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Quality of Life and Functional Capacity in Patients With Atrial Fibrillation and Congestive Heart Failure

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Objectives This study sought to assess the impact of rhythm- versus rate-control treatment strategies and of underlying rhythm on quality of life and functional capacity in patients with atrial fibrillation (AF) and congestive heart failure (CHF).

Background Although intention-to-treat and efficacy analyses have demonstrated similar cardiovascular outcomes in patients with AF and CHF randomized to rhythm or rate control, effects on quality of life remain to be determined.

Methods The AF-CHF (Atrial Fibrillation and Congestive Heart Failure) trial randomized 1,376 patients to rhythm- or rate-control strategies. For this pre-specified substudy, Medical Outcomes Short Form-36 questionnaires were administered at baseline and 4 months. Six-min walk tests were conducted at baseline, 3 weeks, 4 months, and 1 year.

Results Quality of life improved across all domains to a similar extent with rhythm and rate control. However, a higher proportion of time spent in sinus rhythm was associated with a modestly greater improvement in quality of life scores. Six-min walk distance ($p = 0.2328$) and New York Heart Association functional class ($p = 0.1712$) improved to a similar degree with rhythm and rate control. A higher proportion of time spent in sinus rhythm was associated with a greater improvement in New York Heart Association functional class ($p < 0.0001$) but not in 6-min walk distance ($p = 0.1308$).

Conclusions Improvements in quality of life and functional capacity were similar in patients with AF and CHF randomized to rhythm- versus rate-control strategies. By contrast, sinus rhythm was associated with beneficial effects on New York Heart Association functional class and modest gains in quality of life. (Atrial Fibrillation and Congestive Heart Failure [AF-CHF]; NCT88597077) (J Am Coll Cardiol 2013;61:455–60) © 2013 by the American College of Cardiology Foundation

Atrial fibrillation (AF) and congestive heart failure (CHF) are considered cardiovascular epidemics of the modern era and often coexist in the same patient. The AF-CHF (Atrial Fibrillation and Congestive Heart Failure) trial randomized 1,376 patients with AF and CHF from 123 centers to rhythm- or rate-control treatment strategies (1). No differences were observed with respect to the primary outcome (i.e., cardiovascular mortality) and all secondary outcomes (e.g., all-cause mortality, worsening heart failure, stroke) over a mean follow-up of 37 months. Efficacy analyses confirmed comparable treatment effects and further extended these findings to include a lack of association between underlying sinus rhythm and morbidity and mortality (2). It remained to be determined whether a particular treatment strategy or maintenance of sinus rhythm should be favored on the basis of quality of life and/or functional capacity. These important pre-specified secondary outcomes constitute the focus of this a priori–defined substudy of the AF-CHF trial.

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Methods

Study population. Inclusion criteria for the AF-CHF trial were previously described (3). In short, patients were required to have a history of electrocardiographically documented AF, a left ventricular ejection fraction ≤35%, and New York Heart Association (NYHA) functional class II to IV symptoms within 6 months of randomization or class I symptoms if the

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Abbreviations and Acronyms

AF = atrial fibrillation

CHF = congestive heart failure

MCS = Mental Component Summary

NYHA = New York Heart Association

PCS = Physical Component Summary

SF-36 = Short Form-36

left ventricular ejection fraction was ≤25% or if the patient was hospitalized for CHF in the preceding 6 months. Patients were excluded if they were expected to live <1 year, had persistent AF for >12 months, were slated for heart transplantation within 6 months, or had decompensated CHF in the 48 h preceding randomization.

The rhythm-control strategy consisted of using antiarrhythmic drugs, predominantly amiodarone, and electrical cardioversion as needed, to maintain sinus rhythm. With the rate-control strategy, atrioventricular nodal blocking agents were prescribed to control the ventricular response rate during AF, without specific measures to restore or maintain sinus rhythm. Targeted heart rates were <80 beats/min at rest and <110 beats/min during 6-min walk tests. The study protocol was approved by each center's institutional review board, and all patients provided written informed consent.

