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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)