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Disparities and Temporal Trends in Stroke Care Outcomes in Patients with Atrial Fibrillation: The FLiPER-AF Stroke Study

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Abstract

Background and Purpose: Atrial Fibrillation (AF) is the most common cardiac cause of ischemic stroke. However, the relation between AF and stroke care outcomes in diverse populations is understudied. We aimed to evaluate sex and race-ethnic disparities associated with AF in hospital stroke outcomes utilizing data from the FLorida PuErto Rico Atrial Fibrillation (FLiPER–AF) Stroke Study.

Methods: The study included 104,308 ischemic stroke cases with available information on AF status enrolled in a state-wide stroke registry from 2010 to 2016. Multivariable logistic regression models were performed to evaluate the association between AF and stroke outcomes and the modification effects on the associations by sex and by race-ethnicity, adjusted for socio-demographic status, vascular risk factors and stroke severity.

Results: AF was present in 23% of ischemic stroke cases. AF was associated with worse disability at discharge (OR=1.11, 95% CI, 1.04-1.18), less discharge to home (OR=0.89, 0.85-0.92), and longer length of hospital stay (LOS>6 days, OR=1.53, 1.46-1.60). Interaction analyses showed that the association between AF and less discharge to home was stronger in women than men (p for interaction <0.001), as well as in FL-whites than in FL-blacks, FL-Hispanics or PR-Hispanics (p for interaction=0.002). The association between AF and prolonged LOS was more prominent in PR-Hispanics than in FL-blacks, FL-Hispanics, or FL-whites (p for interaction <0.001). From 2010 to 2016, the effects of AF on hospital length of stay attenuated (p for interaction<0.001).

Conclusions: AF was associated with poor disability at discharge, less discharge to home, and prolonged hospital length of stay for acute stroke care. The effect of AF on length of stay attenuated over time. Sex and race-ethnic disparities were observed in the effect of AF on being less discharge to home and prolonged hospital stay. Further research is needed to identify and modify the biologic and systems of care contributors to these disparities.

Keywords: Atrial fibrillation; Hospital care; In-hospital mortality; Disability; Discharge disposition; Stroke Severity; Length of stay; Disparity

Introduction

Atrial Fibrillation (AF) is the most common arrhythmia, the major cardiac cause of stroke, and likely the leading cause of cryptogenic stroke or Embolic Stroke of Undetermined Source (ESUS) [1-4]. Population-based studies have demonstrated that AF increases the risk of ischemic stroke by 4 to 5-fold, accounting for approximately 15% to 20% of all ischemic stokes [5,6]. Stroke patients with AF have a greater mortality, worse disability and poorer neurological outcome compared to stroke patients without AF [7-10]. AF is the major contributing factor for in-hospital expenditures for the care of acute stroke patients [11].

Epidemiological patterns, clinical manifestations, and stroke risk have been described for AF patients, however the studies of AF as an independent predictor of stroke mortality and disability have been conducted in relatively small samples of patients [12]. In addition, the relationship between AF and stroke care outcomes in diverse populations has been understudied. Few studies have examined sex and race/ethnic-specific outcomes associated with AF in large stroke populations from diverse populations and even fewer reported on the temporal trends of AF-associated stroke outcomes.

Our FLorida PuErto Rico Atrial Fibrillation Stroke Study (FLiPER–AF) includes AF data in a network of 89 hospitals from a large, multi-ethnic stroke registry of the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD). FLiPER–AF provides a unique opportunity to determine disparities in stroke outcomes for patients with AF. It also represents a great resource to determine the 'real life' practice of AF management and outcomes for stroke patients with AF, particularly among minority race-ethnic groups that are underrepresented in AF-stroke related studies and clinical trials [13-16]. In the present study, we sought to evaluate sex and race-ethnic disparities in-hospital mortality, length of hospital stay, disability at discharge, and disposition to home for stroke patients with AF. We also examined temporal trends in these stroke care outcomes from 2010 to 2016.

Subjects and Methods

The FLiPER–AF Stroke study utilizes the stroke registry data of FL-PR CReSD collected from 89 FL-PR CReSD hospitals (75 in Florida and 14 in Puerto Rico) from January 2010 to December 2016. In this period, a total of 104,308 cases with primary diagnosis of ischemic stroke and AF data were included in the FLiPER–AF Stroke study after excluding the cases with the primary diagnosis of intracerebral hemorrhage, subarachnoid hemorrhage, TIA, stroke not otherwise specified, or ischemic stroke without AF data. The University of Miami's institutional review board approved the study and waived the need for patient consent.

