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Quality of Life in Atrial Fibrillation: Measurement Tools and Impact of Interventions

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Abstract

QoL in AF. Quality of life (QoL) is of central importance in atrial fibrillation as both a treatment goal and an endpoint in the evaluation of new therapies. QoL appears to be impaired in the majority of patients with AF. A number of interventions for AF have been shown to improve QoL, including pharmacologic and nonpharmacologic rate control, antiarrhythmic drugs, and nonpharmacologic rhythm control strategies. This paper will review the rationale, design, strengths, and limitations of the questionnaires most commonly used to assess QoL in AF studies, and present QoL outcomes from major studies of AF interventions.

Keywords

catheter ablation; atrial fibrillation; quality of life; epidemiology; clinical trials

Introduction

The issue of quality of life (QoL) is critically important in both the treatment of atrial fibrillation (AF) and in the study of new therapies for AF. Since few interventions for AF have been shown to reduce mortality and serious morbidity, the treatment of AF remains focused largely on controlling symptoms and improving or preserving QoL. For AF clinical trials, end points focused exclusively on the assessment of rhythm status (e.g., time to first recurrence or rhythm at the end of some follow-up interval) suffer from the potential weakness of not accurately reflecting the degree to which patients feel symptomatically improved by the intervention under study.¹ The evaluation of QoL has therefore also become a crucial issue in AF clinical studies.^{2,3} Given the primacy of QoL issues in AF, we believe practitioners and researchers would benefit from a deeper understanding of QoL methods and published outcomes in AF patients.

Defining QoL

In 1948, the World Health Organization defined health as being not only the absence of disease and infirmity but also the presence of physical, mental, and social well-being.⁴ QoL is a subjective phenomenon that is based on individual perception, developed through experiences, beliefs, and expectations.^{4,5} Some authors conceptualize the combination of symptoms, functional status, and QoL (the latter referring specifically to the relationship between actual and desired health and functioning) using the broader term “health status,”⁶ while others

consider the term QoL, or more precisely “health-related QoL” as incorporating all of these elements. Thus, the distinction between symptom scales and true QoL measures is often indistinct, but it is generally recognized that symptoms, functional status, and patients’ health perceptions are all important.

Measuring QoL

While there is great variation in how QoL is evaluated, there is consensus that QoL, like intelligence, has multiple dimensions (“domains”), is measurable, and is most appropriately measured by asking the individual.⁷ In order to achieve efficient, consistent results and facilitate comparison across populations and over time, the use of standardized questionnaires has become the most common approach. Some QoL questionnaires (or “instruments”) are designed to assess a wide range of domains applicable to a variety of health states and are referred to as “generic” measures. Generic measures permit ready comparison of QoL in disparate populations and are the most likely to have available normative data.

Disease-specific instruments focus on domains or symptoms most relevant to the disease or condition under study and are sometimes more appropriate for clinical trials owing to their greater sensitivity to change.⁸ Investigators commonly take advantage of the relative strengths of each by using a combination of generic and disease-specific instruments in a given study, resulting in the most comprehensive perspective of QoL in that population.

Prior to widespread adoption, QoL instruments generally go through a careful validation process. Included in this process are assessments of the questionnaires’ validity (that they measure what they purport to measure) and reliability (that results are reproducible).

Measuring QoL in AF

At least 34 different QoL instruments have been used in published AF studies to date (see Table 1), reflecting an obvious lack of consensus on a single optimal approach. This variability unfortunately sometimes hinders comparisons between studies. While a detailed description of all of these measures is beyond the scope of this paper, we will review several of the most important and commonly used instruments.

The most consistently used generic QoL scales in AF studies include the Medical Outcomes Study Short Form Health Survey (SF-36), the Short Form-12 (SF-12), which is derived from the SF-36, and the EuroQOL/EQ-5D. The SF-36 consists of a 36 item questionnaire that assesses eight health concepts: general health perception, physical functioning, social functioning, role limitations due to physical problems, bodily pain, mental health, role limitations due to emotional problems, and vitality.⁹ In addition to these eight subscales, the SF-36 also generates physical (PCS) and mental component summary (MCS) scores. The SF-36 is the most widely validated generic instrument available and has been used to study a great variety of cardiac and noncardiac conditions.¹⁰ It has performed reasonably well in a number of prior AF studies (see below), with the largest changes typically seen in the scales relating to physical function. This track record has led to the selection of the SF-36 in most recent major AF studies.

The SF-12 was derived from the SF-36 by selecting the 12 questions from the original survey that appeared to carry the most information.¹¹ The PCS and MCS scores from the SF-12 have been shown to correlate highly with those derived from the SF-36.

The EuroQOL is a descriptive system covering five dimensions of health status: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each rated on three levels ranging from “no problems” to “severe problems.”¹² It has been extensively validated, has a

long track record of use in a variety of medical conditions, and has the additional advantage of having a well-accepted method (the EQ-5D) for transforming raw scores to preference-based utility weights.¹³

Strengths of the generic tools for measuring QoL in AF studies include their extensive validation, generalizability, and the wealth of data already collected on AF patients. The greatest weakness of the generic measures is that, by design, they reflect general health and functioning, and, therefore, scores among AF patients are strongly influenced by patient demographics and comorbid conditions.¹⁴ This makes the generic measures potentially less sensitive to change in the many older AF patients who have multiple health problems.

