# Safety Outcomes Associated with Rate-Controlling Medications to Manage Atrial Fibrillation in Patients with Heart Failure

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## INTRODUCTION

- Atrial fibrillation (AF) and heart failure (HF) are associated with significant mortality and morbidity.
- Lack of consensus over preferred rate control method for patients with AF and HF.[1]
- Amiodarone has potential for cardioversion and stroke. Digoxin and CCB in observational studies worsen clinical outcomes, and BB may also have negative outcomes.[2]
- Use of rate-controlling medications is variable and needs to be further characterized to identify the most appropriate pharmacologic agents for this population.

## PURPOSE

To assess the safety of amiodarone, digoxin, CCBs, and BBs in rate control for patients with AF and HF

## METHODS

### Study Design
- IRB approved, single center, retrospective cohort review

### Cohort
- Hospitalizations between January 1, 2019 - December 31, 2021
- Adults diagnosed with AF and HF via ICD10 codes
- *Inclusion*: medication charge(s) for intravenous amiodarone, digoxin, non-dihydropyridine CCB, and/or BB (carvedilol, metoprolol, bisoprolol, esmolol, sotalol, propranolol, nadolol, nebivolol)
- *Exclusion:* patients who did not receive medication of interest

### Outcomes
- *Primary:* Frequency of adverse drug events (ADE) between rate control agents
- *Secondary:* Frequency of ADE and number of rate control agents
- Adverse events identified through ICD10 codes

### Analysis
- Descriptive statistics, Fisher's exact test, and Kruskal-Wallis test via IBM SPSS software version 28.0.1.1

## RESULTS

### Table 1. Demographics

| Average Age in Years (Std Dev) | 70.73 (12.19) |
|---|---|
| Gender no. (%) | |
| Male | 349 (59.1) |
| Female | 242 (40.9) |
| Race no. (%) | |
| Black or African American | 63 (10.7) |
| White | 490 (82.9) |
| Declined/Race Not Reported/Other | 38 (6.5) |

### Figure 1. Flow Diagram of Patient Inclusion and Exclusion



1285 patients with AF → 88 duplicate visits
1197 patients with AF on index visit → 567 patients without HF
630 patients with AF + HF → 39 patients without medication of interest
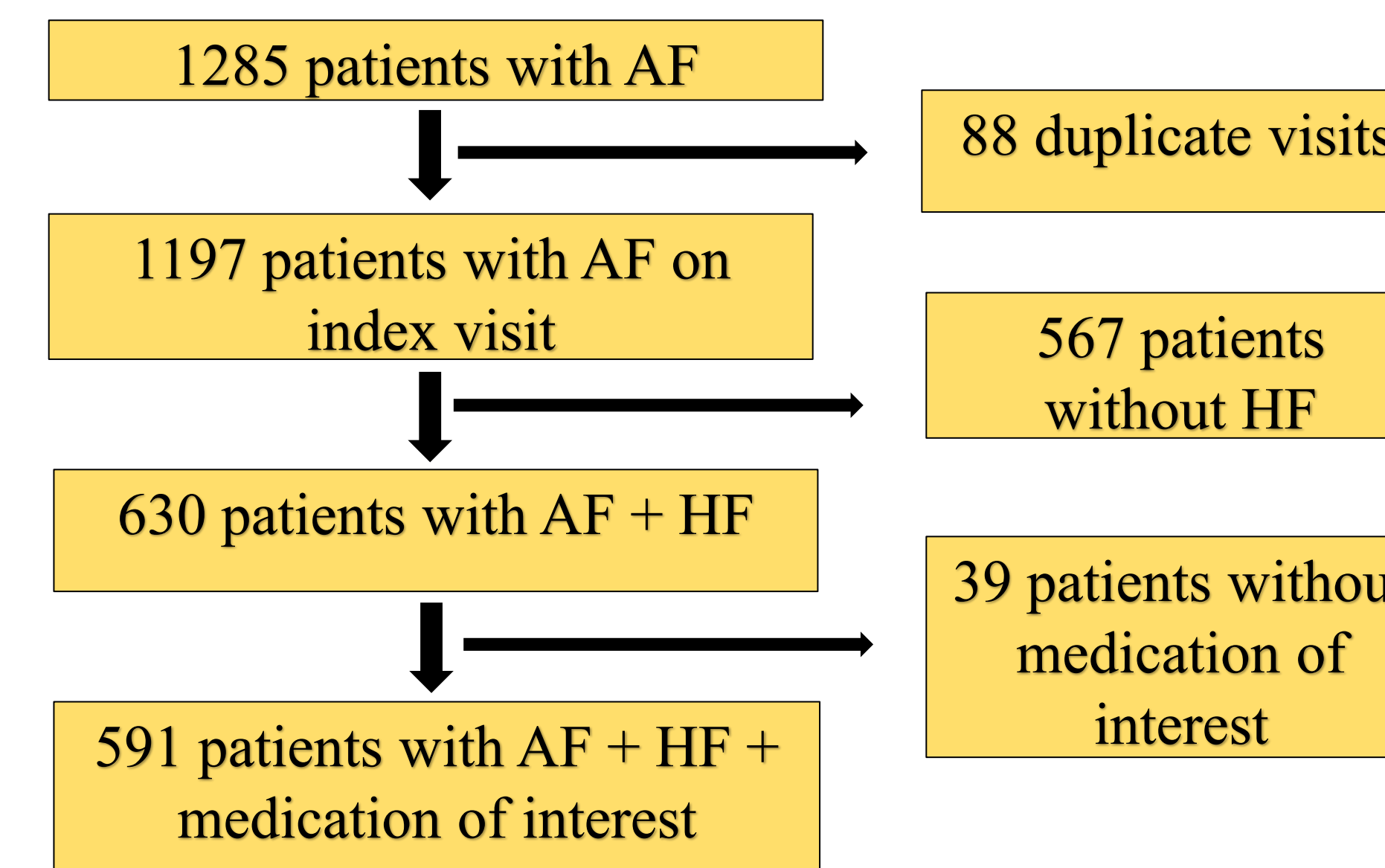591 patients with AF + HF + medication of interest

