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Use of Oral Anticoagulation in Eligible Patients Discharged with Heart Failure and Atrial Fibrillation: Insights from the AHA Get With The Guidelines- Atrial Fibrillation Program

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Abstract

BACKGROUND.—Stroke prophylaxis in patients with atrial fibrillation (AF) and heart failure (HF) in the era of direct anticoagulants (DOAC) is not well characterized. Using data from AHA Get With The Guidelines-Atrial Fibrillation (GWTG-AFIB), we sought to evaluate oral anticoagulation (OAC) use at discharge among AF patients with concomitant HF.

METHODS AND RESULTS.—AF patients with a diagnosis of HF hospitalized from 01/2013 to 03/2017 were included. We compared patient characteristics and use of OAC at discharge among patients with reduced (HFrEF, EF≤40%), borderline (HFbEF, 40%<EF<50%), and preserved (HFpEF, EF≥50%) EF using multivariable mixed logistic regression models. Among 10,883 patients with AF and HF, 1,790 (16.4%) had a reported contraindication to anticoagulation and were excluded from further analysis. Among 9,093 patients eligible for OAC, 3,499 (38.5%) had HFrEF, 1,062 (11.7%) had HFbEF, and 4,532 (49.8%) had HFpEF. The median CHA_2DS_2-VASc score was 5 (Q1, Q3; 3, 6) among all patients and higher among those with HFpEF than HFrEF (5

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[4, 6] vs 4 [3, 5], p<.0001). The proportion of eligible patients discharged on OAC was 94.9%, with 43.6% discharged on warfarin and 50.7% discharged on DOAC. A higher proportion of patients with HFrEF and HFbEF were discharged on DOAC than with HFpEF, but the difference was small (52.8%, 53.1% vs 48.5%, respectively; p=.0002). EF group was not significantly associated with a patient's OAC use at discharge.

CONCLUSIONS.—In the context of AHA GWTG-AFIB, a quality improvement program, the rate of use of OAC at discharge in eligible AF patients with HF was almost 95%. To our knowledge, these rates represent some of the highest use of appropriate anticoagulation for patients in a national registry to date.

As growing and converging epidemics, atrial fibrillation (HF) and heart failure (HF) together portend a worse prognosis than either condition alone.[1-4] In addition, the high risk of ischemic stroke has the potential to further accelerate morbidity for these patients.[5] Though oral anticoagulation (OAC) with warfarin has the ability to reduce stroke risk significantly and has long been recommended in the American College of Cardiology/American Heart Association (ACC/AHA) HF management guidelines,[6, 7] use of OAC among patients with AF and HF has historically remained insufficient (65%) in potentially eligible patients despite attempts to promote guideline adherence.[8] Recent clinical trials have shown direct oral anticoagulants (DOACs) to be equivalent or more efficacious than warfarin for AF stroke prevention, with improved safety profiles and greater ease of use.[9] Additionally, AF coexists across the HF left ventricular ejection fraction (LVEF) spectrum, with prior evidence suggesting that cardiovascular outcomes after AF may differ by HF subtype.[10, 11]

In this study, using data from the Get With The Guidelines (GWTG)-AFIB registry, we examined the clinical characteristics and rate of OAC in patients hospitalized with AF across the HF LVEF spectrum and in a setting of wider availability of DOACs. In addition, we assessed factors associated with appropriate OAC in this population.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Data source

This study utilized data collected through the Get With The Guidelines Atrial Fibrillation (GWTG-AFIB) registry, an ongoing observational, national, inpatient, prospective quality improvement initiative started in 2013 by the American Heart Association (AHA). The program objectives, design, and data elements have been previously described.[12] One primary goal of the registry is to provide active interventions on an institution or health system level to promote rapid-cycle quality improvement. GWTG-AFIB promoted a multifaceted approach including education and outreach, integrated decision support, and ongoing data assessment and feedback geared towards specific institutional change.

Systematic data acquisition was key. Briefly, the registry included consecutive patients aged ≥ 18 years who were hospitalized with a principal or secondary diagnosis of AF or atrial flutter (henceforth included together as AF). Trained personnel at participating hospitals

used an online, interactive Patient Management Tool (QuintilesIMS, Cambridge, Massachusetts) for concurrent as well as retrospective data collection. Collected data included demographics, medical history, medications (including specific antiarrhythmic, anticoagulant, and antiplatelet agents), laboratory data, in-hospital care and procedures specifically related to AF, rate or rhythm strategy, in-hospital outcomes, discharge medications (including contraindications for evidence-based therapies), discharge status, and risk reduction interventions supported by current specialty society guidelines. Contraindications were chosen from a prepopulated list and more than 1 contraindication could be selected. Included in the data collected was assessment of the CHA_2DS_2-VASc and HAS-BLED scores in the evaluation of thromboembolic and bleeding risk, respectively.[13, 14] The CHA_2DS_2-VASc score assesses a point score based on the presence of congestive heart failure, hypertension, age ≧65 years, diabetes mellitus, female sex, and vascular disease (prior myocardial infarction, peripheral vascular disease, or aortic plaque) with additional points given for prior stroke or transient ischemic attack and age >75 years. In current American College of Cardiology (ACC)/AHA guidelines, anticoagulation is recommended for patients with AF and a CHA_2DS_2-VASc score ≥2.[5] Prior HF guidelines have recommended OAC in all HF patients with AF regardless of overall CHA_2DS_2-VASc score.[15] The HAS-BLED score incorporates the risk of bleeding from several risk factors (hypertension, renal disease, liver disease, prior stroke, prior major bleeding or risk of bleeding, labile international normalized ratio, age >65 years, medication usage predisposing to bleeding, and heavy alcohol use), but guidelines do not recommend withholding anticoagulation based on any risk score.[5] Select hospital variables are also available, including total number of beds, US census region, rural/urban status, self-reported teaching versus nonteaching status, and presence or absence of board-certified electrophysiologists on staff.

All participating hospitals were required to comply with local regulatory and privacy guidelines and, if required, to secure institutional review board approval. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the Common Rule. IQVIA is the data collection coordination center for the American Heart Association/American Stroke Association Get With The Guidelines programs. The Duke Clinical Research Institute (Durham, North Carolina) serves as the data analysis center, and institutional review board approval was granted to analyze aggregate de-identified data for research purposes.

Study design and outcomes

For this analysis, we considered and included GWTG-AFIB participants hospitalized between January 2013 and March 2017 with documentation on concurrent diagnosis or history of HF and discharge disposition (Figure 1). HF was determined based on past medical history, primary diagnosis for hospitalization, or first detection during the concurrent hospital admission. Quantitative or qualitative ejection fraction (EF), when available, was submitted by sites based on chart review. From an initial 11,536 patients from 90 hospitals, we further excluded 653 patients without documentation of EF. There were 1,790 patients who had a listed contraindication to anticoagulation; these patients were described but not included in the primary analysis. The final overall study population

included 9,093 admissions from 89 sites, subdivided into 3 groups by EF: HF with preserved EF (HFpEF, EF ≥50% or qualitative description of normal or mild ventricular dysfunction), HF with borderline EF (HFbEF, 40%<EF<50%), and HF with reduced EF (HFrEF, EF ≤40% or qualitative description of moderate/severe ventricular dysfunction).[7]

The primary outcome of interest was use of an oral anticoagulant at discharge among eligible patients with a history of HF without documented contraindications. Other secondary analyses were planned to determine whether OAC varied according to EF groups, direct OAC versus warfarin therapy, risk stratification by CHA_2DS_2-VASc and HAS-BLED scores, and other factors associated with OAC at discharge.