Although a number of AF studies have used cardiac-specific questionnaires (Table 1), only a few of these were specifically designed for AF patients. The most commonly used of these is the Arrhythmia Symptom Checklist: Frequency and Severity. The Symptom Checklist was developed in the late 1980s for evaluating the impact of early catheter ablation and pacing technologies on a variety of arrhythmias.⁵ The Symptom Checklist asks respondents to rate the frequency (from 0 to 4) and severity (from 1 to 3) of 16 symptoms commonly associated with AF. Frequency and severity scores therefore range from 0 to 64 and 0 to 48, respectively.

The Symptom Checklist is straightforward to use, sensitive to change, and has been utilized in a growing number of AF studies. Shortcomings of the Symptom Checklist are the nonspecific nature of a number of the symptoms (e.g., “headache,” “trouble concentrating,” “poor appetite”), and the lack of assessment of functional status or patient satisfaction. For these reasons, the Symptom Checklist is probably inadequate as a stand-alone QoL measure, and some investigators have elected to construct their own symptom scales using a smaller number of items more specific to AF.^{15–17} Published validation data for the AF specific scales are very limited.

QoL in AF: Population Studies

AF is sometimes entirely asymptomatic: 12–21% of patients with documented AF entered into several large studies reported no symptoms on baseline questioning.^{14,18,19} It has also been shown recently that patients with symptomatic paroxysmal AF frequently have asymptomatic episodes both before and after rhythm control interventions.^{20,21} The impact of AF on QoL is therefore strongly influenced by the segment of the AF population that is studied.

Most of the published QoL literature in AF is derived from studies of rate and/or rhythm control interventions, and, therefore, skewed toward selection of highly symptomatic patients. Not surprisingly, baseline scores on standard measures such as the SF-36 tend to be lower than population norms in these studies.^{5,7,22–24} Nonetheless, several important studies of QoL in less selected AF patients have also been completed, and suggest that the majority of AF patients do in fact have reduced QoL.

In a cross-sectional study, Dorian *et al.*²⁵ measured QoL in 142 relatively young (mean age 58) AF patients referred to four arrhythmia clinics using the SF-36, Specific Activity Scale, and AF Symptom Checklist. The AF patients had significantly worse scores on all scales than healthy controls, and similar scores to patients with moderate heart failure or prior coronary events.

Our group recently published QoL outcomes for a large (n = 963) inception cohort of AF patients followed for up to 2.5 years in the FRACTAL registry.¹⁴ At the time of their first AF episodes, FRACTAL patients had SF-12 derived PCS and MCS scores below age-adjusted population norms, and AF Symptom Checklist scores well above historical healthy controls, although, as expected, scores were not as poor as in typical clinical trials. With treatment, QoL

scores improved to approximate population norms within 3–6 months, and generally remained stable thereafter.

It should be noted that not all population studies have found impaired QoL in AF patients. One important group in whom questions persist about the specific impact of AF on overall QoL is the elderly (see below). In one series, 52 “elderly” (mean age 77) patients with “chronic” AF were compared with 48 age-matched controls in sinus rhythm.²⁶ No differences were found on the SF-36, or in exercise duration or LVEF between these groups.

Factors Influencing QoL in AF Patients

Many studies of QoL in AF patients have relied primarily on “generic” instruments—one would therefore expect results to be influenced by age and comorbid medical conditions. In FRACTAL, we found NYHA class, valvular heart disease, and chronic pulmonary disease to have the strongest impact on QoL scores.¹⁴ NYHA class was also found to be an independent predictor of QoL scores by the CTAF investigators,¹ and the baseline presence of coronary artery disease and diabetes were found to predict worsened QoL over time in the RACE trial.²⁴ The potential for comorbid medical conditions to impact scores on generic QoL instruments points to the need for disease-specific scales when studying AF interventions.

Women with AF consistently report significantly poorer QoL and greater symptom burden than men. This was first reported by the CTAF investigators²² using the SF-36, Symptom Checklist, and Duke Activity Status Index, and was confirmed in the RACE trial²⁷ and a cross-sectional study of over 5000 Europeans with recently documented AF.²⁸ Although the gender disparity in QoL scores from these reports was striking, little to no adjustment was made for demographic and clinical factors known to differ between women and men with AF.²⁹ We recently compared QoL by gender in the FRACTAL registry and found that significant differences in PCS, MCS, and Symptom Checklist scores persisted after extensive adjustment for baseline demographic and comorbid health conditions.¹⁴

