Atrial fibrillation (AF) is the most frequent cardiac rhythm disorder and presents a considerable public health burden that is likely to increase in the next decades due to the ageing population. Current management strategies focus on the heart rate and rhythm control, thromboembolism prevention, and treatment of underlying diseases. The concept of quality of life (QoL) has gained significant importance in recent years as an outcome measure in AF studies evaluating therapeutic interventions and as a relevant component of a comprehensive treatment plan. Quality of life is impaired in the majority of patients with AF, and both rate and rhythm control strategies show significant improvement in QoL measures in highly symptomatic patients. This article reviews generic and specialized instruments for measuring QoL in the context of AF, discusses their applications and limitations to integration in clinical practice, and addresses the potential of early therapy for improving QoL outcomes. The development and validation of new QoL assessment tools will have a central role in the advancement of therapies and treatment guidelines for AF.

Keywords: Atrial fibrillation (AF) • Quality of life (QoL) • Rhythm control • Rate control • Cardiac rhythm disorder • Management strategies

Introduction

Atrial fibrillation (AF), the most common arrhythmia resulting in hospital admission, has a significant impact on morbidity and mortality.1,2 While AF is rarely life-threatening in itself, the distress caused by symptom onset can be severe and result in a major reduction in quality of life (QoL). This can be attributed to several factors. Typical arrhythmia-associated complaints include palpitations, chest pain, dizziness, and heart failure-like symptoms.3 Underlying heart disease produces symptoms such as weakness, lightheadedness, and dyspnoea.1 In addition, the consequences of treating AF, including side effects of drugs, interventions, and especially hospitalization, have a negative impact on QoL.

The World Health Organization defines health as not only the absence of disease and infirmity, but also as an aspect of well-being or QoL.4 Nevertheless, there is currently no globally accepted definition for QoL in AF. The term is subjective and may be defined by one or many aspects, including symptoms, functional status, and patients’ health perceptions, experiences, and expectations.4,5 It is therefore important to consider the individual contribution of all these factors when assessing QoL, as well as how intensely perceived AF-related symptoms affect QoL.

Most studies conducted to date have assessed health-related QoL (HRQoL) in symptomatic patients who are intolerant or refractory to antiarrhythmic therapy, or in those treated with ablation. The impact of AF on daily living in less severe or asymptomatic patients is therefore not well known or understood. Moreover, studies directly assessing HRQoL have been hampered by the small sample sizes and lack of control groups. A further confounding factor in the assessment of QoL in patients with AF is the presence of concomitant cardiovascular disease. Cardiovascular disease may dominate the patient’s health preoccupations rather than the atrial dysrhythmia. It is therefore important in clinical studies to separate the impact of HRQoL on patients with AF from that of patients with other cardiac diseases. Studies have also been limited by bias introduced by questionnaires not self-administered by patients.7,8

At present, the management of AF aims to reduce symptoms and prevent severe AF-related complications.3 It is important, however, that the management and treatment of AF take into account not only symptoms, but also individual patient factors such as psychological well-being.9 Patients with AF are known to experience psychological distress, which may manifest as anxiety and/or depression, potentially leading to increased mortality, morbidity, and utilization of health-care resources.10 One-third of patients with AF who

Etienne Aliot1*, Giovanni L. Botto2, Harry J. Crijns3, and Paulus Kirchhof4,5

1 Cardiology Department, Institut Lorrain du Coeur et des Vaisseaux, CHU de Nancy, 54500 Vandoeuvre-lès-Nancy Cedex, France; 2 Cardiology Department, S. Anna Hospital, Como, Italy; 3 Department of Cardiology and CARIM, Maastricht University Medical Centre, Maastricht, The Netherlands; 4 University of Birmingham Centre for Cardiovascular Sciences and SWBH NHS Trust, Institute for Biomedical Research, Birmingham B15 2TT, UK; and 5 Department of Cardiology and Angiology, University Hospital Münster, Münster, Germany

Received 24 June 2013; accepted after revision 27 October 2013; online publish-ahead-of-print 26 January 2014

* Corresponding author. Tel: +33 3 83 15 32 96; fax: +33 3 83 15 38 56. E-mail: e.aliot@chu-nancy.fr