Statistical analysis

We reported descriptive statistics for baseline patient and hospital characteristics for HF patients by EF group using Pearson's chi-squared tests for binary or nominal categorical variables and the Kruskal-Wallis test for continuous or ordinal categorical variables. Proportions and medians with interquartile ranges (IQRs) were reported for categorical and continuous variables, respectively. Percent standardized differences (calculated as the difference in means or proportions divided by a pooled estimate of the standard deviation*100) were also calculated; a standardized difference greater than 10 is typically considered meaningful and may be useful in the interpretation of statistically significant differences that are of small clinical significance. Patient characteristics with <25% missing were imputed before entering into models. Patient medical history or medication prior to admission were imputed to "No" as we assume it was not checked when none applied. Other patient variables were imputed using multiple imputations with 25 datasets. Patient's rate/rhythm strategy was not imputed. Hospital variables were not imputed. Variable missing rates and more imputation details can be found in Table S1 in the Online Supplement. We used adjusted logistic regression models to evaluate covariates associated with anticoagulation at discharge among patients who were anticoagulation naïve on admission. Generalized estimating equations were used to adjust for the clustering of patients within hospitals. Candidate variable selection was based on patients' key baseline demographics and clinical experience. The covariates included were age, sex, race, insurance status, geographic region, hospital type, hospital size, rural status, adult cardiac electrophysiology site, AF type, anemia, coronary artery disease, prior stroke or transient ischemic attack, diabetes, chronic dialysis, HF, hypertension, liver disease, obstructive sleep apnea, peripheral vascular disease, chronic obstructive pulmonary disease, prior hemorrhage or bleeding, prior myocardial infarction, prior history of percutaneous intervention, smoking status, thyroid disease, heart failure medications prior to admission, aspirin and antiplatelet prior to admission, estimated glomerular filtration rate, BMI, and rate versus rhythm control strategy. Adult cardiac electrophysiology site was defined as presence of board certified adult electrophysiologist or availability of AF ablation on site. OAC use was also presented across hospital sites, and by CHA_2DS_2-VASc and HAS-BLED scores in figures. Because some contraindications may be viewed as more relative than absolute, we also conducted a sensitivity analysis that examined the variables associated with OAC excluding "physician preference" and "frequent falls/frailty" as contraindications. All statistical tests were 2-

tailed, with p ≤0.05 considered statistically significant. All analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Baseline characteristics

Among 10,883 patient hospitalizations with AF and HF with documented EF, 1,790 (16.4%) had a reported contraindication to anticoagulation. “High bleeding risk” and “frequent falls/frailty” were the two most prevalent reasons, reported in 51% of those with listed contraindications (Table 1). Patients with HFpEF were slightly more likely to have a contraindication reported (17.8% vs. 15.2 vs.15.0%, p=0.0004) and to have that reason listed as “frequent falls/frailty.” Patients with contraindications were henceforth excluded from further analysis.

Among 9,093 patient hospitalizations eligible for anticoagulation, 3,499 (38.5%) had HFrEF, 1,062 (11.7%) had HFbEF, and 4,532 (49.8%) had HFpEF. As shown in Table 2, for 19.9% of patients, admission was for the first detected episode of AF. Compared with the other EF groups, patients with HFrEF were younger, more likely to be men, a smoker, and had a lower prevalence of hypertension, chronic obstructive pulmonary disease, or thyroid disease. Compared with patients with HFrEF, patients with HFpEF were more likely to have paroxysmal AF (45.0% vs 37.8%, p <.001) and a higher prevalence of prior stroke or TIA (17.0% vs 12.6%, p <.001). Use of beta-blocker therapy ranged from 65-68% on admission in all EF groups. Among eligible patients, 62% were treated with OAC (warfarin, DOAC, or other) before admission. Patients with HFpEF were more likely to be treated with warfarin than HFrEF patients (36.1% vs 30.9%, p <.001), but 27.3% of all HF patients were treated with a DOAC without significant variation among EF groups. Patients with HFrEF were more likely to be treated with a rhythm versus rate control strategy compared with other EF groups (58.1% vs. 52.6% vs. 52.7%, p <.001). Approximately 50% of all patients underwent an AF procedure during the hospitalization.

Oral Anticoagulation at Discharge

Among eligible patients with AF and HF, 94.9% of patients were prescribed OAC at discharge, with 43.6% discharged on warfarin and 50.7% discharged on a DOAC (Table 3). Patients with HFpEF were slightly more likely to not receive oral anticoagulation at discharge (5.7% vs. 4.4% vs. 4.6%, p=0.003). A higher proportion of patients with HFrEF and HFbEF were discharged on DOAC than HFpEF, but the difference was small (52.8%, 53.1% vs 48.5%, respectively; p = .0002). The most commonly prescribed DOAC in our population was apixaban (28% of patients prescribed OAC on discharge).

Patients who were on OAC prior to admission were very likely to have their anticoagulation prescribed at discharge (>94%). In patients who were naïve to OAC (Table 4 and S2, Online Supplement) multivariable logistic regression identified female sex, use of ACEI/ARB prior to admission, a higher eGFR, a higher BMI, and a rhythm control strategy as factors independently associated with higher odds of increased OAC prescription at discharge (all

p<0.05). In the adjusted analysis, the EF group was not significantly associated with a patient's OAC use at discharge.

Consistent with the high overall rate of OAC prescription among eligible patients, hospital level prescription of anticoagulation was high (Figure 2). The median rate of anticoagulation prescription among hospitals was 93.8% (interquartile range: 88.1% - 97.6%), and 10 of 89 hospitals prescribed anticoagulation in all eligible patients. There was no significant association between hospital characteristics and anticoagulation prescription in eligible patients with HF and AF.

Risk stratification and anticoagulation use

The median CHA_2DS_2-VASc score was 5 (Q1, Q3; 3, 6) among all patients and higher among those with HFpEF than HFrEF (5 [Q1, Q3; 4, 6] vs 4 [Q1, Q3; 3, 5], p <.001). The median HAS-BLED score was 2 (Q1, Q3; 2, 3) among all patients. As shown in Figure 3, the highest proportion of OAC use was among patients with CHA_2DS_2-VASc = 4. Lack of anticoagulation remained below 10% among all CHA_2DS_2-VASc scores. Additionally, the odds of being discharged on warfarin was 14% higher than being discharged on DOAC, for every unit increase of CHA_2DS_2-VASc score (OR = 1.14; 95% CI = 1.11, 1.17; p <.0001). Figure 4 shows that rates of non-anticoagulation increased with increasing bleeding risk according to the HAS-BLED risk score. Warfarin prescription also increased relative to DOAC use with increasing HAS-BLED scores (OR = 1.28 for every unit increase HAS-BLED; 95% CI = 1.23, 1.33; p <.0001) Very few patients in this population had a HAS-BLED score above 5.