Age likely has an important impact on QoL scores in AF patients with the effect potentially depending on the assessment tool used. In general, older patients report lower generic QoL scores, particularly on scales related to physical functioning.⁹ Empirical evidence, however, suggests that older patients may have a lesser symptom burden specifically from AF (e.g., lower Symptom Checklist scores) than younger patients.¹⁴ Younger patients may therefore be more likely than older patients to show improvements in QoL with rhythm control interventions, as observed in the RACE trial, in which age <69 predicted a greater likelihood of QoL improving over time.²⁴

Impact of Rate Control on QoL

A number of nonrandomized and randomized studies, most of them involving the strategy of AV junction ablation and permanent pacemaker implantation in patients poorly controlled by medical therapy, have assessed the impact of ventricular rate control on QoL in AF patients. As previously reviewed,³⁰ most of these studies were small (<50 patients), lacked appropriate controls, and used a variety of mainly generic and often not previously validated QoL assessment tools.

The largest nonrandomized “ablate and pace” study assessed 156 patients with “chronic, recurrent, or paroxysmal” AF refractory to drug therapy using the Health Status Questionnaire (essentially identical to the SF-36), Symptom Checklist, and Quality of Life Index, Cardiac Version.³¹ At 3 and 12 months postprocedure, all eight SF-36 subscales showed marked improvement over baseline, and >30% reductions were seen in Symptom Checklist scores.

The AIRCRAFT study³² was the largest randomized study to compare AV junction ablation and pacing with pharmacologic rate control. AIRCRAFT randomized 99 patients with permanent AF and mild to moderate symptoms to these two strategies, and an 18% relative reduction in CAST QoL scores (an arrhythmia symptom scale) was reported favoring “ablate and pace.” However, no significant differences were found using two other generic instruments, suggesting the overall differences were limited.

Impact of Cardioversion and Antiarrhythmic Drugs on QoL

Prior to the completion of randomized rate versus rhythm control studies (see below), remarkably little data were available regarding the impact of cardioversion and antiarrhythmic drugs on QoL in AF patients. One series of 111 patients referred for cardioversion at a single center found 30% and 19% improvements on EuroQol visual analogue scores 1 and 12 months after successful cardioversion among patients who remained in sinus rhythm, while scores slightly decreased in patients who experienced AF recurrence.³³

Two randomized trials comparing alternative antiarrhythmic drugs for patients with persistent³⁴ or both paroxysmal and persistent AF¹ included QoL outcomes, as summarized in Table 2. The CTAF trial, which randomized patients to amiodarone, sotalol, or propafenone, reported improvements in all QoL measures from baseline to 3 months across all patients, but only one of the SF-36 scales (role physical) changed by >10%. The relative changes were somewhat larger for Symptom Checklist scores. No significant differences were found between the randomized groups on any scale. The SAFE-T trial, which included a placebo group in addition to amiodarone and sotalol arms, did not fully report an intention-to-treat analysis, but mentioned no significant between-group findings in their initial publication.³⁴

Both the CTAF and SAFE-T investigators reported posthoc analyses of QoL outcomes based on whether or not patients successfully maintained sinus rhythm.^{1,35} In both cases, the expectation that QoL was better when patients remained in sinus rhythm appeared to be confirmed. However, the magnitude of differences in both studies was modest: 15–20% relative changes in Symptom Checklist scores were seen in both studies, and in SAFE-T only four of eight and two of eight of SF-36 subscales showed statistically significant differences between SR and AF groups at 8 weeks and 12 months, respectively. In addition, these posthoc analyses are no longer randomized comparisons, and are therefore subject to potential confounding by factors that could be associated with the risk of recurrence. Multivariate adjustment could further attenuate the observed differences.

Rate Versus Rhythm Control Studies

QoL was evaluated in four major studies comparing pharmacologic rate control with antiarrhythmic drugs (see Table 2). Across these studies, no significant QoL benefits were observed with rhythm control strategies, compared with rate control.

The PIAF¹⁶ and STAF²³ trials were medium-sized randomized comparisons of antiarrhythmic drugs versus pharmacologic rate control. In both studies, moderate improvements in QoL were seen across several SF-36 subscales from baseline to 12 months for all patients, with no statistically significant differences between treatment groups. Qualitatively similar findings were found in the RACE and AFFIRM QoL substudies,^{7,24} despite their larger size and longer follow-up durations. In AFFIRM, small improvements in most QoL scores were seen within the first year with, for most scales, slight gradual declines over the 4 years of follow-up. At no point were differences observed between the randomized groups.

As with the CTAF and SAFE-T trials, three of the four major rate versus rhythm control studies performed posthoc analyses comparing QoL in patients based on rhythm status. Somewhat surprisingly, two of them—PIAF and AFFIRM—still found no differences in QoL when comparing patients by rhythm status,^{7,10} whereas the RACE investigators did report that sinus rhythm at the end of follow-up was associated with improved QoL.²⁴ It should again be emphasized that these are nonrandomized comparisons, and the adequacy of adjustment for potential confounding in these analyses is not clear.