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2014. For permissions please email: journals.permissions@oup.com.
do not have overt symptoms and are not aware of their condition will report a lower QoL than their peers in sinus rhythm.\textsuperscript{9,11} It is estimated that more than half of the patients in selected populations have episodes of silent AF.\textsuperscript{12} Assessment of the benefits arising from therapeutic interventions in AF have included exercise tolerance and duration of rhythm after cardioversion as study endpoints. However, these endpoints do not correlate well with subjective assessment of the patients’ symptoms. Measures of QoL take into consideration subjective improvements in well-being resulting from pain, psychological, emotional, and physical disturbances, as well as the potential burdens and side effects of therapeutic interventions that cause symptomatic improvement but lead to a reduction in well-being. As a result, QoL is becoming an increasingly important clinical outcome measure in AF,\textsuperscript{9,13} although currently there are no specific guidelines for its assessment in AF patients.\textsuperscript{14} Since multiple factors contribute to QoL (Figure 1), an assessment technique that is able to consider all its different aspects would be ideal. A large number of instruments are available for the assessment of QoL.\textsuperscript{5,15–19} As a result, studies of QoL in AF rarely employ the same scores. This article will explore the various instruments that have been used to assess QoL in AF and their merits and drawbacks, as well as consider the impact of treatment on QoL.

**Comparison of available quality-of-life instruments**

There are several general limitations to the utility of QoL questionnaires in the context of AF. First, they can be highly subjective, both from the clinician’s and the patient’s perspective. Secondly, clinicians rarely use questionnaires as part of their clinical assessment. Thirdly, hospital boards are not convinced of their value; similarly, health insurance companies do not recognize their relevance. Fourthly, QoL questionnaires may vary dramatically, for example, in paroxysmal AF (PAF), rendering spontaneous variability in a patient’s condition a relevant confounder. Finally, the relationship between symptoms and actual rhythm is elusive, and the establishment of an association between the two would be beneficial for the management of AF.\textsuperscript{15} To maximize the clinical utility of QoL, it is important to choose the most appropriate instrument for its assessment. Quality-of-life instruments fall into two classes: generic and symptom scales. Generic QoL instruments are designed to be applicable across a wide range of populations and conditions. Symptom-based HRQoL measures are relevant to particular conditions.

**Generic instruments**

Generic QoL instruments employed in AF include the Medical Outcome Study Short-Form Health Survey (MOS-SF 36, known as SF-36),\textsuperscript{19} the 12-item Short Form Health Survey (SF-12, derived from SF-36),\textsuperscript{20} and the Euro-QoL 5-Dimensional questionnaire (EuroQoL/EQ-5D)\textsuperscript{16} (Table 1). Both the SF-12 and the EuroQoL are validated for measuring QoL in general across different spectra of diseases. The Karnofsky Performance Status Scale,\textsuperscript{21,22} which has been applied to describe global functional status of patients for >50 years in other therapeutic areas such as cancer, has also been utilized in AF.\textsuperscript{23} Generic instruments have the advantages of having been extensively validated and the most commonly used (SF-36) are available in many languages. They tend to be easy to use, and have been used in a large number of clinical investigations of QoL in AF patients. Their main disadvantage is the fact that they measure general health and functioning, rather than symptoms specific to AF, and therefore scores on these questionnaires are influenced by patient demographics and comorbidities, which are prevalent in older patients with AF. The FRACTAL (Fibrillation Registry Assessing Costs, Therapies, Adverse events, and Lifestyle) study concluded that generic tools are not ideal for measuring AF-specific QoL.\textsuperscript{24} There is a need for a comprehensive, validated AF-specific questionnaire to measure the spectrum of QoL domains affected by AF.

The German Competence Network on Atrial Fibrillation (AFNET) has developed a dedicated QoL instrument that makes use of domains covered in generic instruments, such as the SF-12 and EuroQoL, and supplements these with elements from validated depression scales. The usefulness of this generic instrument is currently being assessed in ongoing trials. Both the AFNET and the European Heart Rhythm Association (EHRA) recommend the design, validation, and further use of AF-specific instruments to assess AF-related QoL, particularly when improvement of symptoms and QoL are the desired primary outcomes of a trial.\textsuperscript{15}