Data were collected using the American Heart Association (AHA) Get With The Guidelines-Stroke (GWTG - S), a voluntary, national hospital program established with the goal of improving quality of stroke care. In addition to GWTG-S data, new data collection elements were added for those hospitals participating in FLiPER-AF, including questions on ethnicity, language, education, and AF diagnosis including the use of a prolonged cardiac monitoring and AF management.

Trained personnel at participating hospitals used GWTG-S data-collection tools to collect information on patients presenting to the hospitals with stroke symptoms. Data were collected using AHA's Patient Management Tool, an online, interactive assessment and reporting system. Information collected for each hospitalization included patient demographics (age, sex and race/ethnicity- non-Hispanic white, non-Hispanic black, or Hispanic), health insurance status (private, Medicare, Medicaid/no insurance or unknown), medical history (current smoker, hypertension, diabetes, dyslipidemia, coronary artery disease, peripheral vascular disease, previous stroke/TIA, heart failure and renal insufficiency), mode of hospital arrival (via emergency medical services-EMS from home/scene, private transport, or unknown), stroke severity at presentation assessed by the NIH Stroke Scale (NIHSS) score, modified Rankin Score (mRS) at discharge, in-hospital mortality and discharge disposition. High data quality of the GWTG database is maintained through careful training of chart abstractors, standardized coding instructions, limitations of data fields to realistic entries, audit trails, and required site data quality reports. Data on hospital-level characteristics (academic status, number of beds, and number of years in GWTG-S) were obtained from the AHA database in addition to a self-reported hospital characteristics survey distributed to all hospitals participating in FL-PR CreSD [15].

AF was defined as persistent or paroxysmal AF or flutter diagnosed at or after hospital admission or by medical history of AF or Flutter. Four key clinical stroke outcomes were investigated in relation to AF: (1) in-hospital mortality, (2) disability at discharge (mRS), (3) length of stay (LOS), and (4) discharge disposition. All primary outcomes were coded as binary variables: in-hospital mortality was identified as patients who have either discharge status or discharge disposition as "Expired"; disability at discharge (mRS) was categorized as none to mild disability (mRS 0-2) and moderate to severe disability (mRS 3-5); discharge disposition was categorized as home and non-home/other; LOS was calculated as the time span from hospital admission to discharge and dichotomized to LOS 0-6 days and longer than 6 days (LOS>6).

Statistical Analysis

Univariate analyses were used to compare the frequencies of the pre-specified patient-level and hospital-level characteristics between the ischemic stroke patients with AF and those without AF. Continuous variables were summarized as means with Standard Deviation (SD) and categorical variables were presented as frequencies with percentages. For continuous variables, differences between AF vs. non-AF ischemic stroke cases were assessed using the Student t-test. For categorical variables, the Pearson chi-square test was used. To further analyze the effect of AF on binary clinical outcomes (in-hospital mortality, disability at discharge by mRS, LOS, discharge disposition) we conducted multilevel logistic regressions with Generalized Estimating Equations (GEE) to account for within-hospital and between-hospital variability. Models were built to adjust for pre-specified patient-level and hospital-level characteristics. The pre-specified patient-level factors included age, sex, race/ethnicity, health insurance status, current smoking, hypertension, diabetes, dyslipidemia, Coronary Artery Disease (CAD), Peripheral Vascular Disease (PVD), previous stroke/TIA, heart failure, renal insufficiency, arrival mode, and the NIHSS score. The pre-specified hospital-level factors included academic status, number of beds, years in the GWTG-S program. As sensitivity analysis, we further adjusted for anticoagulation use prior to admission. Model results were presented as Odds Ratios (OR) with 95% confidence intervals (95%CI) and p values. P values less than 0.05 were considered statistically significant. To investigate the potential effect modification by sex and by race-ethnicity, the two-way interactions effects of AF status by sex and by race-ethnicity on the stroke outcomes were tested and the results stratified by sex and by race-ethnicity were presented. We also examined temporal trends in the relationship between AF and stroke care outcomes, and tested for the two-way interaction between AF and discharge year. The results were stratified by a discharge year and plotted. All statistical analyses were performed using SAS version 9.3 software.

Results

Sample characteristics

AF was present in 23% of 104,308 ischemic stroke cases (Table 1). Compared to non-AF ischemic stroke patients, patients with AF were older (79±11 vs. 68±14 years), more likely women (53.8% vs. 48.4%), white (74.3% vs. 57.9%); had Medicare (40.0% vs. 29.9%); hypertension (71.5% vs. 65.2%), dyslipidemia (41.8% vs. 36.9%), CAD/prior MI (30.3% vs. 18.8%), PVD (5.3% vs. 3.4%), previous stroke/TIA (28.7% vs. 25.3%), heart failure (12.4% vs. 3.5%), renal insufficiency (5.5% vs. 3.6%), arrived by EMS (73.3% vs. 56.2%), and had more severe strokes (NIHSS of 6 or greater, 43.9% vs. 26.9%) and the CHA_2DS_2-VASc scores of 4 or greater (61% vs. 40.5%). Patients with AF were less likely current smokers than those without AF (7.4% vs. 18.9%).