There are a few important limitations of the QoL assessments in the rate versus rhythm control studies. First, none of these studies were true comparisons of successful sinus rhythm maintenance versus AF with rate control, since many rhythm control patients had recurrent AF, and some rate control patients remained in sinus rhythm. We further believe the rate versus rhythm control studies were biased toward not finding differences in QoL due to patient selection, because patients who knew they would feel poorly with a rate control strategy may not have been likely to agree to randomization. For both reasons, the question of whether a highly effective rhythm control strategy could improve QoL to a greater extent than rate control remains open.

AF Ablation Studies

A number of nonpharmacologic approaches to sinus rhythm maintenance have been shown to improve QoL in AF patients, mainly in nonrandomized series, including the surgical MAZE procedure.³⁶ Attention in recent years has focused on rapidly evolving approaches to catheter-based ablation.

As shown in Table 3, seven nonrandomized series^{37–43} and two relatively small randomized studies^{15,44} that included QoL and/or symptom assessment among their end points have been published. These studies involved a variety of ablation techniques and included patients with both paroxysmal and persistent forms of AF. Subjects typically were highly symptomatic and had previously failed antiarrhythmic drugs. All of the studies used the SF-36 and/or some type of symptom checklist.

Each of the nonrandomized studies reported positive changes in all or nearly all SF-36 subscales in patients following ablation. The magnitude of change was usually quite large, e.g., 10–20 points in PCS/MCS scores (scored to a population norm of 50) and 20–40 points in individual SF-36 subscales (scored up to 100). The randomized studies likewise showed large improvements in QoL following ablation, which in one of the studies were significantly larger than the gains achieved with antiarrhythmic drugs.⁴⁴

Some degree of caution is needed in interpreting the QoL outcomes presently available for catheter ablation studies. First, it appears that some of the symptomatic benefit of ablation is not due to control of the rhythm, as investigators have shown an increase in the frequency of asymptomatic AF following ablation.²¹ Second, there is great potential for placebo and “nocebo” effects³ based on the subjective nature of QoL endpoints and the lack of blinding in these studies. It has been convincingly shown that invasive cardiac procedures, even under “sham” conditions, can improve patient reported well-being.^{45,46} Third, catheter ablation for AF has not been directly compared with sustained treatment with the most effective antiarrhythmic drug for AF (amiodarone) or with the strategy of pacing and AV junction ablation. Despite these caveats, catheter ablation for AF does appear to be more effective than antiarrhythmic drugs for rhythm control, and available data suggest that successful procedures are associated with large gains in QoL in highly symptomatic patients.

Future Directions

QoL measures have become a routine outcome of AF clinical trials. This will continue as alternative ablation energy sources (e.g., laser, ultrasound, cryothermal) and catheter designs are tested, and ablation in general is evaluated in comparison with alternative treatments in wider segments of the AF population. However, the assessment of QoL is not standardized, and available tools for measuring QoL in AF patients are not ideal. We believe that development of a comprehensive disease-specific QoL measurement tool that goes beyond the current symptom checklist approach could be useful in the conduct of future studies. Whether or not this occurs, we are convinced that clinicians who face decisions regarding AF management should have some familiarity with QoL and its measurement in order to put published claims in the proper context.

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References

1. Dorian P, Paquette M, Newman D, Green M, Connolly SJ, Talajic M, Roy D. Quality of life improves with treatment in the Canadian Trial of Atrial Fibrillation. *Am Heart J* 2002;143:984–990. [PubMed: 12075253]
2. McNamara RL, Brass LM, Drozda JP Jr, Go AS, Halperin JL, Kerr CR, Levy S, Malenka DJ, Mittal S, Pelosi F Jr, Rosenberg Y, Stryer D, Wyse DG, Radford MJ, Goff DC Jr, Grover FL, Heidenreich PA, Peterson ED, Redberg RF. ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association task force on clinical data standards. *Circulation* 2004;109:3223–3243. [PubMed: 15226233]
3. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJG, Damiano RJ, Davies DW, Haines DE, Haissaguerre M, Iesaka Y, Jackman W, Jais P, Kottkamp H, Kuck KH, Lindsay BD, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Natale A, Pappone C, Prystowsky E, Raviele A, Ruskin JN, Shemin RJ. HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Personnel, Policy, Procedures and Follow-Up. *Heart Rhythm* 2007;4:816–861. [PubMed: 17556213]
4. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. *N Engl J Med* 1996;334:835–840. [PubMed: 8596551]
5. Bubien RS, Knotts-Dolson SM, Plumb VJ, Kay GN. Effect of radiofrequency catheter ablation on health-related quality of life and activities of daily living in patients with recurrent arrhythmias. *Circulation* 1996;94:1585–1591. [PubMed: 8840848]
6. Spertus JA, Tooley J, Jones P, et al. Expanding the outcomes in clinical trials of heart failure: The quality of life and economic components of the EPHEsus (EPherone's neuroHormonal Efficacy and Survival Study). *Am Heart J* 2002;143:636–642. [PubMed: 11923800]
7. The AFFIRM Investigators. Quality of life in atrial fibrillation: The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;149:112–120. [PubMed: 15660042]
8. Luderitz B, Jung W. Quality of life in patients with atrial fibrillation. *Arch Intern Med* 2000;160:1749–1757. [PubMed: 10871967]
9. Ware, JEJ. SF-36 Health Survey: Manual and Interpretation Guide. Boston: The Health Institute, New England Medical Center; 1993.
10. Gronefeld GC, Lilienthal J, Kuck KH, Hohnloser SH. Impact of rate versus rhythm control on quality of life in patients with persistent atrial fibrillation. Results from a prospective randomized study. *Eur Heart J* 2003;24:1430–1436. [PubMed: 12909072]
11. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–233. [PubMed: 8628042]