**Specific atrial fibrillation quality-of-life instruments and atrial fibrillation symptom scales**

The main advantage of developing AF-specific HRQoL questionnaires is their specificity; they enable assessment of domains that are relevant and exclusive to AF and increase the sensitivity to changes in patients’ health status. In clinical trials, they have greater statistical power than generic instruments regarding discrimination between patients with AF recurrence and arrhythmia-free patients.\textsuperscript{25}
Several AF-specific QoL instruments have been validated in the last few decades. The Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) questionnaire assesses the QoL based on the four parameters: symptoms (four items), daily activities (eight items), treatment concerns (six items), and treatment satisfaction (two items).8,26 This questionnaire combines symptoms, functional status, and QoL in a single measure and has found to be reliable and sensitive to clinical changes.27 Other AF-specific QoL questionnaires include the Atrial Fibrillation Quality of Life (AF-QoL) questionnaire,28 the QoL in AF (QLAF) questionnaire,29 and the Quality of Life of Atrial Fibrillation (AFQLQ) questionnaire,30,31 details of which are summarized in Table 2.

To provide a more accurate assessment of changes to QoL in response to therapeutic interventions, symptom scales have been devised (Table 3). The Specific Activity Scale is frequently used in AF studies but covers cardiovascular disease as a whole.37 The most commonly employed symptom scales for AF are the Arrhythmia Symptom Checklist, Frequency, and severity (SCL),5 and the University of Toronto Atrial Fibrillation severity Scale (AFSS).32,33 The SCL is straightforward and sensitive and has been employed in many clinical studies. However, several of the symptoms are non-specific, for example, ‘trouble concentrating’, and there is no assessment of functional status or patient satisfaction. The AFSS and SCL have been used with a similar frequency in trials of AF therapy, although generally they did not detect between-group differences related to treatment. The evidence of responsiveness for these measures is limited, and the results are mixed.

---

**Table 1** Generic QoL instruments most commonly used in AF

<table>
<thead>
<tr>
<th>QoL instrument</th>
<th>QoL domains measured</th>
<th>Scoring</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-1220</td>
<td>Limitations in physical activities due to health problems</td>
<td>Summary scores for physical health and mental health, standardized to population norms with the mean score set at 50 (SD = 10)</td>
<td>Extensively validated</td>
<td>By design, reflects general health and functioning</td>
</tr>
<tr>
<td></td>
<td>Bodily pain</td>
<td></td>
<td>Generalizability</td>
<td>Scores among AF patients strongly influenced by patient demographics and comorbid conditions</td>
</tr>
<tr>
<td></td>
<td>General mental health (psychological distress and well-being)</td>
<td></td>
<td>Extensive data on AF already collected using this method</td>
<td>Less sensitive to change in older AF patients with multiple health problems</td>
</tr>
<tr>
<td></td>
<td>Limitations in usual role activities due to emotional problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vitality (energy and fatigue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>General health perceptions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EuroQoL16</td>
<td>Self-care</td>
<td>Rated on three levels</td>
<td>Extensively validated</td>
<td>May not be sensitive to HRQoL-related aspects of AF not covered by the five generic dimensions</td>
</tr>
<tr>
<td></td>
<td>Usual activities</td>
<td>Range from ‘no problems’ to ‘severe problems’</td>
<td>Ease of use</td>
<td>By design, reflects general health and functioning</td>
</tr>
<tr>
<td></td>
<td>Pain/discomfort</td>
<td></td>
<td>Validated for most languages</td>
<td>Scores among AF patients strongly influenced by patient demographics and comorbid conditions</td>
</tr>
<tr>
<td></td>
<td>Anxiety/depression</td>
<td></td>
<td>Long track record of use in a variety of medical conditions</td>
<td>Less sensitive to change in older AF patients with multiple health problems</td>
</tr>
<tr>
<td></td>
<td>Complemented by visual aid score</td>
<td></td>
<td>Has a well-accepted method for transforming raw scores to preference-based utility weights</td>
<td>By design, reflects general health and functioning</td>
</tr>
<tr>
<td>SF-3619</td>
<td>Limitations in physical activities due to health problems</td>
<td>0–100 scoring system</td>
<td>Most widely validated generic instrument</td>
<td>Scores among AF patients strongly influenced by patient demographics and comorbid conditions</td>
</tr>
<tr>
<td></td>
<td>Bodily pain</td>
<td></td>
<td>Has been used to study a great variety of cardiac diseases</td>
<td>Less sensitive to change in older AF patients with multiple health problems</td>
</tr>
<tr>
<td></td>
<td>General mental health (psychological distress and well-being)</td>
<td></td>
<td>Validated for most languages</td>
<td>By design, reflects general health and functioning</td>
</tr>
<tr>
<td></td>
<td>Limitations in usual role activities due to emotional problems</td>
<td></td>
<td>Extensive data on AF already collected using this method</td>
<td>Scores among AF patients strongly influenced by patient demographics and comorbid conditions</td>
</tr>
<tr>
<td></td>
<td>Vitality (energy and fatigue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>General health perceptions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SF-12, 12-item Short Form Health Survey; SF-36, Medical Outcome Study Short-Form Health Survey (MOS-SF 36); QoL, quality of life; SD, standard deviation.
The EHRA recently proposed an AF symptom scale based exclusively on patient-reported symptoms and their impact on daily activities. The EHRA instrument relates specifically to the time when the patient feels to be in the arrhythmia and its classification scales are summarized in Table 4. Latest guidelines for AF suggest that the EHRA score should be used in the clinical evaluation of patients to guide decisions on rhythm control therapy. However, validation of the EHRA score has not yet been