	All		Atrial Fibrillation				
			Yes		No		p
	N	%	N	%	N	%	
All	104308	100	24040	100	80268	100	
Age (mean±SD), years	71±14		79±11		68±14		<.0001
Women	51734	49.6	12923	53.8	38811	48.4	<.0001
Race-Ethnicity							<.0001
FL-white	64209	61.6	17732	73.8	46477	57.9	
FL-black	19564	18.8	2354	9.8	17210	21.4	
FL-Hispanic	14305	13.7	3034	12.6	11271	14.0	
PR-Hispanic	6230	6.0	920	3.8	5310	6.6	
Insurance							<.0001
Private	37831	36.3	8744	36.4	29087	36.2	
Medicare	33614	32.2	9612	40.0	24002	29.9	
No Insurance/Medicaid	10907	10.5	917	3.8	9990	12.4	
Unknown	21956	21.0	4767	19.8	17189	21.4	

Smoker	16957	16.3	1793	7.5	15164	18.9	<.0001
Hypertension	69502	66.6	17181	71.5	52321	65.2	<.0001
Diabetes Mellitus	31500	30.2	6268	26.1	25232	31.4	<.0001
Dyslipidemia	39638	38.0	10055	41.8	29583	36.9	<.0001
CAD/prior MI	22391	21.5	7277	30.3	15114	18.8	<.0001
PVD	4032	3.9	1264	5.3	2768	3.4	<.0001
Previous Stroke/TIA	27213	26.1	6896	28.7	20317	25.3	<.0001
Carotid Stenosis	3418	3.3	860	3.6	2558	3.2	0.0028
Heart Failure	5789	5.5	2982	12.4	2807	3.5	<.0001
Renal insufficiency	4219	4.0	1323	5.5	2896	3.6	<.0001
Prior anticoagulation	2905	2.8	1990	8.3	915	1.1	<.0001
NIHSS							<.0001
0 to 5	41611	39.9	7657	31.9	33954	42.3	
6 and above	32128	30.8	10555	43.9	21573	26.9	
Missing	30569	29.3	5828	24.2	24741	30.8	
Arrival Mode							<.0001
EMS-Yes	62799	60.2	17631	73.3	45168	56.3	
EMS-No	34675	33.2	5023	20.9	29652	36.9	
Unknown/missing	6834	6.6	1386	5.8	5448	6.8	
CHADS score							<.0001
0 and 1	44264	42.4	7356	30.6	36908	46.0	
2 and 3	44546	42.7	12012	50.0	32534	40.5	
4 and above	15498	14.9	4672	19.4	10826	13.5	
CHA_2DS_2-VASc score							<.0001
0 and 1	18917	18.1	1625	6.8	17292	21.5	
2 and 3	38218	36.6	7737	32.2	30481	38.0	
4 and above	47173	45.2	14678	61.0	32495	40.5	
SD=Standard Deviation; FL=Florida; PR=Puerto Rico; CAD=Coronary Artery Disease; MI=Myocardial Infarct; PVD=Peripheral Vascular Disease; TIA=Transient Ischemic Attack; NIHSS= NIH Stroke Scale; EMS=Emergency Medical Service.							

Table 1: Characteristics of stroke patients with and without atrial fibrillation.

Effects of AF on stroke care outcomes

In comparison to non-AF patients, ischemic stroke patients with AF had (1) higher in-hospital mortality (5% vs. 3%); (2) more severe disability at discharge (mRS 3-5: 68% vs. 51%); (3) were less likely discharged home (34% vs. 52%), and (4) had prolonged hospital stay (LOS>6 days, 36% vs. 26%) (Supplemental Table 1).