Quality of life. To assess quality of life, the Medical Outcomes Short Form-36 (SF-36) questionnaire was administered to patients speaking English, French, Spanish, Portuguese, or Danish at baseline and at 4 months. The pre-defined 4-month time frame was considered a reasonable trade-off to assess treatment effects while minimizing inaccuracies resulting from crossovers and attrition (3).

The SF-36 is a multipurpose, short-form health survey that incorporates 36 items and yields the following 8 subscales: 1) physical functioning; 2) general health; 3) bodily pain; 4) mental health; 5) role function: emotional; 6) vitality; 7) social functioning; and 8) role function: physical (4). Using predefined algorithms, scores from these subscales were transformed to create the Physical Component Summary (PCS) score and Mental Component Summary (MCS) score. Scores may range from 0 to 100, with higher values indicating better perceived health-related quality of life (5). These scores have been extensively validated (5,6).

Functional status. The NYHA functional class was determined at baseline, 3 weeks, 4 months, and at 4-month intervals thereafter until the end of follow-up (maximum 6 years). Six-min walk tests (7) were conducted at baseline, 3 weeks, 4 months, 1 year, and annually thereafter until 4 years.

Data analysis. The proportion of time spent in sinus rhythm was modeled as a continuous variable, as previously described (2). In short, time intervals between visits were divided into quartiles (2). Sinus rhythm or AF was assigned to each time point for every patient on the basis of electrocardiographic documentation and the investigators' determination of AF occurrence between visits. The proportion of time spent in sinus rhythm was calculated by dividing the total time in sinus rhythm by follow-up duration. Patients were divided into 2 groups based on whether their proportion of time spent in sinus rhythm was equal or superior (high prevalence), or inferior (low prevalence) to the median value.

Quality-of-life analyses were limited to compliant participants who successfully completed SF-36 questionnaires at baseline and 4 months. Baseline characteristics of patients who did and did not complete SF-36 questionnaires, those randomized to rhythm versus rate control, and groups with high versus low prevalence of sinus rhythm were compared by Student *t* tests or chi-square tests, where appropriate. Quality-of-life analyses were completed for each of the 8 SF-36 subscales and PCS and MCS composite scores. Intrapatient improvements in quality of life from baseline to 4 months were compared by paired Student *t* tests separately for patients randomized to rhythm versus rate control, and in patients with high versus low prevalence of sinus rhythm. Differences in the degree of change in quality of life were assessed by analyses of covariance comparing changes from baseline to 4 months, using baseline scores as a covariate. Baseline variables associated with higher quality of life scores on follow-up were assessed in univariate and multivariate linear regression models. Variables significant at the 0.2 level in univariate analyses were considered in automated backward selection multivariate models. Variables associated with p values <0.01 were retained in the final models.

The proportion of time spent in sinus rhythm was modeled as a covariate in multivariate linear regression models for each of the 8 SF-36 subscales and PCS and MCS. To assess the independent predictive value of proportion of time spent in sinus rhythm, this parameter was included in automated backward selection multivariate models that retained variables associated with p values <0.01.

Generalized estimating equations and repeated-measures analysis of variance were used to assess NYHA functional class and 6-min walk distance, respectively. In generalized estimating equation analyses, an exchangeable correlation structure was specified. Due to the multiplicity of calculations, 2-tailed p values <0.01 were considered statistically significant. Analyses were performed using SAS release 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

Baseline characteristics. From the 1,376 patients enrolled in the AF-CHF trial, 833 patients completed the baseline quality-of-life assessment before randomization. Of these, 749 patients (66 ± 11 years of age, 82.9% male) also completed the 4-month follow-up questionnaire. Differences in baseline characteristics of participants in the quality-of-life analysis and nonparticipants are summarized in Table 1. The cardiovascular mortality rate was higher in nonparticipants compared with participants (p = 0.0007), with no differences in worsening heart failure (p = 0.5661)

Table 1 Baseline Characteristics in the Subgroup of Patients From the AF-CHF Trial Who Were and Were Not Included in the Quality-of-Life Substudy