### Table 2. Incidence of ADE by Medication Class

| | Amiodarone (%) N= 241 | Digoxin (%) N = 71 | CCB (%) N = 163 | BB (%) N = 544 | Total Patients (%) N= 591 |
|---|---|---|---|---|---|
| Digoxin Toxicity | 1 (0.2) | 3 (0.5) | 2 (0.3) | 2 (0.3) | 3 (0.5) |
| Pacemakers | 9 (1.5) | 4 (0.7) | 6 (1.0) | 35 (5.9) | 37 (6.3) |
| AV Block | 8 (1.4) | 3 (0.5) | 6 (1.0) | 16 (2.7) | 16 (2.7) |
| Torsades De Pointes | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Ventricular Tachycardia | 56 (9.5) | 7 (1.2) | 16 (2.7) | 69 (11.7) | 83 (14.0) |
| Atrial Tachycardia | 41 (6.9) | 8 (1.4) | 17 (2.9) | 49 (8.3) | 58 (9.8) |
| Ventricular Fibrillation | 22 (3.7) | 0 (0) | 6 (1.0) | 24 (4.1) | 27 (4.6) |
| Hyperthyroidism | 2 (0.3) | 1 (0.2) | 2 (0.3) | 6 (1.0) | 7 (1.2) |
| Hypothyroidism | 25 (4.2) | 10 (1.7) | 20 (3.4) | 80 (13.5) | 86 (14.6) |
| Stroke | 5 (0.9) | 0 (0) | 0 (0) | 5 (0.9) | 5 (0.9) |
| Hepatic Failure | 26 (4.4) | 8 (1.4) | 7 (1.2) | 32 (5.4) | 33 (5.6) |
| Liver Toxicity | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Bradycardia | 7 (1.2) | 2 (0.3) | 7 (1.2) | 16 (2.7) | 17 (2.9) |
| Hypotension | 38 (6.4) | 12 (2.0) | 20 (3.4) | 74 (12.5) | 80 (13.5) |
| Cardiogenic Shock | 77 (13.0) | 17 (2.9) | 11 (1.9) | 70 (11.8) | 88 (14.9) |

