretics	45 (44%)	1021 (45%)	0.796
Lipid lowering agents	1 (1%)	450 (20%)	<0.001
One year mortality			
Unadjusted events	4 (4%)	117 (5%)	0.566
Unadjusted hazard ratio (95% CI)	Reference (1)	1.36 (0.52–3.69)	0.543
Age-sex-race adjusted hazard ratio (95% CI)	Reference (1)	1.29 (0.48–3.50)	0.616
Six-year mortality			
Unadjusted events	29 (28%)	462 (21%)	0.056
Unadjusted hazard ratio (95% CI)	Reference (1)	1.24 (0.83–1.83)	0.292
Age-sex-race adjusted hazard ratio (95% CI)	Reference (1)	1.15 (0.77–1.70)	0.494