Characteristic	Patients in QoL Substudy (n = 749)	Patients Not in QoL Substudy (n = 627)	p Value*
Age at randomization, yrs	66 ± 11	68 ± 11	<0.0001
Body mass index, kg/m^2	28.2 ± 5.5	27.6 ± 4.9	0.0511
Male	82.9	80.2	0.1993
Coronary artery disease	44.2	52.1	0.0035
Hypertension	43.9	52.2	0.0023
Diabetes	19.0	22.5	0.1067
Stroke or transient ischemic attack	8.0	10.2	0.1564
Left ventricular ejection fraction	26.5 ± 6.3	27.3 ± 5.7	0.0074
Paroxysmal AF	31.1	31.6	0.8356
History of atrial fibrillation, months			0.0006
0–6	58.9	54.2	
6–12	18.2	26.6	
>12	23.0	19.1	
QRS duration, ms	114 ± 30	114 ± 30	0.9377
ACE inhibitor or ARB	96.1	94.9	0.2689
Digoxin	63.3	65.7	0.3494
Beta-blocker	83.0	73.8	<0.0001
Antiarrhythmic drug	46.5	40.2	0.0195
Statin	40.2	45.3	0.0563
Aldosterone antagonist	39.4	51.2	<0.0001
Oral anticoagulant	90.3	86.0	0.0137
Antiplatelet agent	36.9	43.4	0.0137
Left atrium size, mm	49 ± 7	50 ± 8	0.0424
Moderate or severe mitral regurgitation	38.6	37.5	0.0082
Serum sodium, mmol/l	139 ± 4	139 ± 4	0.6723
Serum creatinine, μmol/l	109 ± 34	116 ± 49	0.0035
Implantable cardioverter-defibrillator	7.3	6.7	0.6418

Values are median ± SD or %. *p < 0.01 was considered statistically significant.
ACE = angiotensin-converting enzyme; AF = atrial fibrillation; ARB = angiotensin receptor blocker; QoL = quality of life.

or stroke (p = 0.1564). As shown in Table 2, baseline characteristics of participants randomized to rhythm- versus rate-control treatment strategies were similar.

Quality of life: rhythm versus rate control. Composite scores for physical and mental health improved significantly from baseline to 4 months in both rhythm- and rate-control groups. This improvement was consistent across all domains of the SF-36, as summarized in Table 3. However, a similar degree of improvement in quality of life was observed in rate- and rhythm-control groups. The comparative degree of change remained nonsignificant on all subscales.

An analysis that excluded the 118 patients (15.8%) who crossed over (83 from rhythm control, 35 from rate control) yielded similar results, with no significant difference in any quality-of-life metric compared with the primary intention-to-treat approach. Moreover, amiodarone discontinuation due to side effects (n = 14) was not associated with lower quality-of-life scores.

Quality of life: high versus low prevalence of sinus rhythm. Of 749 patients who completed SF-36 forms at baseline and 4-month visits, the proportion of time spent in sinus rhythm could be ascertained in 738 (98.5%), irrespective of randomized treatment assignment. Compared with patients with a low (<61%) prevalence of sinus rhythm, patients with a high (≥61%) prevalence of sinus rhythm had significantly lower body mass indexes (p = 0.0002), a shorter history of AF (p < 0.0001), and a smaller left atrium (p = 0.0020) and were more likely to have paroxysmal forms of AF (p < 0.0001). They were less likely to receive anticoagulation therapy (p = 0.0002), with a trend toward a higher prevalence of stroke (10.35% vs. 5.93%, p = 0.0279).

As noted in Table 4, most quality-of-life scores significantly improved in both groups. In patients with a high prevalence of sinus rhythm, all subscores improved. In patients with a low prevalence of sinus rhythm, all subscores improved except for "bodily pain" and "mental health." Nonsignificant trends toward greater improvement in PCS

Table 2 Baseline Characteristics of Patients Randomized to Rhythm- Versus Rate-Control Strategies and Included in the Quality-of-Life Analysis

