Is Rhythm-Control Superior to Rate-Control in Patients with Atrial Fibrillation and Diastolic Heart Failure?

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Background: Although no clinical trial data exist on the optimal management of atrial fibrillation (AF) in patients with diastolic heart failure, it has been hypothesized that rhythm-control is more advantageous than rate-control due to the dependence of these patients' left ventricular filling on atrial contraction. We aimed to determine whether patients with AF and heart failure with preserved ejection fraction (EF) survive longer with rhythm versus rate-control strategy.

Methods: The Duke Cardiovascular Disease Database was queried to identify patients with EF > 50%, heart failure symptoms and AF between January 1, 1995 and June 30, 2005. We compared baseline characteristics and survival of patients managed with rate- versus rhythm-control strategies. Using a 60-day landmark view, Kaplan-Meier curves were generated and results were adjusted for baseline differences using Cox proportional hazards modeling.

Results: Three hundred eighty-two patients met the inclusion criteria (285 treated with rate-control and 97 treated with rhythm-control). The 1-, 3-, and 5-year survival rates were 93.2%, 69.3%, and 56.8%, respectively in rate-controlled patients and 94.8%, 78.0%, and 59.9%, respectively in rhythm-controlled patients ($P > 0.10$). After adjustments for baseline differences, no significant difference in mortality was detected (hazard ratio for rhythm-control vs rate-control = 0.696, 95% CI 0.453–1.07, $P = 0.098$).

Conclusions: Based on our observational data, rhythm-control seems to offer no survival advantage over rate-control in patients with heart failure and preserved EF. Randomized clinical trials are needed to verify these findings and examine the effect of each strategy on stroke risk, heart failure decompensation, and quality of life.

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Atrial fibrillation (AF) and the clinical syndrome of diastolic heart failure characterized by heart failure signs and symptoms with preserved ejection fraction (EF) are common pathologic problems. AF affects over 2 million patients in the United States with an annual incidence of 0.1% and prevalence of up to 10% in people older than 80 years.¹ Similarly, in the United States, 1.7 million patients have isolated diastolic heart failure and its reported prevalence approaches 50% in patients older than 70 years.²

AF and diastolic heart failure appear to be interrelated. In the recent EuroHeart Failure Survey,

25% of congestive heart failure (CHF) patients with preserved systolic function had AF.³ Almost 10% of patients with abnormal left ventricular diastolic function have new onset AF within 4 years of follow-up and the risk of developing AF appears proportional to the severity of left ventricular diastolic dysfunction.^{4,5}

Studies of the impact of AF on cardiovascular event risk and life expectancy among all CHF patients generally indicate increased risk and mortality; however, most of these studies included few patients with preserved systolic function.^{6,7} A retrospective subgroup analysis of AF in patients with

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diastolic heart failure who were enrolled into The Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) study found AF was associated with greater increased hazard for major cardiovascular risk in patients with diastolic heart failure compared with those who had systolic heart failure.⁸

To date, no studies have compared a rate- versus rhythm-control strategy in patients with AF and isolated diastolic heart failure. It is unknown to what degree or which of the physiologic changes (loss of atrial contraction, reduction in stroke volume, elevation in filling pressures, increase in ventricular rate or its irregularity) found in AF contribute to the worse outcomes in patients with diastolic heart failure. Theoretically, restoration of sinus rhythm would reverse all or some of these physiologic changes and could prove to be beneficial. We aimed to evaluate a large database to examine whether a rhythm- versus rate-control strategy for patients with AF and diastolic heart failure affected survival.

METHODS

Patient Population

The approval of our institutional review board was obtained at the inception of the study. The patient population was identified using the Duke Cardiovascular Disease Database, which systematically collects information about the in-hospital clinical course and clinical characteristics of all patients undergoing a cardiac catheterization at Duke University Medical Center. Data collected at the time of cardiac procedures include: symptoms, history and physical examination, diagnoses, medications, severity of coronary artery disease, and measures of left ventricular function. Follow-up data are collected at 6 months, 1 year and annually thereafter for patients with at least 1-vessel coronary artery disease. Data on vital status are complete in 93% of patients enrolled in the database. In some cases, when follow-up was not otherwise available, the National Death Index was used to ascertain the vital status.⁹