12. The EuroQol Group. Euro-Qol: A new facility for measurement of health-related quality of life. *Health Policy* 1990;16:199–208. [PubMed: 10109801]
13. Rabin R, de Charro F. EQ-5D: A measure of health status from the EuroQol group. *Ann Med* 2001;33:337–343. [PubMed: 11491192]
14. Reynolds MR, Lavelle T, Essebag V, Cohen DJ, Zimetbaum P. Influence of age, sex, and atrial fibrillation recurrence on quality of life outcomes in a population of patients with new-onset atrial fibrillation: The Fibrillation Registry Assessing Costs, Therapies, Adverse events and Lifestyle (FRACTAL) study. *Am Heart J* 2006;152:1097–1103. [PubMed: 17161061]
15. Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F Jr, Bates ER, Lehmann MH, Vicedomini G, Augello G, Agricola E, Sala S, Santinelli V, Morady F. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;354:934–941. [PubMed: 16510747]
16. Hohnloser SH, Kuck KH, Lilienthal J. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): A randomised trial. *Lancet* 2000;356:1789–1794. [PubMed: 11117910]
17. Brignole M, Gianfranchi L, Menozzi C, Alboni P, Musso G, Bongiorni MG, Gasparini M, Raviele A, Lolli G, Paparella N, Acquarone S. Assessment of atrioventricular junction ablation and DDDR mode-switching pacemaker versus pharmacological treatment in patients with severely symptomatic paroxysmal atrial fibrillation: A randomized controlled study. *Circulation* 1997;96:2617–2624. [PubMed: 9355902]
18. Kerr CR, Boone J, Connolly SJ, Dorian P, Green M, Klein G, Newman D, Sheldon R, Talajic M. The Canadian Registry of Atrial Fibrillation: A noninterventional follow-up of patients after the first diagnosis of atrial fibrillation. *Am J Cardiol* 1998;82(7 suppl 1):82N–85N. [PubMed: 9671014]
19. Flaker GC, Belew K, Beckman K, Vidaillet H, Kron J, Safford R, Mickel M, Barrell P. Asymptomatic atrial fibrillation: Demographic features and prognostic information from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;149:657–663. [PubMed: 15990749]
20. Page RL, Tilsch TW, Connolly SJ, Schnell DJ, Marcello SR, Wilkinson WE, Pritchett EL. Asymptomatic or “silent” atrial fibrillation: Frequency in untreated patients and patients receiving azimilide. *Circulation* 2003;107:1141–1145. [PubMed: 12615792]
21. Hindricks G, Piorkowski C, Tanner H, Kobza R, Gerds-Li JH, Carbucicchio C, Kottkamp H. Perception of atrial fibrillation before and after radiofrequency catheter ablation: Relevance of asymptomatic arrhythmia recurrence. *Circulation* 2005;112:307–313. [PubMed: 16009793]
22. Paquette M, Roy D, Talajic M, Newman D, Couturier A, Yang C, Dorian P. Role of gender and personality on quality-of-life impairment in intermittent atrial fibrillation. *Am J Cardiol* 2000;86:764–768. [PubMed: 11018197]
23. Carlsson, Jo; Miketic, S.; Windeler, Ju; Cuneo, A.; Haun, S.; Micus, S.; Walter, S.; Tebbe, U.; Investigators, S. Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation: The Strategies of Treatment of Atrial Fibrillation (STAF) study. *J Am Coll Cardiol* 2003;41:1690–1696. [PubMed: 12767648]
24. Hagens VE, Ranchor AV, Van Sonderen E, Bosker HA, Kamp O, Tijssen JG, Kingma JH, Crijns HJ, van Gelder IC. RACE Study Group. Effect of rate or rhythm control on quality of life in persistent atrial fibrillation. Results from the Rate Control versus Electrical Cardioversion (RACE) Study. *J Am Coll Cardiol* 2004;43:241–247. [PubMed: 14736444]
25. Dorian P, Jung W, Newman D, Paquette M, Wood K, Ayers GM, Camm J, Akhtar M, Luderitz B. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: Implications for the assessment of investigational therapy. *J Am Coll Cardiol* 2000;36:1303–1309. [PubMed: 11028487]
26. Howes CJ, Reid MC, Brandt C, Ruo B, Yerkey MW, Prasad B, Lin C, Peduzzi P, Ezekowitz MD. Exercise tolerance and quality of life in elderly patients with chronic atrial fibrillation. *J Cardiovasc Pharmacol Ther* 2001;6:23–29. [PubMed: 11452333]
27. Rienstra M, Van Veldhuisen DJ, Hagens VE, Ranchor AV, Veeger NJGM, Crijns HJGM, Van Gelder IC. Gender-related differences in rhythm control treatment in persistent atrial fibrillation. Data of the Rate Control versus Electrical Cardioversion (RACE) study. *J Am Coll Cardiol* 2005;46:1298–1306. [PubMed: 16198847]