Combination antithrombotic therapy

In the analysis population of 9,093 patients, 43.2% were prescribed aspirin, with 40.0% of patients taking both aspirin and OAC (Table 3). Use of aspirin was higher in patients with HFrEF than HFbEF and HFpEF (47.4% vs. 43.4% and 39.8%, p<.001). The use of so-called triple therapy—a combination of aspirin, other non-aspirin antiplatelet, and OAC—was documented in 3.1% of patients, with higher use among patients with HFrEF than other EF groups (4.1% vs. 2.4% and 2.6%, p<.001). While aspirin use prior to admission was not significantly associated with OAC at discharge in adjusted models (OR 1.03; 95% CI 0.74-1.43; p=0.86), a higher proportion of patients discharged with aspirin did not receive appropriate anticoagulation (7.3% vs. 3.1%, p<.0001).

Sensitivity Analyses

We excluded two stated contraindications to anticoagulation in a sensitivity analysis, "physician preference" and "frequent falls/frailty." As expected, in this increased eligible population of patients with AF and HF, stroke prophylaxis was slightly lower, prescribed in 89.6% of patients. Congruent with the main analysis, EF group was not significantly associated with OAC at discharge in adjusted models. However, increased patient age and permanent/long standing persistent AF was now associated with significantly lower odds of OAC (Table S3 in Supplement). Use of ACEI/ARB prior to admission and eGFR were no longer independently associated with OAC use, but other results were consistent with the

primary analysis. Additionally, Table S4 in the Online Supplement presents a comparison of how imputations for missing variables affected the multivariable modeling.

DISCUSSION

In the context of a national quality improvement initiative, we examined the characteristics and management of over 9000 admissions for patients with AF and HF. In the modern era of widely available DOAC therapy, stroke prophylaxis among eligible patients with AF and HF was almost 95%, regardless of EF. To our knowledge, these rates represent some of the highest rates of appropriate anticoagulation use for patients in a national registry to date. These results strongly support the efforts of large-scale quality improvement initiatives and creation of learning health systems to promote successful implementation of evidenced-based care. There was no significant association between hospital characteristics and anticoagulation prescription in eligible patients with HF and AF.

Published evidence of patients in observational registries—particularly in those with HF—generally suggest that the use of stroke prophylaxis has been low. Registries in the late 1990s-2000s suggested only around 60% of eligible patients with AF received anticoagulation.[16] An earlier analysis from the GWTG-Heart Failure program data on anticoagulation between 2005-2008 also suggested rates of appropriate stroke prophylaxis around 65%, and no improvement over time despite participation in a GWTG quality improvement program.[8] The rate of use of appropriate anticoagulation in outpatients treated by cardiovascular specialists in the ACC National Cardiovascular Data Registry's PINNACLE (Practice Innovation and Clinical Excellence) Registry—a quality improvement program—between 2008 and 2012 also did not exceed 50%.[17] In contrast, in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)—a voluntary registry of US outpatients with AF, rates of OAC were generally higher at around 77%, and even higher among HF patients at 81% (irrespective of contraindications).[18, 19] In these registries the predominant drug prescription for anticoagulation was warfarin. In the era of increasing DOAC availability and prescription, an updated analysis of the PINNACLE registry with data up to 2014 showed an increasing anticoagulation rate of 61%, though warfarin remained the predominant drug used.[20] Updated data from GWTG-HF to include 2014 also showed higher anticoagulation rates of ~73% in patients with AF and HF.[21]

Anticoagulation to prevent stroke and systemic embolism in patients with AF has been a principal target of quality improvement in AF. Compared to prior registries, use of anticoagulation in our analysis is very high. Given the voluntary nature and design of GWTG-AFIB to target quality improvement in AF care and specifically anticoagulation, some degree of bias will be inherent. Additionally, over 50% of patients in the current analysis underwent AF procedures such as cardioversion or ablation during the hospitalization, potentially heightening attention to the risk of stroke and its prevention. Nevertheless, prior work within HF has shown that focused patient data collection, targeted decision support tools, and performance feedback in a large-scale care improvement intervention can improve the use of guideline-recommended HF therapies.[22] Within GWTG-AFIB, analysis of temporal trends show sustained improvement in OAC rates over time and is also >95% in the last quarter of enrollment.[23] Prior analyses in HF and stroke have

suggested variations in care and outcomes based on hospital characteristics like bed size and academic status, but we saw no significant associations between different hospital characteristics and anticoagulation prescription in eligible patients with HF and AF.[24, 25] This finding may suggest iterative improvement in the successful implementation of quality improvement methods across different hospital settings within GWTG-AFIB. Combined with increasing availability of DOACs, these data suggest concrete performance improvement techniques can have a lasting impact on promoting sustainable evidence-based treatment.

In the primary analysis, about 16% of patients were deemed ineligible for anticoagulation due to a selected contraindication, with the most common causes being “frequent falls/ frailty” and “high bleeding risk.” An additional 257/1,790 (14.9%) of patient were deemed ineligible due to “patient refusal.” In contrast, in the recent PINNACLE analysis, only 0.09% of patients had a documented contraindication to anticoagulation.[20] Our high rate of selected contraindications may be attributed to a sicker, hospitalized patient population. However, the increased accountability associated with a reportable quality metric of a quality improvement program could have contributed a significant role. Nevertheless, these contraindications reflect the challenging balance between the risk of stroke against risk of bleeding complications, especially among older patients. Prior research of elderly patients, however, suggests that their risk of ischemic stroke is greater than the risk for hemorrhagic stroke, and they may indeed derive the greatest net benefit from anticoagulation.[26, 27] Additionally, most older patients with a personal history or a perceived high risk for falls still derive net benefit from anticoagulation when balanced against the absolute risk of fall-related major bleeding.[28, 29] Thus, under a more rigorous analysis of risk versus benefit, it is likely that more of the patients excluded in the current analysis could be considered good candidates for OAC. Identifying and properly communicating risk in a shared decision model will be an important next target for quality improvement in AF management.

Our results suggest a potential mismatch in the risk-benefit assessment between DOACs and warfarin. In large clinical trials, 4 DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) consistently showed statistically lower rates of major bleeding (with the exception of rivaroxaban and dabigatran 150 mg) and intracranial bleeding when compared to warfarin.[30-33] However, in our cohort, for every unit increase of HAS-BLED bleeding risk, the odds of warfarin prescription increased 28% relative to DOAC use. Risk scores including HAS-BLED can help quantify hemorrhage risk for individual patients, with a score ≥3 indicating “high risk” for bleeding. However, given their uncertain clinical utility, current practice guidelines do not make absolute recommendations based on any one absolute score.[5] Renal dysfunction is a component of HAS-BLED and may have contributed to the increased warfarin use. Nevertheless, recent evidence supports the safety and effectiveness of standard-dose apixaban for stroke prevention in dialysis patients with AF.[34] In appropriate patients represented by clinical trials, evidence suggests that use of DOACs may be safer in patients with a higher risk of bleeding.