For this study, diastolic heart failure was defined as the presence of signs and/or symptoms of CHF in a patient with preserved EF > 50% by cardiac angiography.¹⁰ Patients with clinical evidence of CHF, EF > 50% and AF enrolled in the database from January 1995 through June 2005 were iden-

tified. Patients were considered to have AF only if AF was listed as a discharge diagnosis or as a diagnosis in a subsequent outpatient visit to a cardiology clinic during the study period. We were unable to further classify patients with AF as having paroxysmal versus long-standing persistent AF. Study entry date was determined to be the onset date of AF provided that other inclusion criteria were met. Both patients with ischemic and non-significant coronary artery disease were included in this study. Patients with prior history of myocardial infarction, coronary revascularization, or at least two significantly diseased arterial systems were defined to have an ischemic etiology of their diastolic heart failure.¹¹ Patients with single-vessel coronary disease with significant stenosis ($\geq 75\%$) of the proximal left anterior descending artery were also defined to have an ischemic etiology. Excluded were patients with congenital heart disease, moderate to severe valvular disease, hypertrophic cardiomyopathy as determined by clinical, echocardiographic, and catheterization findings by experts, constrictive pericarditis, moderate to severe primary pulmonary hypertension or pulmonary hypertension secondary to connective tissue disease, hepatopulmonary disease, severe pulmonary disease, advanced cancer, or carcinoid. Patients were further excluded if they had no CHF symptoms, if CHF was only documented in the setting of an acute coronary syndrome, or for whom anatomic catheterization descriptors were not available. One of the authors (Sana M. Al-Khatib) reviewed medical records on all patients to adjudicate their eligibility for inclusion in this study.

The onset of AF, that is, time zero, was determined in one of three ways: (1) date of the cardiac catheterization if AF was a diagnosis; (2) outpatient clinic date associated with the diagnosis of AF; or (3) midpoint between admission and discharge during a hospitalization subsequent to the catheterization if AF was a discharge diagnosis. If the catheterization date occurred prior to the midpoint between admission and discharge, then the catheterization date was used for the onset of AF.

Treatment

Patients were classified into two groups based on whether they were managed with a rate-control strategy versus a rhythm-control strategy at baseline. Treatments with catheter ablation or therapies other than either a rate- or a rhythm-control

strategy were not examined in this analysis. The rhythm-control group included patients treated with any Class I or III antiarrhythmic drug (AAD) and the rate-control group included patients not treated with a Class I or III AAD, but who were treated with a beta-blocker, calcium-channel blocker, and/or digoxin. It was not possible to verify whether an individual patient was actually rate-controlled or rhythm-controlled, but only whether they were receiving a rate-controlling medication or an AAD. Given the small number of patients with ventricular tachyarrhythmias and because it is not common practice to treat premature ventricular contractions with antiarrhythmic medications at our institution, we felt that it was reasonable to assume that the AADs were being used to treat AF. Data on medications were obtained from a pharmacy database that captures all in-hospital medications; our institution's Cardiovascular Disease database that incorporates follow-up data; and clinic visit notes. Crossovers between treatment groups could not be verified. The endpoint for this analysis was all-cause mortality.

Statistical Analysis

Baseline characteristics and outcomes of the rate-control group were compared with those of the rhythm-control group. Categorical variables are presented as percentages and continuous variables are presented as medians and interquartile ranges. Statistical comparisons were performed using two-sided significance tests with the results declared significant at $P < 0.05$. Unordered categorical variables were compared using the Pearson chi-square test (or Fisher's exact test if appropriate). Continuous and ordered categorical measures were compared using the Wilcoxon rank-sum test.

To compare and illustrate the survival of patients treated with rhythm-control versus rate-control, "landmark analyses" were performed.^{12,13} A landmark analysis is a type of survival analysis that classifies patients into a nonoutcome event, such as treatment, that occurs during study follow-up. In our analyses, we define landmark time and study outcomes in terms of elapsed time from a patient's AF diagnosis and prognosis is assessed from this landmark time point. Patients who died prior to the chosen time point were not included in the analysis. The landmark analyses in this study were performed at 60 days post-AF diagnosis. This time was chosen because it adequately covered the dis-

tribution of time when patients would have likely had medical therapy for AF initiated, and relatively few deaths occurred prior to this time. The Kaplan-Meier method was used to graphically display the cumulative percentage of patients surviving over time for the rhythm- versus rate-control groups. Differences in survival of the two treatment groups were assessed using the log rank test and differences were adjusted using weighted Cox proportional hazards regression modeling with the inverse probability weighted estimators method to adjust for AAD usage.¹⁴ Candidate variables for multivariable adjustment in these survival models included age, gender, race, heart rate, blood pressure, vascular disease, diabetes, history of hypertension, CHF severity, prior myocardial infarction, severity of coronary artery disease, third heart sound, mild valvular heart disease, patient comorbidities, and medications. The linearity assumption for all continuous and ordinal variables was checked and appropriate transformations were performed to satisfy this assumption.