Table 2 Atrial fibrillation-specific QoL symptom scales

<table>
<thead>
<tr>
<th>QoL instrument</th>
<th>QoL domains measured</th>
<th>Scales/scoring</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFEQT/AF-QoL-18</td>
<td>Initially developed as a 42-item questionnaire to assess the impact of AF and its treatment</td>
<td>Five-point Likert scale</td>
<td>Totally agree</td>
<td>Applicable to all types of AF (paroxysmal and permanent)</td>
</tr>
<tr>
<td></td>
<td>on patients’ symptoms, functioning, and daily activities through six domains: symptoms, social functioning, physical functioning, emotional functioning, treatment concerns, and treatment satisfaction</td>
<td>Sufficiently agree</td>
<td></td>
<td>Limited clinical data; unknown validity, and reproducibility</td>
</tr>
<tr>
<td></td>
<td>Later refined and renamed AF-QoL-18 questionnaire comprising two parts: (i) AF-QoL-7, comprising seven items</td>
<td>Neither agree nor disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>which deal with the psychological domain; (ii) AF-QoL-11, comprising</td>
<td>Sufficiently disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 items which deal with physical activity</td>
<td>Totally disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AF-QoL</td>
<td>Psychological Physical Sexual activity</td>
<td>Five-point Likert scale</td>
<td>Totally agree</td>
<td>Able to capture changes over time in patients’ HRQoL</td>
</tr>
<tr>
<td></td>
<td>Domains numbered sequentially (I–VII) Questions containing items to be scored</td>
<td>Sufficiently agree</td>
<td></td>
<td>Uncertain generalizability. Scores among AF patients may be influenced by patient demographics</td>
</tr>
<tr>
<td></td>
<td>sequentially numbered 1–22</td>
<td>Neither agree nor disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>‘Yes/no’ questions leading into domains not numbered or scored</td>
<td>Sufficiently disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Higher numbers indicate worse QoL</td>
<td>Totally disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scoring</td>
<td>0–100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QLAF</td>
<td>Palpitation Breathlessness Chest pain Dizziness Drug Direct-current cardioversion Ablation</td>
<td>Five-point Likert scale</td>
<td>Totally agree</td>
<td>Simple Practical Rapidly administered (useful in the outpatient setting) Internally consistent Responsive</td>
</tr>
<tr>
<td></td>
<td>Variety and frequency of symptoms (Questions 1–6) Severity of symptoms (Questions 7–12) Limitations of daily and special activities and mental anxiety (Questions 13–26)</td>
<td>Sufficiently agree</td>
<td></td>
<td>Relatively time-consuming Uncertain generalizability</td>
</tr>
<tr>
<td>AFQLQ</td>
<td>Scales</td>
<td>Neither agree nor disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Physical functioning Role functional-physical Role functional-emotional Bodily pain General health perceptions Vitality Social functioning Mental health</td>
<td>Sufficiently disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subscales transformed to create Physical and Mental Component Summary scores (PCS and MCS, respectively), range 0–100 points</td>
<td>Totally disagree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Higher scores indicate a well health status Scoring Questions 1–6: 0–24 points Questions 7–12: 0–18 points Questions 13–26: 0–56 points Higher scores for each subscale indicate a well health status as with SF-36</td>
<td>0–100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This list is not exhaustive.