28. Dagres N, Nieuwlaat R, Vardas PE, Andresen D, Levy S, Cobbe S, Kremastinos DT, Breithardt G, Cokkinos DV, Crijns HJ. Gender-related differences in presentation, treatment, and outcome of patients with atrial fibrillation in Europe: A report from the Euro Heart Survey on Atrial Fibrillation. *J Am Coll Cardiol* 2007;49:572–577. [PubMed: 17276181]
29. Humphries KH, Kerr CR, Connolly SJ, Klein G, Boone JA, Green M, Sheldon R, Talajic M, Dorian P, Newman D. New onset atrial fibrillation: Sex differences in presentation, treatment, and outcome. *Circulation* 2001;103:2365–2370. [PubMed: 11352885]
30. Thrall G, Lane D, Carroll DLGYH. Quality of life in patients with atrial fibrillation: A systematic review. *Am J Med* 2006;119:448.e441–448.e419. [PubMed: 16651058]
31. Kay GN, Ellenbogen KA, Giudici M, Redfield MM, Jenkins LS, Mianulli M, Wilkoff B. The Ablate and Pace Trial: A prospective study of catheter ablation of the AV conduction system and permanent pacemaker implantation for treatment of atrial fibrillation. *J Interv Card Electrophysiol* 1998;2:121–135. [PubMed: 9870004]
32. Weerasooriya R, Davis M, Powell A, Szili-Torok T, Shah C, Whalley D, Kanagaratnam L, Heddle W, Leitch J, Perks A, Ferguson L, Bulsara M. The Australian Intervention Randomized Control of Rate in Atrial Fibrillation Trial (AIRCRAFT). *J Am Coll Cardiol* 2003;41:1697–1702. [PubMed: 12767649]
33. Berry C, Stewart S, Payne EM, McArthur JD, McMurray JJ. Electrical cardioversion for atrial fibrillation: Outcomes in “real-life” clinical practice. *Int J Cardiol* 2001;81:29–35. [PubMed: 11690662]
34. Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobsen AK, Lewis HD, Raisch DW, Ezekowitz MD. Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;352:1861–1872. [PubMed: 15872201]
35. Singh SN, Tang XC, Singh BN, Dorian P, Reda DJ, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD, Lopez B, Raisch DW, Ezekowitz MD. Quality of life and exercise performance in patients in sinus rhythm versus persistent atrial fibrillation. *J Am Coll Cardiol* 2006;48:721–730. [PubMed: 16904540]
36. Lonnnerholm S, Blomstrom P, Nilsson L, Oxelbark S, Jideus L, Blomstrom-Lundqvist C. Effects of the maze operation on health-related quality of life in patients with atrial fibrillation. *Circulation* 2000;101:2607–2611. [PubMed: 10840012]
37. Chen MS, Marrouche NF, Khaykin Y, Gillinov AM, Wazni OM, Martin DO, Rossillo A, Verma A, Cummings J, Erciyes D, Saad E, Bhargava M, Bash D, Schweikert R, Burkhardt D, Williams-Andrews M, Perez-Lugones A, Abdul-Karim A, Salib W, Natale A. Pulmonary vein isolation for the treatment of atrial fibrillation in patients with impaired systolic function. *J Am Coll Cardiol* 2004;43:1004–1009. [PubMed: 15028358]
38. Erdogan A, Carlsson J, Neumann T, Berkowitsch A, Neuzner J, Hamm CW, Pitschner HF. Quality-of-life in patients with paroxysmal atrial fibrillation after catheter ablation: Results of long-term follow-up. *Pacing Clin Electrophysiol* 2003;26:678–684. [PubMed: 12698667]
39. Goldberg A, Menen M, Mickelsen S, MacIndoe C, Binder M, Nawman R, West G, Kusumoto FM. Atrial fibrillation ablation leads to long-term improvement of quality of life and reduced utilization of healthcare resources. *J Interv Card Electrophysiol* 2003;8:59–64. [PubMed: 12652179]
40. Hsu LF, Jais P, Sanders P, Garrigue S, Hocini M, Sacher F, Takahashi Y, Rotter M, Pasquie JL, Scavee C, Bordachar P, Clementy J, Haissaguerre M. Catheter ablation for atrial fibrillation in congestive heart failure. *N Engl J Med* 2004;351:2373–2383. [PubMed: 15575053]
41. Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P, Gulletta S, Gugliotta F, Pappone A, Santinelli V, Tortorello V, Sala S, Zangrillo A, Crescenzi G, Benussi S, Alfieri O. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: Outcomes from a controlled nonrandomized long-term study. *J Am Coll Cardiol* 2003;42:185–197. [PubMed: 12875749]
42. Tondo C, Mantica M, Russo G, Avella A, De LL, Pappalardo A, Fagundes RL, Picchio E, Laurenzi F, Piazza V, Biscaglia I. Pulmonary vein vestibule ablation for the control of atrial fibrillation in patients with impaired left ventricular function. *Pacing Clin Electrophysiol* 2006;29:962–970. [PubMed: 16981920]