	Rhythm Control (n = 371)	Rate Control (n = 378)	p Value*
Age at randomization, yrs	65 ± 12	66 ± 11	0.3950
Body mass index, kg/m^2	28.0 ± 5.6	28.4 ± 5.4	0.2795
Male	80.3	85.5	0.0624
Coronary artery disease	44.6	43.8	0.8198
Hypertension	45.6	42.3	0.3740
Diabetes	17.3	20.6	0.2374
Stroke or transient ischemic attack	9.4	6.6	0.1552
Left ventricular ejection fraction	26.5 ± 6.5	26.4 ± 6.0	0.8937
Paroxysmal AF	32.6	29.6	0.3776
History of atrial fibrillation, months			0.4436
0–6	61.2	56.6	
6–12	17.3	19.0	
>12	21.6	24.3	
QRS duration, ms	111 ± 30	116 ± 30	0.0381
ACE inhibitor or ARB	96.5	95.8	0.6052
Digoxin	63.6	63.0	0.8539
Beta-blocker	84.1	82.0	0.4468
Antiarrhythmic drug	47.4	45.5	0.5952
Statin	38.8	41.5	0.4477
Aldosterone antagonist	36.1	42.6	0.0698
Oral anticoagulant	88.4	92.1	0.0919
Antiplatelet agent	37.2	36.5	0.8451
Left atrium size, mm	48.2 ± 7.3	49.2 ± 7.0	0.0857
Moderate or severe mitral regurgitation	26.5	34.5	0.0206
Serum sodium, mmol/l	139 ± 4	140 ± 3	0.0742
Serum creatinine, μmol/l	109 ± 35	110 ± 32	0.5728
Implantable cardioverter-defibrillator	7.5	7.1	0.8320

Values are median ± SD or %. *p < 0.01 was considered statistically significant.
Abbreviations as in Table 1.

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Table 3 Analyses of Quality of Life Comparing Covariance Changes From Baseline to 4 Months in Rate- Versus Rhythm-Control Groups

Parameter	Rhythm Control (n = 371)				Rate Control (n = 378)				Between-Group p Value
	Baseline	Follow-Up	Change*	p Value†	Baseline	Follow-Up	Change*	p Value†	
Physical functioning	20.7 ± 5.0	21.7 ± 5.2	1.2 ± 0.2	<0.0001	20.0 ± 5.1	21.3 ± 4.9	1.2 ± 0.2	<0.0001	0.9756
General health	14.7 ± 4.0	15.8 ± 4.3	1.1 ± 0.2	<0.0001	14.7 ± 4.0	15.7 ± 4.2	0.9 ± 0.2	<0.0001	0.5979
Bodily pain	8.9 ± 2.7	9.4 ± 2.6	0.5 ± 0.1	0.0103	8.8 ± 2.7	9.1 ± 2.6	0.3 ± 0.1	0.0366	0.2444
Mental health	22.0 ± 4.8	22.7 ± 4.9	0.6 ± 0.2	0.0065	22.3 ± 4.9	22.9 ± 4.6	0.7 ± 0.2	0.0039	0.7823
Role function: emotional	4.9 ± 1.2	5.2 ± 1.2	0.3 ± 0.1	<0.0001	4.8 ± 1.2	5.1 ± 1.2	0.2 ± 0.1	0.0001	0.2084
Vitality	13.6 ± 4.1	14.8 ± 4.2	1.3 ± 0.2	<0.0001	13.4 ± 3.9	14.4 ± 4.1	1.0 ± 0.2	<0.0001	0.2449
Social functioning	7.3 ± 2.1	7.9 ± 2.0	0.6 ± 0.1	<0.0001	7.2 ± 2.1	7.8 ± 2.0	0.5 ± 0.1	<0.0001	0.4611
Role function: physical	5.4 ± 1.6	5.9 ± 1.7	0.7 ± 0.1	<0.0001	5.1 ± 1.5	5.7 ± 1.7	0.6 ± 0.1	<0.0001	0.4381
PCS score	37.4 ± 9.3	40.2 ± 10.3	2.9 ± 0.4	<0.0001	35.8 ± 9.4	38.9 ± 10.1	3.2 ± 0.4	<0.0001	0.6442
MCS score	47.4 ± 10.5	49.9 ± 10.4	2.3 ± 0.5	<0.0001	47.8 ± 10.0	49.6 ± 9.2	1.9 ± 0.4	0.0003	0.5310

*Adjusted values using the baseline score as a covariate are reported for the change in quality of life subscales from baseline to 4 months. †Intrapatient changes in quality of life from baseline to 4 months were compared by paired Student *t* tests.