RESULTS

Baseline Characteristics

From January 1, 1995 to June 30, 2005, 33,637 patients underwent cardiac catheterization at our institution. Of these patients, 382 patients met our study inclusion criteria. Examining the data available, we determined that including the 22 echocardiographic and nuclear diagnoses of diastolic dysfunction did not substantially augment our patient numbers and as a result, these patients were not included in this analysis.

The onset of AF (time zero) was determined to be the catheterization date for 132 of these patients. For 242 patients time zero was determined to be the midpoint between the inpatient admission and discharge dates. For eight patients time zero was determined to be an outpatient clinic visit date associated with the diagnosis of AF. None of these eight patients had been diagnosed with AF prior to their study inclusion at time zero. The median age for the study population was 70 years with 48% male and 62% having an ischemic etiology of their heart disease. For the landmark view at 60 days, there were 285 patients in the rate-control group and 97 patients in the rhythm-control group. Compared with patients in the rhythm-control group, a larger percentage of patients in the rate-control

Table 1. Baseline Characteristics

Baseline Descriptors	Total n = 382	Rate-Control Group n = 285	Rhythm-Control Group n = 97	P-value
Demography				
Age, years (median IQR)	70 (62,75)	70 (63,76)	70 (59,75)	0.605
Male%	47.9	48.4	46.4	0.730
Race%				0.011
African-American	17.5	20.7	8.2	
Caucasian	74.9	71.2	85.6	
Native American	5.8	6.7	3.1	
Other	1.8	1.4	3.1	
Severity of CHF				
NYHA Class II	31.7	32.6	28.9	0.518
NYHA Class III	46.9	46.3	48.5	
NYHA Class IV	21.5	22.1	22.7	
Clinical features of CHF				
Diagnosis of ischemic etiology	62.3	64.9	54.6	0.071
Left ventricular EF (median IQR)	63 (55,69)	63 (55,69)	62 (56–69)	0.997
Chronic obstructive pulmonary disease	13.9	15.8	8.2	0.063
Cardiovascular burden of disease				
Hypertension	79.8	81.1	76.3	0.312
Hyperlipidemia	55.5	55.1	56.7	0.782
Diabetes mellitus	40.3	42.1	35.1	0.221
Peripheral vascular disease	19.1	17.9	22.7	0.300
Cerebrovascular disease	16.0	15.1	18.6	0.420
History of smoking	50.8	51.6	48.5	0.595
Prior myocardial infarction	26.4	29.1	18.6	0.042
Prior percutaneous coronary intervention	19.6	22.8	10.3	0.007
Prior coronary artery bypass graft	19.4	19.3	19.6	0.950
Number of diseased coronary arteries				0.476
0	33.5	31.9	38.1	
1	20.7	20.7	20.6	
2	16.5	18.6	10.3	
3	29.3	28.8	30.9	

group were nonwhites, had a history of percutaneous coronary intervention, and a prior myocardial infarction. There was no significant difference in either baseline heart failure symptoms ($P = 0.518$) or left ventricular EF ($P = 0.997$) for patients in the rhythm- and rate-control groups. Other patient characteristics were similar for the two groups (Table 1).

Medications

The rates of use of cardiac medications are provided in Table 2. The overall rate of use of warfarin was 55.8%, 53.0% of patients in the rate-control group, and 63.9% in the rhythm-control group; however, there was a trend toward higher use of warfarin in the rhythm-control group compared

Table 2. Baseline Medications Used in the Rate-Control and the Rhythm-Control Groups

Medication	All-Patients n = 382	Rate-Control Group n = 285	Rhythm-Control Group n = 97	P-value
Aspirin	87.4	86.3	90.7	0.258
Warfarin	55.8	53.0	63.9	0.061
Beta-blocker	66.2	63.5	74.2	0.054
Calcium channel blocker	33.0	33.7	30.9	0.618
Angiotensin-converting enzyme inhibitor	58.1	57.2	60.8	0.531
Digoxin	24.6	25.3	22.7	0.610
Diuretic	66.8	61.1	83.5	<0.001