Group	In-hospital mortality, %			Disability at discharge, %			LOS>6 days, %			Discharge to home, %		
	AF	non-AF	P*	AF	non-AF	p*	AF	non-AF	p*	AF	non-AF	p*
All	5.4	3.2	<.0001	68.2	50.9	<.0001	35.9	26.0	<.0001	34.4	52.5	<.0001
Female	5.4	3.1	<.0001	73.7	55.6	<.0001	36.2	25.6	<.0001	29.1	49.6	<.0001
Male	5.4	3.3	<.0001	61.8	46.6	<.0001	35.5	26.4	<.0001	40.5	55.2	<.0001
White	5.1	2.9	<.0001	67.1	49.4	<.0001	31.6	21.8	<.0001	32.3	50.3	<.0001
Black	4.9	2.6	<.0001	69.0	51.7	<.0001	48.2	31.1	<.0001	36.7	52.2	<.0001
FL-Hispanic	5.8	3.2	0.0004	70.5	51.8	<.0001	44.2	28.5	<.0001	38.0	55.2	<.0001
PR-Hispanic	9.9	7.8	0.069	79.9	66.4	<.0001	60.7	41.5	<.0001	57.8	66.5	0.006
2010	6.6	3.2	<.0001				35.8	23.9	<.0001	20.4	39.4	<.0001
2011	6.1	2.9	<.0001				37.1	25.2	<.0001	26.0	43.9	<.0001
2012	6.6	3.0	<.0001	70.3	51.8	<.0001	34.9	23.6	<.0001	33.6	53.4	<.0001
2013	5.3	3.1	<.0001	68.8	50.7	<.0001	37.2	26.3	<.0001	37.0	55.0	<.0001
2014	5.2	3.4	<.0001	69.6	50.5	<.0001	35.4	26.9	<.0001	37.1	56.1	<.0001
2015	4.4	3.3	0.006	67.0	50.5	<.0001	36.8	27.0	<.0001	39.5	56.7	<.0001
2016	4.6	3.3	0.004	67.5	51.4	<.0001	34.4	27.4	<.0001	38.4	55.5	<.0001

*Unadjusted and based on GEE model.

Supplemental Table 1: Outcomes of stroke care by Atrial Fibrillation (AF) status, sex, race-ethnicity and discharge year.

In adjusted models for patient-level and hospital-level covariates (Table 2), ischemic stroke patients with AF (1) had greater disability at discharge (OR=1.11; 1.04-1.18); (2) were less likely discharged home (OR=0.89; 0.85-0.92); and (3) had prolonged hospital stay (LOS>6 days, OR=1.53; 1.46-1.60) than ischemic stroke patients without AF. These associations remained statistically significant and very similar in the sensitivity analyses with further adjustment for anticoagulation use prior to admission (data not shown).

	In-hospital mortality		**Disability at discharge**		**Discharge to home**		**LOS>6 days**	
	OR (95% CI)	**P**	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**
AF (Yes vs. No)	1.07 (0.97, 1.19)	0.182	1.11 (1.04, 1.18)	0.001	0.89 (0.85, 0.92)	<.0001	1.53 (1.46, 1.60)	<.0001
Age (65 to 79 vs. 50-64)	1.32 (1.15, 1.50)	<.0001	1.55 (1.45, 1.66)	<.0001	0.66 (0.63, 0.69)	<.0001	0.96 (0.91, 1.00)	0.050
Age (80+ vs 50-64)	1.57 (1.29, 1.91)	<.0001	3.19 (2.95, 3.46)	<.0001	0.35 (0.33, 0.38)	<.0001	0.83 (0.78, 0.89)	<.0001
Female vs. Male	0.86 (0.83, 0.90)	<.0001	1.25 (1.18, 1.32)	<.0001	0.90 (0.87, 0.93)	<.0001	0.97 (0.94, 1.00)	0.030
FL-black vs FL-white	0.86 (0.73, 1.01)	0.063	1.38 (1.27, 1.51)	<.0001	0.88 (0.84, 0.91)	<.0001	1.32 (1.24, 1.40)	<.0001