The continued high use of concomitant aspirin in our cohort of patients receiving OAC remains another area for further education and improvement. Multiple prior studies have demonstrated increased risk for hemorrhage associated with combined antiplatelet and

anticoagulant use in patients with appropriate indications.[35-39] Additionally, prior registries such as ORBIT have found that nearly 40% of patients receiving combined therapy had no clear indication for the addition of aspirin.[39] In the current analysis, about 40% of patients were on combined aspirin and anticoagulant therapy. This finding is comparable to those described in the ORBIT registry where 35% of the AF cohort received combined therapy and in the large apixaban and dabigatran clinical trials where roughly 30% and 40% of patients, respectively, received concomitant low dose aspirin and oral anticoagulants.[30, 32] Despite increasing concerns regarding the bleeding risk of aspirin and minimal evidence of benefit in stable atherosclerotic disease, concomitant use with oral anticoagulants persists in the modern era.[37] Clinicians should further consider whether the benefits of concomitant aspirin outweigh risks in AF patients on OAC.

Study Limitations

We note several limitations of this study. First, GWTG-AFIB is a voluntary program with the explicit objective to improve adherence to guidelines for AF management and treatment in hospitalized patients. Participating hospitals may have a stronger interest in following guideline recommendations. Findings may not generalize to patients with AF and HF who are not hospitalized. However, prior analyses of other GWTG registries suggest that the patient populations are nationally representative. [40, 41] Second, patient data are collected by chart review and thus dependent on the accuracy and completeness of documentation. Additionally, patients deemed eligible for anticoagulation treatment in our analysis may have had other reasons that prevented treatment not well captured by the medical record or case report form. Lastly, post-discharge initiation or adherence and persistence to therapy is not currently available.

Conclusions

In the context of a national quality improvement initiative and of increasing DOAC availability, we found almost 95% OAC among eligible hospitalized patients with HF across the LVEF spectrum and AF. Quality improvement initiatives including clinical decision support, education outreach, performance profiling, and real-time feedback can be implemented successfully with sustainable impact on patient outcomes on a national scale. In other areas of chronic AF care—such as prevention of HF, appropriate antiarrhythmic selection, and careful review of concomitant antiplatelet use—these efforts should serve as a framework for future performance improvement programs that support implementation of evidence-based care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is new?

- Guidelines strongly recommend use of oral anticoagulation for stroke prophylaxis in patients with atrial fibrillation and heart but prior studies have showed significant gaps in medication use
- In the setting of a quality improvement initiative and availability of contemporary direct oral anticoagulants, we show that there was nearly universal prescription of stroke prophylaxis among patients with atrial fibrillation and heart failure

What are the clinical implications?

- These results support the use of systematic, scalable quality improvement initiatives to help implement evidence-based therapies into clinical care

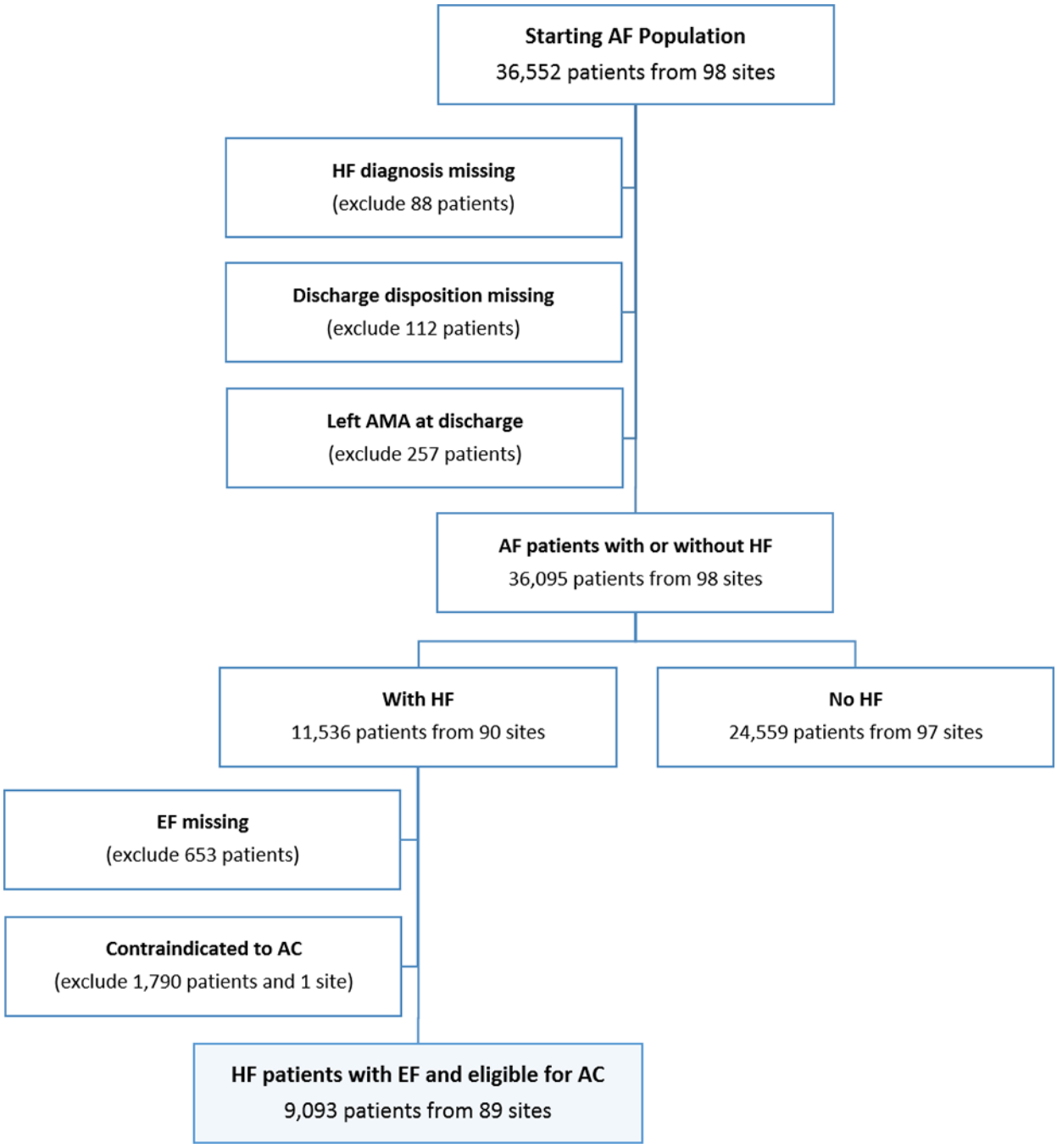

Figure 1.
Flow diagram of the study design. This figure displays the initial study population, through exclusions, to the final study population.