Table 3. Type of Antiarrhythmic Medications Used in the Rhythm-Control Group*

Class I Antiarrhythmic n = 23		Class III Antiarrhythmic n = 73	
Procainamide	60.9	Amiodarone	60.3
Quinidine	30.4	Sotalol	38.4
Disopyramide	4.4	Dofetilide	1.4
Propafenone	4.4		

*It was noted that one patient was receiving antiarrhythmic medication, but the drug was not specified.

with the rate-control group ($P = 0.061$). In most of the reviewed charts, no reason was given as to why the patient was not on warfarin. Compared with patients in the rate-control group, patients in the rhythm-control group were more likely to receive beta-blockers and diuretics ($P = 0.054$ and $P < 0.001$, respectively). No significant differences were observed for aspirin, digoxin, or angiotensin-converting enzyme-inhibitor usage.

In the rhythm-control group, 76% received a Class III AAD and 24% received a Class I AAD. Data on the type of antiarrhythmic medication used were missing for only 1 patient, as the specific medication could not be verified (Table 3).

Patient Outcomes

Using the 60-day landmark view, 66 patients died within 60 days or did not have follow-up beyond 60 days (47 patients in the rate-control group and 19 patients in the rhythm-control group) and thus, these patients were not included in the landmark analysis. Of these patients, 30 died and 36 were missing follow-up beyond 60 days. Of the 30 deaths, 23 patients were in the rate-control group and 7 patients were in the rhythm-control group. This difference was not statistically significant ($P = 0.372$).

The 1-year survival rate was 93.2% in patients treated with rate-control versus 94.8% in patients treated with rhythm-control. At 3 years, the survival rate was 69.3% in patients treated with rate-control versus 78.0% in patients treated with rhythm-control ($P = 0.171$). At 5 years, the survival rate was only 56.8% in the rate-control group and 59.9% in the rhythm-control group. After adjusting for patient clinical characteristics and AAD usage in a weighted Cox proportional hazards regression model with inverse probability weighted adjustment (Table 4), there was a trend toward better survival in patients managed with rhythm-control that did not meet statistical significance likely due to lack of statistical power (HR for rhythm-control vs rate-control = 0.696, 95% CI 0.453–1.07, $P = 0.098$). Of note, treatment with warfarin was associated with a significant mortality reduction after adjustment with multivariable analysis (HR for rhythm-control vs rate-control = 0.656, 95% CI 0.469–0.917, $P = 0.014$). As warfarin was administered to a larger proportion of patients treated with a rate-control strategy, it is possible that the higher rate of warfarin anticoagulation contributed to the marginally significant survival benefit of the rate-control strategy; however, the interaction between rate-control and warfarin therapy in the multivariable model was not significant ($P = 0.640$). Figure 1 shows adjusted survival curves for the two groups using a landmark analysis view at 60 days. The distribution of mode of death for the 151 patients included in the 60-day landmark analysis is provided in Table 5.

DISCUSSION

Our study indicates that patients with AF and diastolic heart failure undergoing cardiac catheterization at our institution are more likely to be treated with a rate-control strategy than a rhythm-control strategy. We found no statistically different effect

Table 4. Results of Multivariable Model

Characteristic	Wald χ^2	P-value	HR	95% CI
Charlson Index (max of 4 to satisfy linearity)	18.4524	<0.0001	1.412	1.206,1.653
Aspirin	16.9296	<0.0001	0.406	0.264,0.623
BMI (max of 26 to satisfy linearity)	14.1459	0.0002	0.867	0.805,0.934
Age (HR per 10 year increment)	10.0593	0.0015	1.332	1.116,1.590
Warfarin	6.0921	0.0136	0.656	0.469,0.917
Diabetes, end organ damage	5.5449	0.0185	1.977	1.121,3.485
CHF class	5.0996	0.0239	1.295	1.035,1.620
Antiarrhythmic medication	2.7375	0.0980	0.696	0.453,1.069

Figure 1. Adjusted survival curves by treatment group using landmark analysis at 60 days.

on survival between the rate- and rhythm-control strategies. Adjusted analyses revealed a rhythm-control strategy to be associated with a modest trend toward better survival than a rate-control strategy.