FL-Hispanic vs. FL-white	0.97 (0.86, 1.09)	0.606	1.10 (0.96, 1.27)	0.166	1.15 (1.09, 1.21)	<.0001	1.14 (1.06, 1.22)	0.000
PR-Hispanic vs. FL-white	2.48 (1.81, 3.41)	<.0001	1.65 (0.77, 3.51)	0.198	3.62 (2.55, 5.13)	<.0001	1.79 (1.36, 2.35)	<.0001
Health insurance (Medicare vs. private)	1.03 (0.94, 1.12)	0.518	1.14 (1.04, 1.24)	0.003	0.79 (0.75, 0.84)	<.0001	1.11 (1.06, 1.17)	<.0001
Health insurance (No Insurance/medicaid vs. private)	1.30 (1.07, 1.59)	0.008	1.11 (1.00, 1.23)	0.045	1.23 (1.11, 1.35)	<.0001	1.47 (1.35, 1.59)	<.0001
Health insurance (Unknown vs. private)	1.09 (0.94, 1.26)	0.240	0.82 (0.66, 1.03)	0.084	1.05 (0.94, 1.18)	0.399	1.09 (1.01, 1.17)	0.020
Smoker vs. non-smoker	0.72 (0.62, 0.83)	<.0001	0.91 (0.85, 0.97)	0.005	1.08 (1.03, 1.14)	0.003	0.98 (0.93, 1.03)	0.471
Hypertension (yes vs. no)	0.95 (0.86, 1.06)	0.375	1.14 (1.06, 1.22)	<.001	0.92 (0.88, 0.96)	<.0001	1.01 (0.97, 1.04)	0.771
Diabetes Mellitus (Yes. No)	1.11 (1.04, 1.18)	0.001	1.38 (1.32, 1.45)	<.0001	0.78 (0.75, 0.81)	<.0001	1.16 (1.13, 1.20)	<.0001
Dyslipidemia (Yes vs. No)	0.79 (0.74, 0.83)	<.0001	0.90 (0.85, 0.95)	<.001	1.13 (1.09, 1.17)	<.0001	0.90 (0.87, 0.93)	<.0001
CAD/prior MI (Yes vs. No)	1.23 (1.13, 1.33)	<.0001	0.98 (0.94, 1.03)	0.510	1.00 (0.97, 1.04)	0.898	1.07 (1.04, 1.11)	<.0001
PVD (Yes vs. No)	1.27 (1.06, 1.51)	0.008	1.31 (1.15, 1.49)	<.0001	0.87 (0.78, 0.96)	0.008	1.18 (1.08, 1.29)	<.001
Previous Stroke/TIA (Yes vs. no)	0.85 (0.78, 0.92)	0.001	1.35 (1.27, 1.43)	<.0001	0.84 (0.80, 0.87)	<.0001	1.05 (1.02, 1.09)	0.003
Heart Failure (Yes vs. no)	1.43 (1.27, 1.61)	<.0001	1.27 (1.12, 1.44)	<.001	0.81 (0.76, 0.86)	<.0001	1.12 (1.05, 1.21)	0.001
Renal insufficiency - chronic ((Yes vs. no)	1.28 (1.10, 1.50)	0.001	1.26 (1.13, 1.40)	<.0001	0.95 (0.88, 1.02)	0.129	1.40 (1.32, 1.49)	<.0001
EMS (Yes vs. no)	3.50 (3.15, 3.89)	<.0001	2.12 (1.97, 2.27)	<.0001	0.42 (0.40, 0.45)	<.0001	1.72 (1.65, 1.81)	<.0001
EMS (Yes vs. Unknown)	2.93 (2.51, 3.41)	<.0001	1.03 (0.39, 2.69)	0.951	0.51 (0.46, 0.56)	<.0001	1.38 (1.24, 1.52)	<.0001
NIHSS (>=6 vs. 0-5)	6.09 (5.26, 7.06)	<.0001	4.15 (3.69, 4.66)	<.0001	0.26 (0.24, 0.28)	<.0001	2.38 (2.25, 2.53)	<.0001
NIHSS(missing vs. 0-5)	3.28 (2.69, 4.00)	<.0001	1.01 (0.88, 1.15)	0.937	0.74 (0.65, 0.83)	<.0001	1.54 (1.40, 1.68)	<.0001
Teaching hospital (Yes vs. No)	1.30 (0.98, 1.73)	0.064	0.60 (0.43, 0.84)	0.003	1.21 (1.04, 1.42)	0.017	1.13 (0.95, 1.34)	0.177
Number of beds (tertile 2 vs tertile 1)	1.24 (0.95, 1.62)	0.118	1.37 (0.93, 2.01)	0.116	0.97 (0.86, 1.10)	0.636	1.39 (1.18, 1.64)	<.0001
Number of beds (tertile 3 vs tertile 1)	2.21 (1.71, 2.87)	<.0001	1.42 (0.96, 2.10)	0.080	0.95 (0.81, 1.12)	0.545	1.39 (1.11, 1.75)	0.005

Years in GWTG-S (tertile 2 vs tertile 1)	1.02 (0.79, 1.31)	0.884	0.91 (0.59, 1.43)	0.694	0.93 (0.82, 1.06)	0.282	0.98 (0.80, 1.19)	0.827
Years in GWTG-S (tertile 3 vs tertile 1)	1.07 (0.77, 1.48)	0.685	0.82 (0.53, 1.26)	0.359	0.97 (0.84, 1.11)	0.641	0.90 (0.74, 1.09)	0.262
LOS=Length Of Stay; CI=Confidence Interval; FL=Florida; PR=Puerto Rico; CAD=Coronary Artery Disease; MI=Myocardial Infarct; PVD=Peripheral Vascular Disease; TIA=Transient Ischemic Attack; NIHSS= NIH Stroke Scale; EMS=Emergency Medical Service; GWTG-S= Get With The Guidelines–Stroke.								

Table 2: Multivariable-adjusted odds ratio (OR) for stroke care outcomes.