MCS = Mental Composite Summary; PCS = Physical Composite Summary.

(p = 0.0332) and MCS (p = 0.0652) scores were observed in patients with a higher compared with lower prevalence of sinus rhythm. Patients with lower MCS values at baseline were more likely to improve.

Univariate and multivariate predictors of a lower PCS score on follow-up are listed in Table 5. A trend toward better self-perceived health favored the rhythm-control treatment arm (p = 0.0479), without reaching the threshold for significance (p < 0.01). A higher prevalence of sinus rhythm was associated with a nonsignificant trend toward higher PCS scores on follow-up (p = 0.0313). No factor was significantly associated with a lower MCS score on follow-up in univariate analyses, including higher prevalence of sinus rhythm (p = 0.3602) and rhythm versus rate control (p = 0.7292) or in multivariate analyses.

Six-min walk test. The 6-min walk test was completed by 1,099, 1,083, 1,054, and 948 patients at baseline, 3 weeks, 4 months, and 1 year, respectively. The 6-min walk distance progressively increased from 317.0 ± 120.0 m to 373.7 ± 118.4 m in the rhythm-control group over a 12-month period and from 319.9 ± 120.7 m to 359.4 ± 117.7 m in the rate-control group, with no significant treatment effect (p = 0.2328). Similar results were obtained by comparing changes in the 6-min walk test distance in the high (318.3 ± 125.3 m to 372.0 ± 119.3 m) versus low (319.2 ± 115.9 m to 359.2 ± 118.2 m) prevalence of sinus rhythm group (p = 0.1308).

NYHA functional class. All 1,376 patients had complete NYHA functional class data at baseline. NYHA functional class III or IV symptoms were present in 215 patients (31.5%) and 216 patients (31.1%) randomized to rhythm and rate control, respectively. Of the remaining 1,134 patients at 12 months of follow-up, 100 (17.9%) and 116 (20.1%) in the rhythm- and rate-control groups, respectively, had NYHA functional class III or IV symptoms. The assigned treatment arm was not associated with an improvement in functional class (p = 0.1712).

From a total of 1,316 patients in whom the proportion of time spent in sinus rhythm was assessed, 178 patients (26.9%) with a high and 229 patients (35.1%) with a low prevalence of sinus rhythm had NYHA functional class III or IV symptoms at baseline. At 12 months of follow-up, the

Table 4 Analyses of Quality of Life Comparing Covariance Changes From Baseline to 4 Months According to Whether Patients Had a High or Low Prevalence of Sinus Rhythm

Parameter	High Prevalence of Sinus Rhythm (n = 367)				Low Prevalence of Sinus Rhythm (n = 371)				Between-Group p Value
	Baseline	Follow-Up	Change*	p Value†	Baseline	Follow-Up	Change*	p Value†	
Physical functioning	20.9 ± 4.9	22.1 ± 5.1	1.4 ± 0.2	<0.0001	19.9 ± 5.2	21.0 ± 4.9	1.0 ± 0.2	<0.0001	0.1555
General health	14.7 ± 4.0	15.9 ± 4.3	1.2 ± 0.2	<0.0001	14.8 ± 4.1	15.6 ± 4.2	0.8 ± 0.2	<0.0001	0.1044
Bodily pain	8.9 ± 2.7	9.4 ± 2.6	0.5 ± 0.1	0.0010	8.9 ± 2.7	9.0 ± 2.6	0.2 ± 0.1	0.3263	0.0595
Mental health	21.8 ± 4.8	22.8 ± 4.8	0.8 ± 0.2	0.0004	22.5 ± 4.9	23.0 ± 4.7	0.6 ± 0.2	0.0391	0.5938
Role function: emotional	4.9 ± 1.2	5.2 ± 1.1	0.4 ± 0.1	<0.0001	4.8 ± 1.2	5.0 ± 1.2	0.2 ± 0.1	0.0005	0.0186
Vitality	13.6 ± 4.0	15.1 ± 4.1	1.6 ± 0.2	<0.0001	13.3 ± 4.0	14.0 ± 4.2	0.7 ± 0.2	0.0008	0.0004
Social functioning	7.2 ± 2.1	8.0 ± 2.0	0.7 ± 0.1	<0.0001	7.4 ± 2.1	7.7 ± 2.0	0.4 ± 0.1	0.0015	0.0147
Role function: physical	5.4 ± 1.6	6.0 ± 1.7	0.8 ± 0.1	<0.0001	5.1 ± 1.4	5.6 ± 1.7	0.5 ± 0.1	<0.0001	0.0123
PCS	37.5 ± 9.2	40.8 ± 10.2	3.6 ± 0.4	<0.0001	35.8 ± 9.3	38.4 ± 10.2	2.2 ± 0.4	<0.0001	0.0332
MCS	47.1 ± 10.6	50.1 ± 10.0	2.8 ± 0.5	<0.0001	48.1 ± 10.0	49.4 ± 9.6	1.6 ± 0.4	0.0084	0.0652