That patients with AF and diastolic heart failure were more likely to be treated with a rate-control strategy is not surprising given the results of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial that showed a trend toward worse survival with antiarrhythmic medications compared with rate-control therapy in patients older than 65 years of age with

minimally symptomatic AF. Clinical trials like AFFIRM, Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE), Pharmacological Intervention in Atrial Fibrillation (PIAF), and Strategies of Treatment of Atrial Fibrillation (STAF), provide objective evidence that a rhythm-control strategy is not superior to a rate-control strategy.^{15–17} Though none of these trials focused on patients with heart failure, we now have the results of two randomized controlled trials comparing rate- with rhythm-control strategies in patients with systolic heart failure. The AF and CHF (AF-CHF) trial showed no difference in

Table 5. Distribution of Mode of Death in the Rate-Control and the Rhythm-Control Groups

Mode of Death	All-Patients n (%)	Rate-Control Group n (%)	Rhythm-Control Group n (%)
Definite myocardial infarction	6 (4.0)	2 (1.6)	4 (13.8)
During or postcardiac surgery	3 (2.0)	2 (1.6)	1 (3.5)
Congestive heart failure	4 (2.7)	2 (1.6)	2 (6.9)
Sudden	6 (4.0)	6 (4.9)	0 (0)
Unobserved	3 (2.0)	3 (2.5)	0 (0)
Postresuscitation	1 (0.7)	0 (0)	1 (3.5)
Other cardiac causes	40 (26.5)	28 (23.0)	12 (41.4)
Vascular causes	14 (9.3)	14 (11.5)	0 (0)
Trauma	3 (2.0)	3 (2.5)	0 (0)
Noncardiac, medical	56 (37.1)	51 (41.8)	5 (17.2)
Noncardiac, procedure-related	2 (1.3)	1 (0.8)	1 (3.5)
Undetermined	13 (8.6)	10 (8.2)	3 (10.3)
Total	151	122	29

cardiovascular mortality with rate- (25.2%) compared with rhythm-control (26.7%) in patients with AF and left ventricular systolic dysfunction (HR 1.06, 95% CI 0.86–1.30, $P = 0.59$).^{18,19} Meanwhile, the chronic atrial fibrillation and heart failure (CAFE-II) study examined patients with persistent AF, heart failure, and impaired left ventricular function and found that at 1-year follow-up, although symptoms and exercise capacity were similar, patients treated with a rhythm-control strategy had improved left ventricular function and quality of life compared with those treated with a rate-control strategy.²⁰ Nonetheless, the recent evidence from AF-CHF and CAFE-II only focuses on patients with AF and depressed left ventricular function—not those patients with AF and heart failure with preserved EF, who are clinically and pathophysiologically distinct.

Further highlighting the dearth of evidence addressing the subgroup of patients with AF and diastolic dysfunction is a systematic literature review of 32 clinical trials on the optimal management of AF in patients with heart failure by Khand et al., in 2000, in which not a single study addressed AF in heart failure with preserved EF.²¹ Although in AFFIRM there was a trend toward better survival with rate-control, only 23.1% had a history of CHF and the HR for death was higher in patients with left ventricular EF $\geq 50\%$ compared to the group with EF $< 50\%$, who were treated with rhythm-control.¹⁵ Similarly, although RACE suggests that rate-control is not inferior to rhythm-control, the mean EF was $30\% \pm 10$ and only half of the patients had a history of heart failure, precluding extrapolation of these results to the growing subgroup of patients with AF and preserved systolic function.¹⁶ A randomized clinical trial in patients with AF and diastolic heart failure would provide additional information pertinent to optimal treatment strategies as consensus practice guidelines do not currently address the management of this subset of patients.²²

Despite the paucity of data on the optimal management of AF in diastolic heart failure, many physicians prefer to restore and maintain sinus rhythm in such patients. They reason that patients will do better if they remain in sinus rhythm because left ventricular filling in diastolic heart failure occurs primarily in late diastole and is therefore more dependent than normal hearts on atrial contraction, which disappears in AF. As logical as this argument may sound, to date it has not been validated by data from randomized controlled