Sex, racial-ethnic differences in effects of AF on stroke care outcomes

We observed sex and race-ethnic differences in the effect of AF on discharge to home and length of hospital stay. For discharge home, the effect of AF was more prominent in women (29% in AF vs. 50% in non-AF; adjusted OR=0.84, 0.80-0.88) than in men (41% in AF vs. 55% in non-AF; adjusted OR=0.94, 0.89-0.99), with a p-value for interaction <0.001; and in FL-whites (32% in AF vs. 50% in non-AF; adjusted OR=0.87, 0.83-0.91) than in FL-blacks (37% in AF vs. 52% in non-AF; adjusted OR=0.92, 0.83-1.01), FL-Hispanics (38% in AF vs. 55% in non-AF; adjusted OR=0.98, 0.88-1.09) and PR-Hispanics (58% in AF vs. 67% in non-AF; adjusted OR=0.99, 0.84-1.17), with a p-value for interaction=0.002. For LOS>6 days, the effect of AF was greater in PR-Hispanics (61% in AF vs. 42% in non-AF; adjusted OR=1.91, 1.66-2.19) than in FL-whites (32% in AF vs. 22% in non-AF; adjusted OR=1.52, 1.43-1.61), FL-blacks (48% in AF vs. 31% in non-AF; adjusted OR=1.60, 1.47-1.75) and FL-Hispanics (44% in AF vs. 29% in non-AF; adjusted OR=1.57, 1.44-1.72), a p-value for interaction of 0.001. (Supplemental Table 1, and Table 3).

Subgroup	In-hospital Mortality		Disability at discharge		Discharge to home		LOS > 6 days	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Men	1.06 (0.92, 1.22)	0.406	1.10 (1.04, 1.18)	0.002	0.94 (0.89, 0.99)	0.027	1.47 (1.38, 1.56)	<.001
Women	1.09 (0.96, 1.24)	0.172	1.13 (1.03, 1.24)	0.012	0.84 (0.80, 0.88)	<.001	1.59 (1.49, 1.69)	<.001
P value for AF-by-sex interaction	0.875		0.467		**<.001**		0.529	
FL-white	1.15 (1.03, 1.27)	0.011	1.10 (1.02, 1.19)	0.014	0.87 (0.83, 0.91)	<.001	1.52 (1.43, 1.61)	<.001
FL-black	1.19 (0.86, 1.65)	0.293	1.20 (0.99, 1.45)	0.066	0.92 (0.83, 1.01)	0.092	1.60 (1.47, 1.75)	<.001
FL-Hispanic	0.97 (0.74, 1.26)	0.793	1.06 (0.95, 1.19)	0.274	0.98 (0.88, 1.09)	0.683	1.57 (1.44, 1.72)	<.001
PR-Hispanic	0.83 (0.69, 0.99)	0.043	1.31 (1.00, 1.70)	0.046	0.99 (0.84, 1.17)	0.891	1.91 (1.66, 2.19)	<.001
P value for AF-by-race-ethnicity interaction	0.416		0.753		**0.002**		**0.001**	
LOS=Length Of Stay; CI=Confidence Interval; FL=Florida; PR=Puerto Rico.								

Table 3: Multivariable-adjusted Odds Ratio (OR) of stroke care outcomes for Atrial Fibrillation (AF) by sex and race-ethnicity.

Temporal trends in effects of AF on stroke outcomes

The effects of AF on all stroke outcomes attenuated from 2010 to 2016. Significant trends were observed for reduced in-hospital mortality and length of stay. The effect of AF on in-hospital mortality changed from 1.34 (95% CI: 1.13-1.59) in 2010 to 0.85 (0.66-1.11) in 2016, with a p-value for interaction<0.001. The effect of AF on LOS >6 days changed from 1.71 (1.53-1.92) in 2010 to 1.27 (1.16-1.39) in 2016, with a p-value for interaction<0.001 (Figure 1).