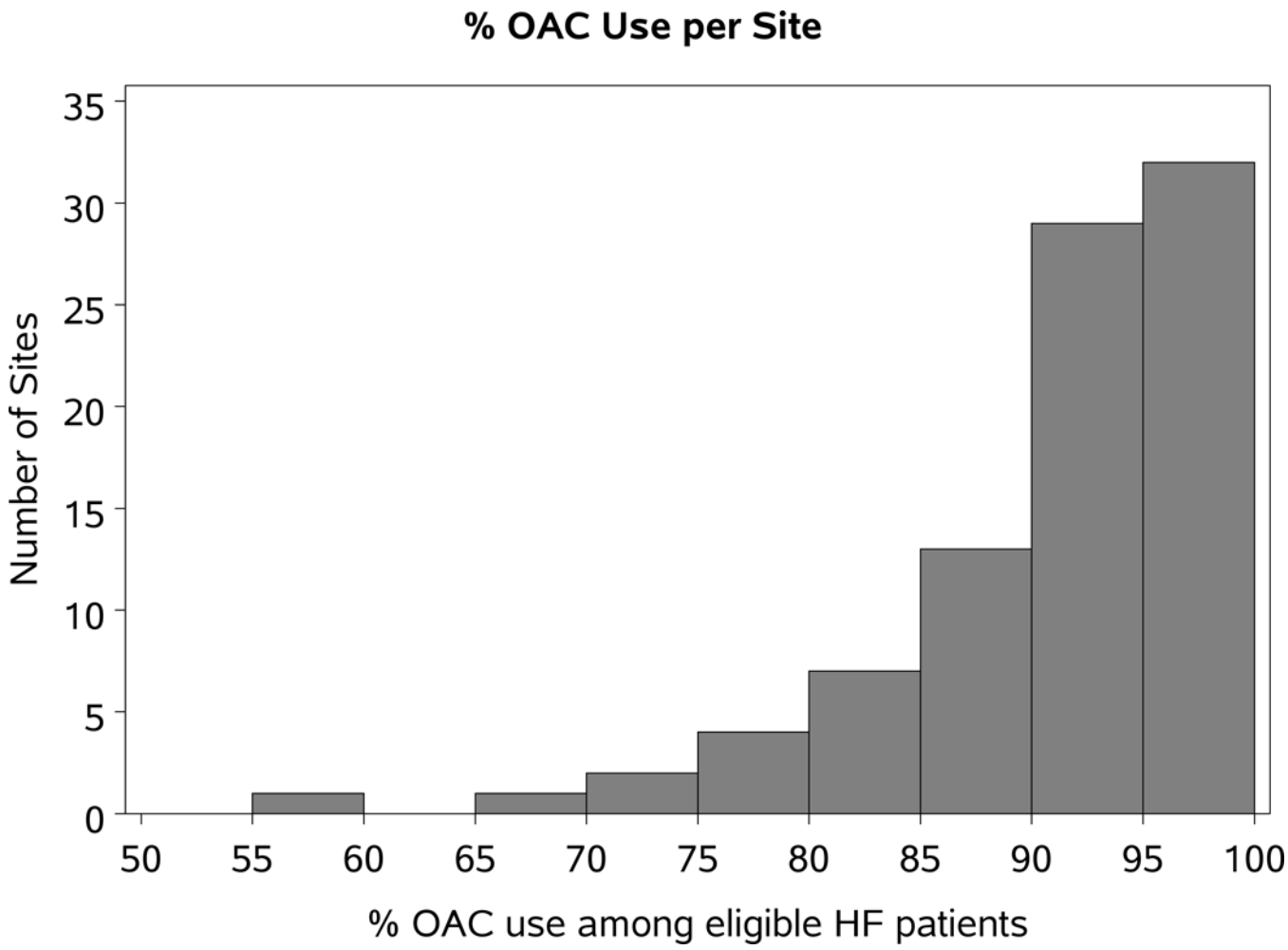

Figure 2.
Oral anticoagulation at discharge per site among eligible heart failure patients.

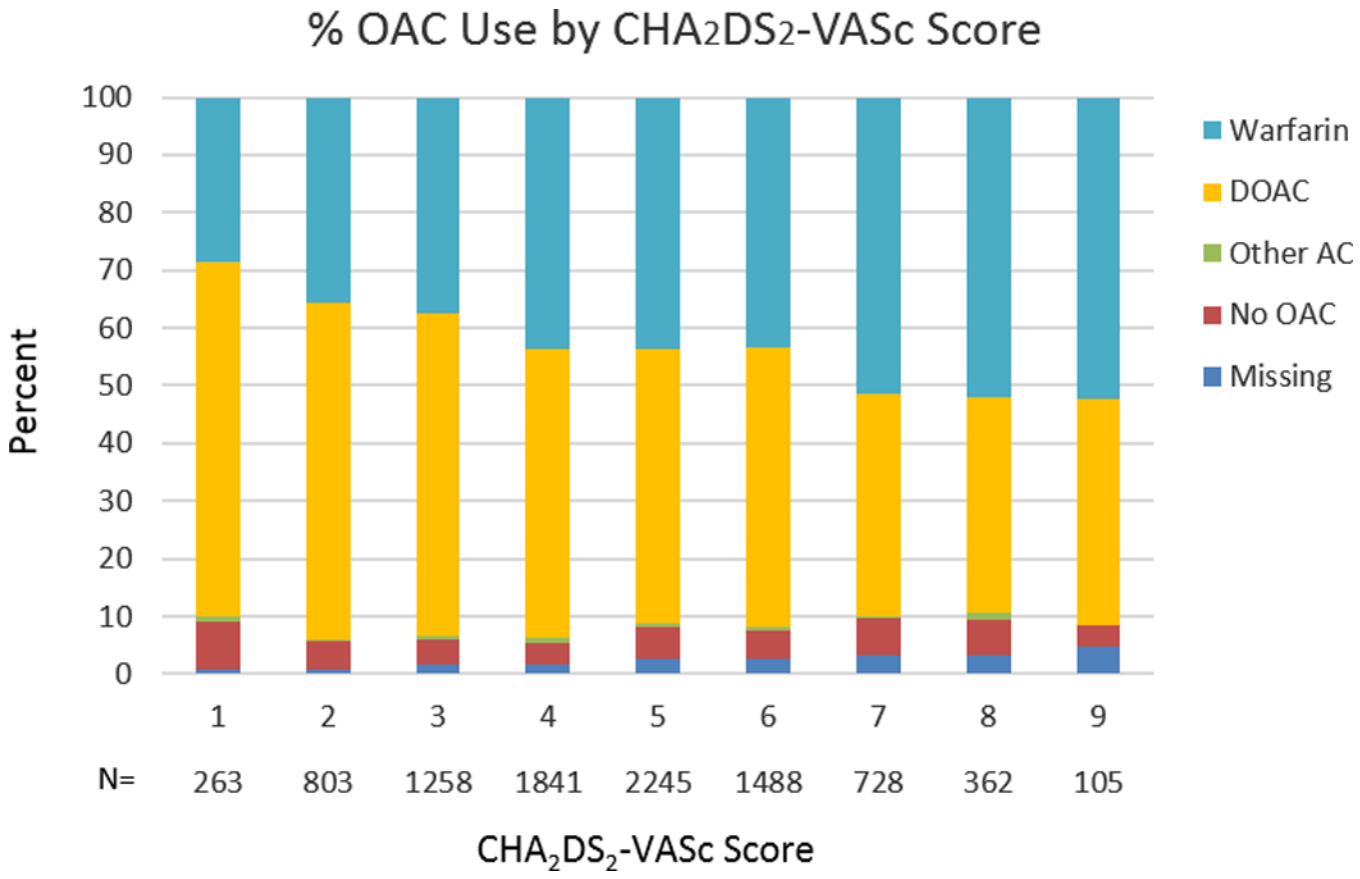

Figure 3.