43. Weerasooriya R, Jais P, Hocini M, Scavee C, MacLe L, Hsu LF, Sandars P, Garrigue S, Clementy J, Haissaguerre M. Effect of catheter ablation on quality of life of patients with paroxysmal atrial fibrillation. *Heart Rhythm* 2005;2:619–623. [PubMed: 15922270]
44. Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, Bash D, Schweikert R, Brachmann J, Gunther J, Gutleben K, Pisano E, Potenza D, Fanelli R, Raviele A, Themistoclakis S, Rossillo A, Bonso A, Natale A. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: A randomized trial. *JAMA* 2005;293:2634–2640. [PubMed: 15928285]
45. SoRelle R. Direct myocardial revascularization a “placebo effect,” according to study chief. *Circulation* 2000;102:E9036–9037.
46. Sud S, Massel D, Klein GJ, Leong-Sit P, Yee R, Skanes AC, Gula LJ, Krahn AD. The expectation effect and cardiac pacing for refractory vasovagal syncope. *Am J Med* 2007;120:54–62. [PubMed: 17208080]

TABLE 1**Quality of Life Measures Used in Atrial Fibrillation Studies**

Generic Measures	Disease-Specific Measures
SF-36	Quality of life index: Cardiac version
SF-12	Karolinska questionnaire
PGWB index (Psychological General Well Being)	Minnesota Living with Heart Failure Questionnaire
McMaster Health Index	Arrhythmia Syndrome scale
WHO-26	Arrhythmia Symptoms Checklist: Frequency and Severity
Quality of life diaries	University of Toronto AF Severity Scale
Nottingham Health Profile	Specific Symptoms Scale
Ladder of Life	Specific Activity Scale
EuroQOL	Quality of Life of Atrial Fibrillation Scale
SF-6	CAST QoL
Health Locus of Control Scale	Symptom Specific Checklist
Hopkins Symptom Checklist	Symptom Severity Questionnaire
Psychosocial Adjustment to Illness scale	
Global Health Status Questionnaire	
Coping Strategies Questionnaire	
Psychosocial Adjustment to Illness	
State-Trait Anxiety Inventory	
Medical Outcomes Study Depression Scale	
Health Status Questionnaire	
Assessment of Quality of Life Instrument (AQoL)	
Sickness Impact Profile	
Duke Activity Status Index	

TABLE 2
Selected Quality of Life Studies in Atrial Fibrillation

Trial Name	Population	Study Design	Measure of QoL	Results
Anti-Arrhythmic Drug Studies				
CTAF ¹	264 patients with recent paroxysmal or persistent AF without prior AAD exposure	Randomized (2:1:1) to amiodarone, sotalol, or propafenone	SF-36, Symptom Checklist, Duke Activity Status Index, University of Toronto AF Severity Scale	Modest improvements in SF-36 PCS and MCS scores and ~20% reduction in Symptom Checklist scores. No differences between groups, despite less AF in amio group
SAFE-T ^{34,35}	665 patients (99% men) with persistent AF	Randomized to amiodarone, sotalol, or placebo. Those in AF after 4 weeks were electrically cardioverted	SF-36, Symptom Checklist, Specific Activity Scale, University of Toronto AF Severity Scale	By intention to treat, no differences between groups at 1 year except for decreased mental health score in amio group
Rate Versus Rhythm Control Studies				
PIAF ^{10,16}	252 patients with AF between 7 and 360 days duration	Randomized to rhythm control (amiodarone +/- cardioversion) versus rate control. QoL data obtained at baseline and 12 months	SF-36	4/8 subscales improved in rhythm control versus 6/8 in rate control. No significant differences observed between groups
STAF ²³	AF for >4 weeks, excluding those with low and very high risk of recurrence (N = 200)	Randomized to rhythm control (cardioversion + AAD) versus rate control (drugs). QoL data obtained at baseline and 12 months	SF-36	At 12 months, 2/8 subscales improved in rhythm control group versus 5/8 in rate control group. No overall between-group differences
RACE ²⁴	352 patients with persistent AF included in the RACE study	Randomized to rate (drugs) or rhythm control (cardioversion, AADs). QoL data collected at baseline, 1 year, and 24–36 months	SF-36	QoL similar between groups at study end. Rate control group had improvement in 3 subscales versus 0 subscales in rhythm control group
AFFIRM ⁷	25% of AFFIRM sites participated in QoL substudy (N = 716)	Patients randomly assigned to rate or rhythm control group. QoL data collected at baseline, 2 months, 12 months, and annually for 4 years	Perceived health, Ladder of life, SF-36, QoL index, Symptom Checklist	Quality of life scores improved modestly and to a similar degree in rate and rhythm control groups

AAD = antiarrhythmic drug; PCS = physical component summary score; MCS = mental component summary score.