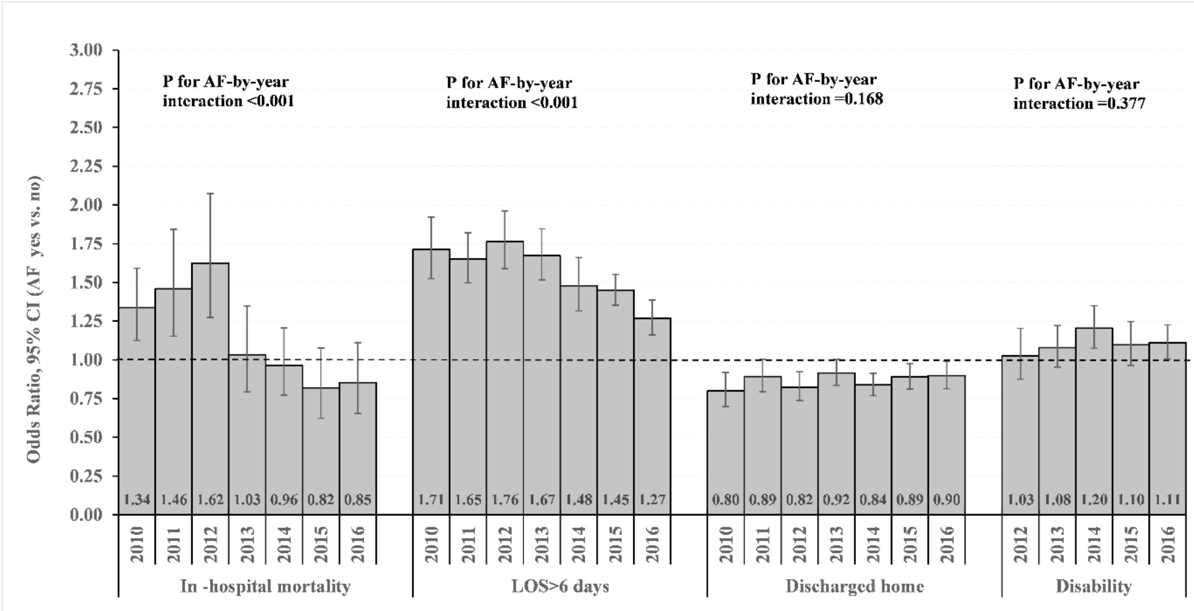

Figure 1: Atrial fibrillation and stroke care outcomes by discharge year in ischemic stroke patients. Odds Ratio (OR) and 95% Confidence Interval (CI) of Atrial Fibrillation (AF) for stroke care outcomes by discharge year. The effects of AF on all stroke outcomes attenuated from 2010 to 2016, with significant change in in-hospital mortality (p value for interaction <0.001) and Length Of Stay (LOS>6 days) (p value for interaction <0.001).

Discussion

The present study contributes novel data on sex, race-ethnic, and temporal variations in the effect of AF on stroke outcomes in a diverse and largely understudied stroke population of Florida and Puerto Rico. Women with stroke and AF were less likely discharged home than women without AF and Puerto Rican stroke patients with AF had almost two times longer hospital stay than Puerto Ricans without AF. These findings were not explained by greater stroke severity or disability at discharge, indicating that other biological, socioeconomic and cultural factors, and systems of care factors not accounted in our study are important contributors. Nevertheless, improvements in the management of AF and systems of care for all stroke patients may be a solution for eliminating most of the observed disparities, as indicated in our temporal trend analyses for in-hospital mortality. However, disability is still a major issue after a stroke. Even more pronounced, disability continues to be considerably greater in stroke patients with AF than without AF. Further advances in hospital and pre-hospital stroke care for patients with AF is critically needed to improve stroke outcomes and eliminate disparities in stroke outcomes in patients with AF, particularly in vulnerable minority populations.

In the FLiPER–AF Stroke Study, almost one fifth of stroke patients had AF. This proportion is similar to that reported in other studies [5,6]. Stroke patients with AF are typically older, and more often women, Caucasian and on Medicare. They more likely have a high burden of vascular risk factors including hypertension, dyslipidemia and prior heart disease and stroke. Therefore, stroke patients with AF usually have high CHA_2DS_2-VASc scores, present with more severe strokes, and have increased mortality. Similar was observed in our FLiPER–AF Stroke Study. Stroke patients with AF had a 1.7-fold greater in-hospital mortality (5% in-hospital mortality for those with AF vs. 3% without AF), 2-fold greater disability at discharge (68% with AF vs. 51% without AF), 38% less likely discharged home (34% with AF vs. 52% without AF), and had a 1.8-fold greater hospital stay 6 days or longer (36% with AF vs. 26% without AF). These odds substantially decreased after adjustment however, suggesting that most disparities in stroke outcomes in patients with AF could be reduced by controlling for the known modifiable vascular risk factors and by improving AF management and stroke hospital systems of care. Regardless, stroke patients with AF in our study continue to have worse disability at discharge after acute stroke hospitalization than those without AF, and this finding could not be explained by stroke severity, current AF management, or stroke hospital systems of care. Other biological and non-biological factors not included to our analyses may be important to evaluate in further studies. The residual factors potentially contributing to worse disability in patients with AF may include poor cerebral collateral circulation, reduced use of thrombolysis/antithrombotic therapy and/or contraindications or bleeding on antithrombotic therapy, as suggested in the literature [17]. These and other factors, such as delay in recognizing stroke symptoms, women specific stroke symptoms, need for more prolonged diagnostic testing [18], and socioeconomic and cultural factors may be particularly important for stroke patients with AF and deserve further study [19], particularly in diverse minority populations [20].