Oral anticoagulation at discharge among eligible AF patients with HF according to CHA_2DS_2-VASc score.

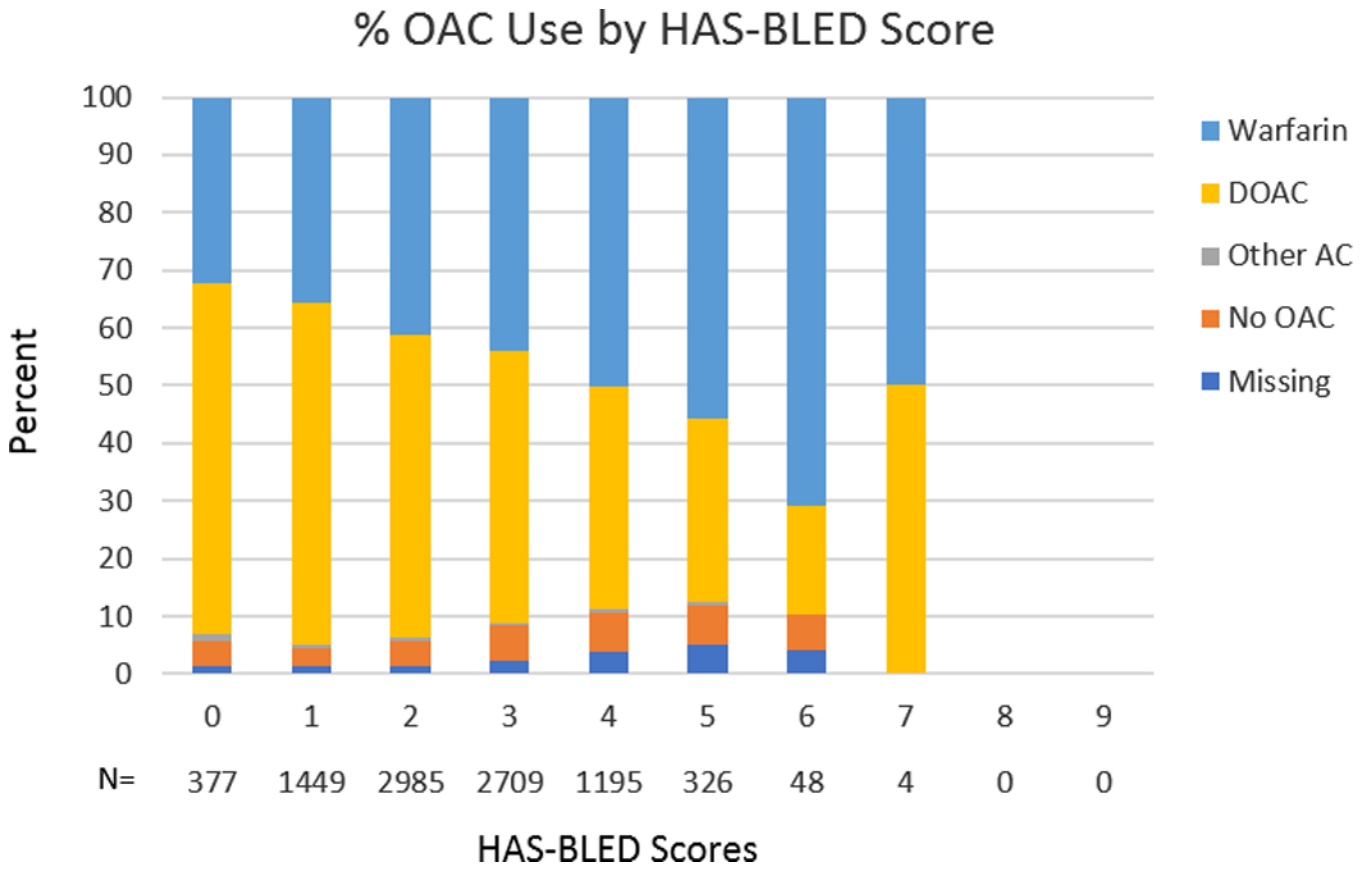

Figure 4.
Oral anticoagulation at discharge among eligible AF patients with HF according to HAS-BLED score.

Table 1

. **Oral Anticoagulation (OAC) Contraindication in AF patients with HF by EF groups.**

Variable	Overall N=10,883	HF*r*EF (EF ≤40%) N=4,115	HF*b*EF (EF 41–49%) N=1,252	HF*p*EF (EF ≥50%) N=5,516	P Value
OAC Contraindications					
Anticoagulation Contraindicated	1,790 (16.4)	616 (15.0)	190 (15.2)	984 (17.8)	0.0004
Reasons					
Allergy	11 (0.6)	5 (0.8)	1 (0.5)	5 (0.5)	0.74
Unable to adhere/monitor	126 (7.0)	79 (12.8)	10 (5.3)	37 (3.8)	<.0001
Occupational risk	5 (0.3)	2 (0.3)	0 (0.0)	3 (0.3)	0.74
High Bleeding risk	495 (27.7)	132 (21.4)	62 (32.6)	301 (30.6)	<.0001
Prior intracranial hemorrhage	48 (2.7)	13 (2.1)	5 (2.6)	30 (3.0)	0.53
Bleeding event	335 (18.7)	104 (16.9)	42 (22.1)	189 (19.2)	0.23
Frequent falls/frailty	503 (28.1)	147 (23.9)	53 (27.9)	303 (30.8)	0.01
Patient refusal/preference	267 (14.9)	98 (15.9)	30 (15.8)	139 (14.1)	0.58
Physician preference	332 (18.5)	112 (18.2)	35 (18.4)	185 (18.8)	0.95
Recent operation	41 (2.3)	17 (2.8)	5 (2.6)	19 (1.9)	0.53
Comorbid illness (e.g. renal/liver)	134 (7.5)	53 (8.6)	17 (8.9)	64 (6.5)	0.22
Need for dual antiplatelet therapy	25 (1.4)	13 (2.1)	2 (1.1)	10 (1.0)	0.18

Data shown number (percent).