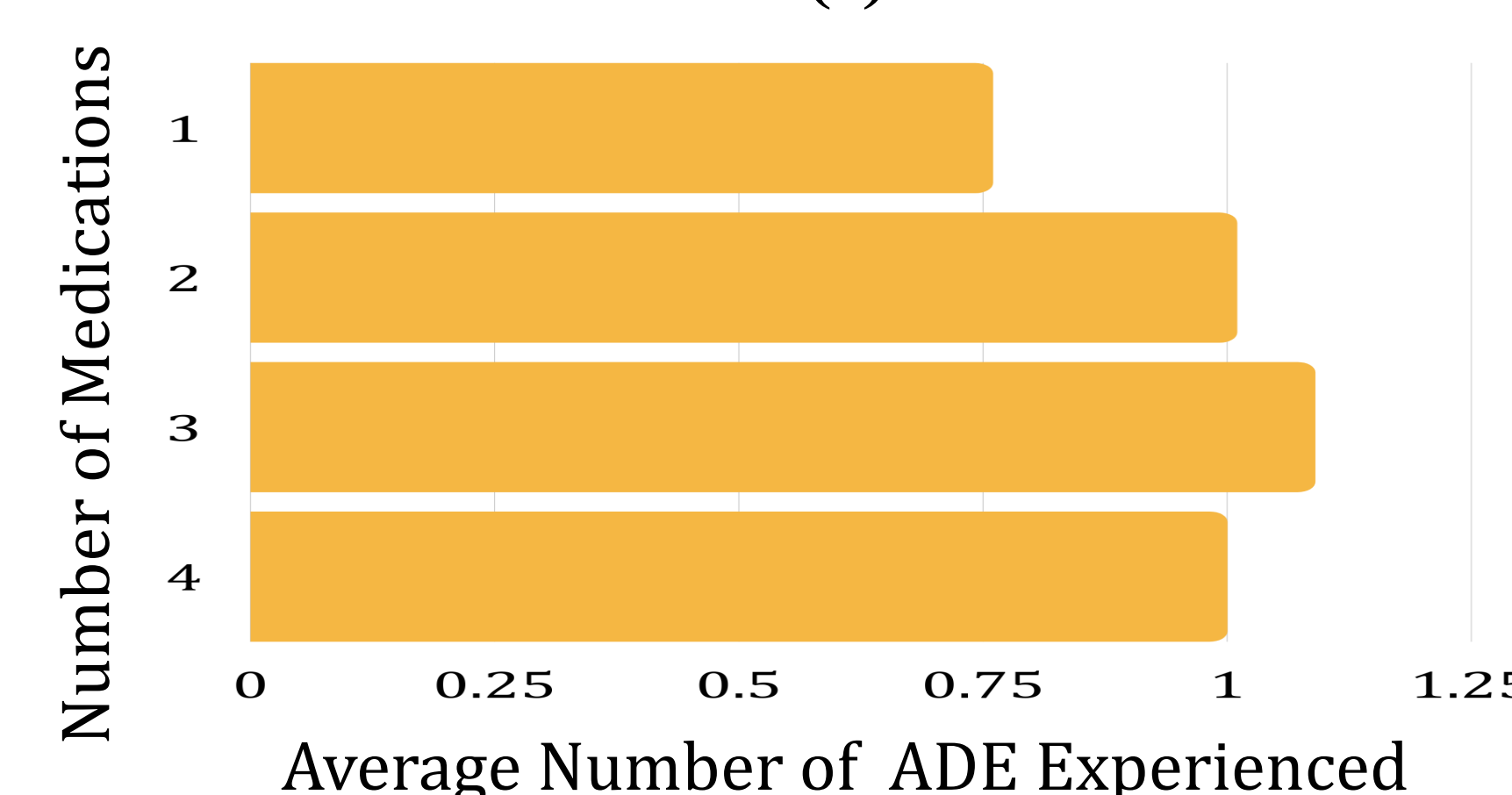### Figure 2. Average ADE Per Number of Medication(s) Received



Average Number of ADE Experienced (x-axis)
Number of Medications (y-axis)

### Table 3. Incidence of ADE Per Number of Medication(s) Received

| Number of Medications | N (%) |
|---|---|
| 1 | 263 (44.5) |
| 2 | 241 (40.8) |
| 3 | 74 (12.5) |
| 4 | 13 (2.2) |

**P-value= 0.012**

## RESULTS (Cont'd)

**Baseline characteristics**
- A total of 591 patients met criteria: 544 (92.0%) BB, 241 (40.8%) amiodarone, 163 (27.6%) CCB, and 71 (12.0%) digoxin.
- The mean (standard deviation) age of was 70.7 (12.2) years old and consisted mainly of White males.

**Primary outcome**
- Amiodarone had the highest incidence of adverse events with an average of 1.3 adverse events per patient. Digoxin was the second most common (1.0 ADE/patient), followed by BB (0.87 ADE/patient), and CCB last (0.73 ADE/patient).
- The most common adverse event was cardiogenic shock (14.9%).

**Secondary outcome**
- 263 patients (44.5%) received one class of medication, 241 patients (40.8%) received two classes, 74 (12.5%) received three classes, and 13 (2.2%) received four classes.
- There was a statistically significant difference (0.012, $p<0.05$) between the number of medications received and number of adverse effects.

## LIMITATIONS

- Single center, retrospective study
- Patients in medication classes are not mutually exclusive, leading to association only analysis

## CONCLUSIONS

- Although current guidelines recommend amiodarone and digoxin for rate control, those receiving BBs and CCBs were associated with fewer adverse events per patient compared to other medication classes.
- Prospective studies should be conducted to refine guidelines.
- There was an association with greater adverse events and number of rate control medications per patient, suggesting optimization of medication classes should be done before augmentation with another class.

## ACKNOWLEDGEMENTS & REFERENCES

1. Gopinathannair R, Chen LY, Chung MK, et al. Managing atrial fibrillation in patients with heart failure and reduced ejection fraction: a scientific statement from the American Heart Association. *Circ Arrhythm Electrophysiol.* 2021;14(6):HAE0000000000000078.
2. January CT, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. Circulation