trials. Concerns have also been raised about the safety of AADs in patients with CHF, particularly the risk for proarrhythmia or sudden death.^{23–25} Amiodarone and dofetilide are the only AADs that have been found to be safe in patients with systolic heart failure. In patients with isolated diastolic heart failure, the safety of AADs has not been proven, and thus, some physicians favor a rate-control strategy. While there are theoretical benefits to using beta-blockers and calcium-channel blockers in patients with AF and pure diastolic dysfunction due to their negative inotropic and rate-controlling effects, very little conclusive evidence exists to guide the treatment of heart failure with preserved systolic function.²⁶ In a population-based study of new-onset CHF and normal EF as it presents in the community, beta-blockers were independently associated with improved survival ($P = 0.02$); however, only 81% of the included patient population met criteria for “probable diastolic heart failure” and only 29% had AF or atrial flutter.²⁷ In a small, prospective, randomized trial, beta-blockers resulted in a significant reduction in mortality (56% vs 76%, $P = 0.007$) and mortality plus nonfatal myocardial infarction (59% vs 65%, $P = 0.002$) in patients with New York Heart Association class II–III CHF, prior q-wave myocardial infarction, and EF $\geq 40\%$ after 2 months of treatment with an angiotensin-converting enzyme-inhibitor and diuretics.²⁸ Similarly, verapamil, has been shown to improve short-term clinical status, exercise capacity, and diastolic filling in patients with isolated diastolic dysfunction.²⁹ Digoxin has been a traditional agent used for rate-control in patients with both AF and CHF and remains a first-line agent in the presence of systolic heart failure; however, it has no proven benefit in patients with isolated diastolic heart failure. For patients with AF and structural heart disease, there is consensus that anticoagulation is important to prevent systemic embolization. Despite current guidelines, the rate of warfarin usage in our database population was low. Although the reason for this remains unclear, it is possible that most arrhythmias were transient and appeared in proximity to the index hospitalization.

Our study has some limitations. First, this is an observational study of clinical data prospectively collected from an inherently biased study cohort given that patients were selected from a cardiac catheterization database of patients referred for coronary angiography possibly due to symptomatic

coronary artery disease. Due to the nature of the database, we were unable to accurately determine the number of patients that underwent coronary revascularization during the index hospitalization. As such, this patient population may not fully represent the characteristics of diastolic heart failure patients in the general population. Second, we were unable to retrospectively verify that a patient treated with a rate-controlling medication was actually rate-controlled or that a patient treated with an AAD was actually rhythm-controlled and we were unable to verify crossovers from one treatment group to another during study follow-up. However, continuous electrocardiographic monitoring is not routine in clinical practice and was not performed in the large randomized trials comparing these strategies. Third, patients were only considered to have AF if it was listed as a discharge diagnosis or diagnosis during a clinic visit during the predefined study period. The fact that data regarding AF are only captured at one time point precludes determination of AF duration, an important risk factor for outcome. Similarly, the duration of treatment with an AAD before or after inclusion in the study remains unknown. Fourth, stroke data, heart failure hospitalizations, and quality of life measures were unavailable. Fifth, due to our relatively small sample size, our study lacked statistical power to detect a significant difference in survival between patients treated with a rate- versus rhythm-control strategy. Based on our observed trend toward better survival in patients treated with rhythm-control, our study's calculated current power to detect a significant result was only 64%. In the absence of a randomized trial where patients are randomized to rate- or rhythm-control therapy at the onset of AF, using a landmark analysis allowed us to assess prognosis from the onset of AF, classifying patients based on the use of rate- or rhythm-control over the ensuing 60-day period, essentially providing an intent-to-treat analysis in this observational setting. Finally, while inherent difficulties exist in diagnosing diastolic dysfunction, our study defined diastolic dysfunction based on clinical evidence of CHF and a preserved EF. Despite the inherent limitations of these observational data, we have previously published data from this database on the subset of patients with AF who have systolic heart failure (defined as $EF < 50\%$).³⁰ After adjusting for baseline characteristics and medications, we found no significant difference in mortality between patients treated with

rate- versus rhythm-control—essentially predicting the results of the prospectively randomized AF-CHF trial. To more closely replicate AF-CHF using our database, we have also examined the subset of patients with AF and CHF with $EF \leq 35\%$ and again, there was no significant difference in survival for patients treated with rate- compared with rhythm-control.

CONCLUSIONS

Based on our observational data, there was no advantage of a rate-control over a rhythm-control approach for AF in patients with diastolic heart failure. Statistical adjustments resulted in the appearance of a trend toward better survival in patients with AF and heart failure with preserved EF managed with rhythm-control; however, large randomized clinical trials are needed to verify this hypothesis-generating finding, and to examine the effect of each strategy on the risk of stroke, heart failure decompensation, and quality of life.

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