Table 2

. **Baseline characteristics in atrial fibrillation (AF) patients with heart failure (HF) by ejection fraction (EF) groups.**

Variable	Overall N=9,093	HF*r*EF (EF ≤40%) N=3,499	HF*b*EF (EF 41-49%) N=1,062	HF*p*EF (EF ≥50%) N=4,532	P Value	% Std. Diff. HF*b*EF vs HF*r*EF	% Std. Diff. HF*p*EF vs HF*r*EF
Demographics							
Age, years	72 (63 - 81)	68 (59 - 78)	73 (64 - 81)	75 (66 - 83)	<.001	31.4	48.9
Female	47.60	31.15	44.82	60.94	<.001	28.4	62.6
Race/Ethnicity					<.001		
White/Caucasian	81.32	78.24	79.22	84.20		2.4	15.3
Black/African American	9.83	12.03	9.82	8.14		7.1	13.0
Hispanic (any race)	5.73	6.65	6.96	4.73		1.2	8.3
Insurance status					0.004		
No Insurance	8.70	9.32	7.44	8.52		6.8	2.8
Medicare - Private/HMO/Other	19.74	17.89	20.06	21.09		5.5	8.1
Medicare (Title 18)	20.21	19.41	20.43	20.79		2.6	3.4
Medicaid (Title 19)	13.12	14.03	12.71	12.51		3.9	4.5
Private/HMO/Other	38.23	39.35	39.36	37.09		<0.1	4.7
LVEF, %	48 (33 - 58)	30 (23 - 35)	45 (43 - 47)	58 (55 - 63)			
Systolic blood pressure, mm Hg	131 (115 - 147)	127 (111 - 143)	133 (117 - 149)	133 (118 - 150)	<.001	23.6	26.8
Heart Rate, bpm	104 (79 - 130)	107.5 (81 - 132)	106 (81 - 132)	100 (77 - 129)	<.001	3.4	15.5
Body mass index, kg/m^2	30.1 (25.6 - 35.9)	29.9 (25.4 - 35.6)	30.1 (25.8 - 35.1)	30.2 (25.7 - 36.1)	0.30	1.2	5.8
Atrial Arrhythmia Type					0.003		
Atrial Flutter	11.42	12.86	10.64	10.48		6.9	7.4
Atrial Fibrillation	88.58	87.14	89.36	89.52		-	-
Type of AF					<.001		
Permanent/long standing Persistent AF	14.43	13.65	13.75	15.18		0.3	4.4
Persistent AF	23.85	25.28	26.76	22.10		3.4	7.5
Paroxysmal AF							
Paroxysmal AF	41.77	37.79	40.88	44.96		6.3	14.6
First Detected AF	19.94	23.28	18.61	17.76		11.5	13.7
Medical History							
Anemia	12.98	10.12	14.41	14.85	<.001	13.1	14.4
Coronary Artery Disease	37.40	38.35	42.00	35.58	<.001	7.4	5.8
Prior Stroke or TIA	15.00	12.58	14.60	16.97	<.001	5.9	12.4
Diabetes	34.98	33.92	36.53	35.42	0.20	5.5	3.1
Dialysis	1.87	1.71	1.69	2.03	0.53	0.2	2.3
Heart Failure	80.85	78.85	82.30	82.06	0.001	8.7	8.1

Variable	Overall N=9,093	HF*r*EF (EF ≤40%) N=3,499	HF*b*EF (EF 41-49%) N=1,062	HF*p*EF (EF ≥50%) N=4,532	P Value	% Std. Diff. HF*b*EF vs HF*r*EF	% Std. Diff. HF*p*EF vs HF*r*EF
Hypertension	79.12	74.51	79.10	82.70	<.001	10.9	20.1
Obstructive Sleep Apnea	19.41	18.29	20.24	20.08	0.10	5.0	4.6
Peripheral Vascular Disease	8.46	7.60	9.51	8.87	0.05	6.8	4.6
COPD	24.69	20.61	23.73	28.07	<.001	7.5	17.5
Prior Hemorrhage	2.56	1.83	2.73	3.09	0.002	6.0	8.1
Prior MI	14.27	17.06	15.25	11.87	<.001	4.9	14.8
Prior PCI	15.05	16.46	17.89	13.29	<.001	3.8	8.9
Smoker	11.81	15.52	9.60	9.47	<.001	17.9	18.4
Thyroid Disease	18.82	14.03	19.30	22.40	<.001	14.2	21.8
Prior AF Procedure							
Cardioversion	24.04	24.42	26.10	23.25	0.13	3.9	2.8
Ablation	11.37	10.43	11.24	12.13	0.07	2.6	5.4
AF Surgery (Surgical MAZE)	1.40	1.62	1.61	1.18	0.23	0.1	3.8
None	69.11	68.82	67.37	69.76	0.30	3.1	2.1
Medications at Admission							
ACEi/ARB	49.40	54.18	47.98	46.02	<.001	12.4	16.4
Aldosterone Antagonist	10.18	14.97	7.71	7.04	<.001	23.1	25.5
Beta-Blocker	67.02	68.60	68.21	65.53	0.01	0.8	6.5
Anticoagulation Therapy					<.001		
Warfarin	33.60	30.94	31.70	36.10		1.6	11.0
DOAC	27.26	27.34	30.06	26.55		6.0	1.8
Other AC/not specified	1.19	0.70	1.93	1.40		10.8	6.9
No OAC	37.95	41.02	36.32	35.95		9.7	10.5
Aspirin	41.44	43.45	41.33	39.91	0.007	4.3	7.2
Antiplatelet agent (not aspirin)	8.62	8.19	10.60	8.49	0.05	8.3	1.1
Triple Therapy (aspirin + non-aspirin antiplatelet + OAC)	2.02	2.37	1.83	1.79	0.18	3.8	4.1
Laboratory Data at Admission							
Serum Creatinine	1.1 (0.9 - 1.4)	1.1 (0.9 - 1.5)	1.1 (0.9 - 1.4)	1.1 (0.8 - 1.4)	<.001	3.2	1.3
Blood urea nitrogen, mg/dL	21 (16 - 29)	21 (16 - 31)	20 (15 - 29)	21 (15 - 29)	0.001	8.3	6.4
NT-pro BNP, pg/mL	3183 (1469 - 6290)	4180 (1731 - 7989)	3284 (1435 - 7008)	2640 (1305 - 5025)	<.001	22.2	35.1
BNP, pg/mL	522 (264.5 - 1048.5)	649.1 (334 - 1289)	539.4 (222 - 985)	423 (237 - 853)	<.001	23.5	18.7
eGFR, mL/min per 1.73 m^2	60 (43 - 77)	61 (44 - 77)	61 (45 - 78)	59 (42 - 76)	0.003	1.8	6.4
Rate/Rhythm Control Strategy					<.001		
Rate Control Strategy	45.22	41.89	47.41	47.35		11.1	11.0
Rhythm Control Strategy	54.78	58.11	52.59	52.65		-	-
Procedures During This Hospitalization							