TABLE 3
AF Catheter Ablation Studies with Quality of Life Assessment

Authors	Population	Study Design/Ablation Approach	Measure of QoL	Results
Nonrandomized Series				
Erdogan <i>et al.</i> ³⁸	30 patients with paroxysmal AF refractory to multiple AADs	Linear RF ablation in the right atrium only ("catheter Maze"). QoL data obtained pre- and 3, 6, 9, 12, 24, 36 months postablation	SF-36, symptom specific checklist (locally derived)	Patients without AF recurrence (9/30) had statistically significant improvements in all eight SF-36 subscales over 2 years. Pts with AF recurrence had little change
Goldberg <i>et al.</i> ³⁹	33 patients with paroxysmal AF who failed multiple AADs	RF ablation of focal triggers in pulmonary veins and RA. QoL measures obtained at baseline, 1, and 3 years of follow up	SF-36	At 1 and 3 years post-ablation, significant improvements seen in all SF-36 scales except bodily pain
Pappone <i>et al.</i> ⁴¹	589 ablation patients with drug-refractory AF (70% paroxysmal), compared with 582 patients who declined ablation	109 ablated and 102 medically treated patients did QoL surveys every 3 months for 1 year. Patients were treated with circumferential isolation of all PVs using RF	SF-36	PCS and MCS scores significantly rose from ~40 to ~50 within 6 months after ablation, but did not change in reference cohort treated with drugs
Hsu <i>et al.</i> ⁴⁰	58 pts with CHF, LVEF <45% and AF (>90% persistent or permanent)	Cohort matched (by age, sex, AF type) to additional 58 pts without CHF. RF ablation: PVI, usually with linear in ablation in LA roof and/or mitral isthmus	SF-36, Symptom Checklist	Significant improvements in Symptom Checklist and SF-36 scores reported for both groups after ablation. PCS/MCS increased 24/21 points in CHF group, 18/14 points in control group
Chen <i>et al.</i> ³⁷	377 consecutive patients with symptomatic AF refractory to AADs. Study focused on 94 patients with LVEF <40%	Ostial PVI performed with closed internally irrigated RF catheter; 10% also underwent cavotricuspid isthmus ablation	SF-36	Significant improvement in on all SF-36 subscales 6 months following PVI irrespective of LV function. Scores more than doubled on most scales
Weerasooriya <i>et al.</i> ⁴³	63 consecutive patients with symptomatic paroxysmal AF refractory to ≥2 AADs	PVI plus linear ablation in mitral isthmus and cavotricuspid isthmus using externally irrigated RF catheter. QoL data collected at baseline, 3 and 12 months	SF-36, Symptom Checklist	Significant improvement in 8/8 SF-36 subscales and Symptom Checklist scores at 3 and 12 months postablation. Largest changes in role physical (36 points) and bodily pain (31 points) scales
Tondo <i>et al.</i> ⁴²	105 patients with paroxysmal and persistent	PV "vestibule" ablation plus linear ablation in mitral isthmus and cavotricuspid isthmus using externally	SF-36	Improvement in at least 6 SF-36 measures 6 months after

Authors	Population	Study Design/Ablation Approach	Measure of QoL	Results
Randomized Studies	(75%) AF refractory to AADs. 40 patients with LVEF <40% compared to 65 without	irrigated RF. QoL collected at baseline and 6 months		ablation. Improvements similar whether or not LV dysfunction present
	Wazni <i>et al.</i> ⁴⁴ 70 patients with at least monthly symptomatic PAF for at least 3 months and no prior treatment with AADs	Patients randomized to antral PVI using RF (8 mm tipped catheter) or AAD (flecainide or sotalolol). QoL data obtained at enrollment and 6 months	SF-36	Improvement in QoL significantly greater (by 6–20 points) in PVI group than AAD group in 5/8 subscales of the SF-36
	Oral <i>et al.</i> ¹⁵ 146 patients with “chronic” AF	Randomly assigned to 1–2 cardioversions over 3 months or ablation (circumferential PVI + linear ablation in LA roof and mitral isthmus with 8 mm RF catheter). Both groups received amiodarone for 3 months	Symptom Severity Questionnaire (locally derived, 5 symptoms)	12 months after ablation, symptom scores fell from 17±4 to 6±2 in patients without AF recurrence and from 17±4 to 12±4 in patients with AF recurrence. Recurrence less common with ablation. High rate of crossover to ablation

AAD = antiarrhythmic drug; PCS = physical component summary score; MCS = mental component summary score; PV = pulmonary vein; PVI = pulmonary vein isolation; CHF = congestive heart failure.