*Adjusted values using the baseline score as a covariate are reported for the change in quality-of-life subscales from baseline to 4 months. †Intrapatient changes in quality of life from baseline to 4 months were compared by paired Student *t* tests.

Abbreviations as in Table 3.

Table 5 Univariate and Multivariate Predictors of a Poorer Physical Composite Score of Quality of Life at Follow-Up

	β Coefficient	Standardized β Coefficient	p Value*
Univariate analyses			
Rate vs. rhythm control	−1.3 ± 0.7	−0.1	0.0944
High vs. low prevalence of sinus rhythm	2.4 ± 0.8	0.1	0.0016
Age, per year	−0.11 ± 0.03	−0.13	0.0005
Body mass index, per kg/m^2	−0.3 ± 0.1	−0.1	<0.0001
Female	−4.9 ± 1.0	−0.2	<0.0001
Coronary artery disease	−3.1 ± 0.7	−0.2	<0.0001
Hypertension	−2.5 ± 0.7	−0.1	0.0007
Statins	−2.8 ± 0.8	−0.1	0.0002
Diabetes	−3.5 ± 0.9	−0.1	0.0002
Stroke or transient ischemic attack	−3.3 ± 1.4	−0.1	0.0163
Paroxysmal atrial fibrillation	−1.1 ± 0.8	−0.05	0.1937
Oral anticoagulant	1.8 ± 1.3	0.1	0.1594
Antiplatelet agent	−1.8 ± 0.8	−0.1	0.0210
Left atrial size, per mm	−0.15 ± 0.05	−0.11	0.0068
Moderate or severe mitral regurgitation	−1.9 ± 0.8	−0.1	0.0211
Serum sodium, per mmol/l	0.17 ± 0.10	0.06	0.1075
Serum creatinine, per μmol/l	−0.04 ± 0.01	−0.1	0.0001
Multivariate analysis			
Body mass index, per kg/m^2	−0.2 ± 0.1	−0.1	0.0019
Female sex	−6.1 ± 1.0	−0.2	<0.0001
Coronary artery disease	−2.8 ± 0.8	−0.1	0.0003
Left atrium size, per mm	−0.16 ± 0.05	−0.12	0.0022
Serum creatinine, per μmol/l	−0.03 ± 0.01	−0.11	0.0048

Values are mean ± SE unless otherwise indicated.

NYHA functional class was more likely to improve in patients with a high prevalence of sinus rhythm ($p < 0.0001$). Notably, the greatest improvement in NYHA functional class occurred during the first 4 months and was most pronounced between baseline and the 3-week visit ($p < 0.0001$).

Discussion

The main finding of this quality-of-life and functional status analysis in patients with AF and CHF is the absence of superiority of 1 treatment strategy (i.e., rhythm vs. rate control) over the other. The modest benefit observed in patients with a higher proportion of time spent in sinus rhythm suggests that the potential for sinus rhythm is a marker of favorable outcomes. Interestingly, although patients with a higher prevalence of sinus rhythm were more likely to have paroxysmal AF and smaller left atria, a greater proportion experienced strokes. This likely reflects their lower likelihood of receiving anticoagulants and underscores the importance of adhering to anticoagulation guidelines, which presuppose a similar thromboembolic risk for paroxysmal and persistent forms of AF (8).