Variable	Overall N=9,093	HF*r*EF (EF ≤40%) N=3,499	HF*b*EF (EF 41-49%) N=1,062	HF*p*EF (EF ≥50%) N=4,532	P Value	% Std. Diff.	
						HF*b*EF vs HF*r*EF	HF*p*EF vs HF*r*EF
No Procedures	49.73	43.58	49.14	54.64	<.0001	11.2	22.3
Cardioversion	35.14	39.37	36.12	31.64	<.0001	6.7	16.2
A-Fib Ablation	7.36	7.79	7.13	7.08	0.46	2.5	2.7
A-Flutter Ablation	5.47	6.49	4.66	4.86	0.003	8.0	7.1
PCI	4.15	6.96	4.28	1.95	<.0001	11.6	24.5
Pacemaker	2.91	1.62	2.38	4.03	<.0001	5.4	14.6
Hospital Characteristics							
Rural Location	7.22	6.33	6.86	7.98	0.02	2.2	6.4
Academic/Teaching Hospital	85.58	87.38	87.12	83.85	<.001	0.8	10.1
Hospital Size (Number of Beds)					0.002		
500+	44.78	47.30	46.99	42.34		0.6	10.0
400-499	14.40	14.38	14.47	14.40		0.2	<0.1
300-399	11.17	10.10	10.77	12.08		2.2	6.3
200-299	13.03	11.92	12.14	14.08		0.7	6.4
100-199	14.36	14.29	13.09	14.71		3.5	1.2
50-99	2.26	2.01	2.53	2.39		3.5	2.6
Region					0.006		
West	11.47	11.92	12.24	10.94		1.0	3.1
South	26.99	27.46	28.25	26.32		1.7	2.6
Midwest	24.73	25.81	25.14	23.81		1.5	4.6
Northeast	36.81	34.81	34.37	38.92		0.9	8.5
Adult Cardiac Electrophysiology Hospital	86.81	88.28	88.13	85.39	0.001	0.5	8.6

Data shown number (percent) or median (Q1-Q3). Percent standardized differences is calculated as the difference in means or proportions divided by a pooled estimate of the standard deviation*100; a standardized difference greater than 10 is typically considered meaningful. HFrEF = heart failure reduced ejection fraction; HFbEF = heart failure borderline ejection fraction; HFpE = heart failure preserved ejection fraction; HMO = health maintenance organization; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; DOAC = direct oral anticoagulant; OAC = oral anticoagulant; NT- BNP = N-Terminal pro brain natriuretic peptide; eGFR = estimated glomerular filtration rate.

Table 3

. Discharge medications and risk scores in atrial fibrillation (AF) patients with heart failure (HF) by ejection fraction (EF) groups.

Variable	Overall N=9,093	HF*r*EF (EF ≤40%) N=3,499	HF*b*EF (EF 41–49%) N=1,062	HF*p*EF (EF ≥50%) N=4,532	P Value	% Std. Diff	
						HF*b*EF vs HF*r*EF	HF*p*EF vs HF*r*EF
Medications at Discharge							
Overall Anticoagulation, %	94.9	95.4	95.6	94.4	0.003		
Warfarin	3,876 (43.6)	1,437 (42.0)	432 (41.7)	2,007 (45.2)		0.8	6.3
DOAC	4,510 (50.7)	1,805 (52.8)	551 (53.1)	2,154 (48.5)		0.7	8.6
Apixaban	2,397						
Rivaroxaban	1,724						
Dabigatran	373						
Edoxaban	15						
Other AC/not specified	57 (0.6)	19 (0.6)	8 (0.8)	30 (0.7)		2.7	1.5
No OAC	456 (5.1)	158 (4.6)	46 (4.4)	252 (5.7)		0.9	4.8
Missing	194 (2.1)	80 (2.3)	25 (2.4)	89 (2.0)			
Aspirin	3,579 (43.2)	1,520 (47.4)	423 (43.4)	1,636 (39.8)	<.001	7.9	15.2
Antiplatelet(s) (not aspirin)	598 (7.2)	244 (7.6)	75 (7.7)	279 (6.8)	0.35	0.1	3.1
Triple Therapy (aspirin + non-aspirin antiplatelet + OAC)	280 (3.1)	141 (4.1)	25 (2.4)	114 (2.6)	<.001	9.7	8.7
Risk Scores							
HAS-BLED Score	2 (2 - 3)	2 (1 - 3)	2 (2 - 3)	3 (2 - 3)	<.001	18.7	28.2
CHA2DS2-VASc Score	5 (3 - 6)	4 (3 - 5)	5 (4 - 6)	5 (4 - 6)	<.001	30.7	47.6

Data shown number (percent) or median (Q1-Q3). Percent standardized differences is calculated as the difference in means or proportions divided by a pooled estimate of the standard deviation*100; a standardized difference greater than 10 is typically considered meaningful. HFrEF = heart failure reduced ejection fraction; HFbEF = heart failure borderline ejection fraction; HFpE = heart failure preserved ejection fraction; DOAC = direct oral anticoagulant; OAC = oral anticoagulant. CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥75 years [doubled], Diabetes mellitus, Prior Stroke or TIA or thromboembolism [doubled], Vascular disease, Age 65 to 74 years, Sex category). HAS-BLED score (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly).

Table 4

. **Multivariable Factors Associated with Oral Anticoagulation (OAC) use in OAC Naïve Patients**

Variables	Unadjusted Model OR (95% CI)	*P Value*	Adjusted Model OR (95% CI)	*P Value*
EF group		0.07		0.08
HF*p*EF (EF ≥50%)	0.76 (0.60, 0.96)	0.02	0.77 (0.52, 1.16)	0.21
HF*b*EF (EF 41-49%)	1.00 (0.74, 1.33)	0.97	1.16 (0.75, 1.79)	0.50
HF*r*EF (EF ≤40%)	Reference		Reference	
Female vs. male			1.42 (1.09, 1.85)	0.009
AF Type: AFib	-	-		
Permanent/long standing Persistent AF	-	-	0.45 (0.16, 1.27)	0.13
Persistent AF	-	-	0.64 (0.31, 1.31)	0.22
Paroxysmal AF	-	-	0.41 (0.22, 0.75)	0.004
First Detected AF	-	-	1.06 (0.52, 2.17)	0.87
AFib, type missing	-	-	0.33 (0.15, 0.74)	0.007
AF Type: AFlutter	-	-	Reference	
Past Medical History: Heart Failure	-	-	0.60 (0.37, 0.99)	0.04
ACEi/ARB Prior to Admission	-	-	1.36 (1.00, 1.85)	0.05
eGFR, per 10 unit increase	-	-	1.10 (1.00, 1.22)	0.05
BMI, per unit increase	-	-	1.05 (1.02, 1.08)	0.0008
Control Strategy: Rate vs. Rhythm	-	-	0.59 (0.39, 0.91)	0.02

Other covariates included in multivariable model were age, sex, race, insurance status, geographic region, hospital type, hospital size, rural status, adult cardiac electrophysiology site, AF type, anemia, coronary artery disease, prior stroke or transient ischemic attack, diabetes, chronic dialysis, HF, hypertension, liver disease, obstructive sleep apnea, peripheral vascular disease, chronic obstructive pulmonary disease, prior hemorrhage or bleeding, prior myocardial infarction, prior history of percutaneous intervention, smoking status, thyroid disease, heart failure medications prior to admission, aspirin and antiplatelet prior to admission, estimated glomerular filtration rate, BMI, and rate versus rhythm control strategy. Full model results included in Online Supplement.