The novel findings of the present analysis are sex and race-ethnic disparities in the effect of AF on length of hospital stay and discharge disposition in stroke patients, even after adjustment for biologic factors (age, vascular risk factors, stroke severity), health insurance status, and hospital characteristics representative of systems of hospital stroke care (e.g., teaching hospitals vs. non-teaching or large hospitals vs. small) in Florida and Puerto Rico. Although sex, race-ethnicity and AF are well-established factors associated with increased stroke incidence, mortality and disability [21], there are no large studies in multi-ethnic populations that evaluated their interaction effects on the hospital stroke outcomes. A prolonged hospital stay among stroke patients with known or newly diagnosed AF during hospitalization may be due to the higher risk of in-hospital medical complications and a need for further treatments and diagnostic procedures before discharge [22]. As reported by other studies [20], our study showed that the minorities have prolonged LOS in comparison to whites. Particularly prolonged LOS was observed in Puerto Rico, where acute stroke care continues to be extremely challenging due to limited resources, a lack of stroke units and stroke specialists, lower delivery of quality stroke care, and less participation and shorter time in the GWTG-S quality improvement program in comparison to Florida hospitals [13].

Women with stroke and AF were less likely discharged home in our study. This may reflect a more severe stroke at presentation, more motor deficits and greater disability, and the need for longer and more intense rehabilitation in women than in men with stroke and AF. However, most of these factors were included in our analyses but did not explain the sex disparity in discharge disposition. Our previous analyses in FL-PR CReSD showed that women less likely received thrombolysis and had longer time to treatment than men [14,16]. In current analyses however, we did not consider acute stroke treatment as we included all ischemic hospitalized stroke cases regardless of their eligibility for acute thrombolysis. Other factors, such as social isolation (e.g., leaving alone) and cultural (e.g., not being able to care for family or being probably more willing to take care of their male partners than vice versa) may be particularly important in the decision-making regarding home disposition for women, but were not available for our analyses.

We did not specifically investigate disparity in the use of anticoagulation and the type of anticoagulant in AF patients and its effect on stroke outcomes. These analyses were discussed in our recent publication [23]. However, our sensitivity analysis with additional adjustment for anticoagulation use did not change the man effects of AF on stroke outcomes nor observed race-ethnic disparities. Underuse of anticoagulation in women and minorities have been suggested as a contributing factor to poor stroke outcomes, although these disparities are not well understood [24-26].

Our temporal trend analyses showed that the effect of AF on all of the unfavorable outcomes attenuated over time, particularly for in-hospital mortality and length of hospital stay. Interestingly, we did not find significant sex and race-ethnic differences in effect of AF on in-hospital mortality, suggesting an overall improvement in the management of AF and stroke in all hospitalized stroke patients. In our previous analyses, we observed temporal improvements in defect-free-care and in AHA acute ischemic stroke care performance metrics in women and across all racial-ethnic subgroups [13]. Therefore, it is evident that adherence to evidence-based guidelines and quality improvement hospital stroke care programs may effectively reduce stroke disparities in all stroke patients as well as in stroke patients with AF. Nevertheless, more research in needed to investigate whether sex and race-ethnic disparities exist in the effect of AF on immediate in-hospital care performance indicators and how this translates into long-term outcomes after stroke in patients with AF.

Our study has several limitations. First, AF was defined by its detection during stroke admission, discharge, or based on the patient's medical history. No data was available on prolonged cardiac monitoring to ensure that paroxysmal AF was not under diagnosed. Second, our registry does not contain follow up data after discharge, therefore the outcomes are limited to those obtained during the hospital stay or at discharge. In the temporal analyses, in-hospital mortality could have been confounded by the competing risk of LOS i.e. the shorter LOS the lower the risk of dying during hospitalization. Lower in-hospital mortality over time may be in part due to reduced LOS and changes in healthcare delivery such as earlier transition to in-patient rehabilitation or community based models of palliative care. Assessing in-hospital mortality using survival analysis may help reduce some of these biases, but no time-to-event data is available in the registry. And finally, our statistical power was very high due to a large sample size with the small differences between point estimates and therefore clinical relevance of these significant but small differences need further investigations.

Conclusion

AF is associated with poor stroke disability with evident sex and race-ethnic disparities in the effect of AF on prolonged length of hospital stay and less discharge disposition to home. With overall temporal improvements in hospital stroke care, the effect of AF on in-hospital mortality was considerably reduced since 2010 with no evidence of sex and race-ethnic disparities in hospital mortality. However, disability after stroke in patients with AF continues to be greater than in patients without AF. This observation clearly indicates a need for more advances in acute stroke care and management of stroke patients with AF for improved short and long-term stroke outcomes and reduced disparities.

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