Quality of life. The degree of impairment in health-related quality of life in our study population with both AF and CHF was more pronounced than previously reported in patients with predominantly one or the other (6,9–12). Previous studies found that the reduction in quality of life associated with AF is similar to that of CHF (10,13,14). The associations between poorer quality of life, coronary artery disease, and diabetes noted in our study (Table 5) were previously reported in patients with AF (15,16). Improvements in quality of life with rhythm- and rate-control treatment strategies for AF have likewise been observed in patient populations principally without CHF (6,10,15–19). Various antiarrhythmic agents have yielded comparable results (10,15,16). Our findings corroborate and further extend the lack of superiority of one treatment strategy over the other in improving quality of life to patients with both AF and CHF.

Patients with a higher compared with lower proportion of time spent in sinus rhythm experienced modest improvements in mental and physical components of quality-of-life scores. These findings are consistent with previous AF ablation trials comparing interventional approaches with medical therapy (20–22) and to substudies of clinical trials assessing rhythm- versus rate-control treatment strategies (15,16,18). However, the largest such trial, the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study (19), which included 25% of participants (n = 716) in a pre-specified quality-of-life analysis (6), found that underlying rhythm at the follow-up visit was not predictive of quality of life. The authors hypothesized that benefits of sinus rhythm, if any, may be offset by the adverse effects of antiarrhythmic drugs (6,23). Inconsistencies with our results may reflect, in part, the different study populations, treatment strategies, and means of assessing underlying rhythm. Few patients in the AFFIRM trial had left ventricular dysfunction in contrast to all patients in AF-CHF. Unlike the AFFIRM trial, almost all patients in the rhythm-control arm of the AF-CHF trial received amiodarone. Finally, our study design permitted a more comprehensive classification scheme to quantify the proportion of time spent in sinus rhythm rather than relying exclusively on 1 electrocardiogram obtained at a single visit.

Functional capacity. Consistent with the quality-of-life analysis, the 6-min walk distance increased to a similar extent with rhythm- and rate-control treatment strategies and in patients with a high versus lower prevalence of sinus rhythm. Similarly, in a pre-specified substudy of the AFFIRM trial, the 6-min walk test distance improved in both treatment arms (24). However, the extent of improvement was modestly superior in the rhythm control group (94 feet; adjusted $p = 0.049$). Other trials have reported a trend toward longer distances walked in patients with sinus rhythm compared with AF for up to 2 years of follow-up, with benefits dissipating thereafter (17). In a manner similar to the AFFIRM trial (24), the NYHA functional class improved in both treatment arms, with no difference between rhythm- and rate-control strategies. The greater improvement in NYHA functional class in patients with a

high prevalence of sinus rhythm was not associated with an objective increase in the 6-min walk distance, perhaps reflecting an enhanced subjective perception of functional capacity.

Study limitations. Although the current analysis is a prespecified substudy of the AF-CHF trial, assessment of quality of life was necessarily limited to participants who completed questionnaires of interest. To maximize catchment conditions, questionnaires were made available in 5 languages. Although differences between participants and nonparticipants affect generalizability, baseline characteristics of participants randomized to rhythm- and rate-control strategies were similar, such that comparisons remain internally valid.

Although the mean follow-up for the AF-CHF trial was 37 months, analyses of quality of life and functional status were limited to 4 and 12 months, respectively. Although this timeline is well suited to capture treatment effects, which are most pronounced during the initial months of therapy, results cannot be generalized to longer follow-up durations. Finally, the study was subject to limitations inherent in all observational studies in that multivariate analyses adjust for baseline imbalances and potential confounders but cannot control for unknown or unmeasured variables.

Conclusions

Quality of life and functional capacity in patients with AF and CHF are substantially impaired and improve to a similar extent with rate- and rhythm-control treatment strategies. A higher proportion of time spent in sinus rhythm is associated with a greater improvement in NYHA functional class and modest gains in health-related quality of life.

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Key Words: atrial fibrillation ■ functional capacity ■ heart failure ■ quality of life.