AF, atrial fibrillation; HRQoL, health-related quality of life; AFEQT, Atrial Fibrillation Effect on QualiTy-of-Life questionnaire; AF-QoL-18, Atrial Fibrillation Quality of Life 18; AF-QoL, Atrial Fibrillation Quality of Life questionnaire; AF AWARE, Atrial Fibrillation AWareness And Risk Education group; QLAF, Quality of Life in Atrial Fibrillation; QoLAF, Quality of Life and Atrial Fibrillation study; AFQLQ, Atrial Fibrillation Quality of Life Questionnaire; SF-36, Medical Outcome Study Short-form Health Survey.
Table 3  Symptom scales for AF

<table>
<thead>
<tr>
<th>AF instrument</th>
<th>Domains measured</th>
<th>Scales/scoring</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation symptom checklist, Frequency, and Severity</td>
<td>16 items (symptoms associated with AF)</td>
<td>Frequency (0 to 4) Severity (1 to 3) of each symptom Frequency and severity scores are not combined</td>
<td>Straightforward to use, sensitive to change, had been used in many AF studies</td>
<td>Relatively time-consuming Uncertain generalizability</td>
</tr>
<tr>
<td>University of Toronto Atrial Fibrillation Severity Scale AFSS</td>
<td>9 items: Total AF burden = AF frequency + AF duration + AF severity Global well-being AF symptoms healthcare utilization Demographic data Current AF status</td>
<td>Individual symptoms attributable to AF are scored on a five-point Likert scale, such that the total AFSS severity score ranges from 0 to 35, with higher scores indicating increased AFSS</td>
<td>Able to capture changes over time in patients’ HRQoL</td>
<td>Relatively time-consuming Uncertain generalizability</td>
</tr>
<tr>
<td>EHRA AF symptom scale</td>
<td>Symptoms that are attributable to AF and reverse or reduce upon restoration of sinus rhythm or with effective rate control</td>
<td>EHRA 1—IV (see Table 4)</td>
<td>Clinical relevance simplicity</td>
<td>Limited clinical data; unknown validity, generalizability, and reproducibility</td>
</tr>
<tr>
<td>Canadian cardiovascular Society Severity in Atrial Fibrillation Scale (CCS-SA)</td>
<td>AF-related symptoms (palpitations, dyspnoea, dizziness/syncope, chest pain, weakness/fatigue); determination of symptom-rhythm correlation; assessment of the effect of these symptoms on patient daily function, and QoL</td>
<td>4-point scale 0 (asymptomatic) to 4 (severe)</td>
<td>Achieves a balance of simplicity, precision, and comprehensiveness Ease of use at the bedside</td>
<td>Poor correlation with subjective AF burden Uncertain generalizability</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; QoL, quality of life.

Table 4  European Heart Rhythm Association score of AF-related symptoms

<table>
<thead>
<tr>
<th>Classification of AF-related symptoms (EHRA score)</th>
<th>EHRA class</th>
<th>Explanation</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHRA I “No symptoms”</td>
<td>EHRA I</td>
<td>“No symptoms”</td>
<td>Clinical relevance simplicity</td>
<td>Limited clinical data; unknown validity, generalizability, and reproducibility</td>
</tr>
<tr>
<td>EHRA II “Mild symptoms”; normal daily activity not affected</td>
<td>EHRA II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EHRA III “Severe symptoms”; normal daily activity affected</td>
<td>EHRA III</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EHRA IV “Disabling symptoms”; normal daily activity discontinued</td>
<td>EHRA IV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; EHRA, European Heart Rhythm Association. Printed with permission from Camm et al.1

Impact of atrial fibrillation therapies on quality of life

Clinical studies employing the QoL instruments detailed above have found that patients with AF have a marked impairment of HRQoL compared with population norms,38–40 healthy controls,41–43 and other patients with coronary heart disease (CHD).33 However, most of the published QoL literature in AF is derived from studies of rate and/or rhythm control interventions and is therefore biased towards selection of highly symptomatic patients or subgroups of clinical trial patients. Such populations are likely to be biased and have inadequate statistical power. Unsurprisingly, baseline scores on QoL instruments tend to be lower than the general population in these studies.41,43,44

To date, there are limited data assessing QoL in a general AF patient population.33,40,44–46 Most studies have examined the impact of specific interventions, including ablation and pacemaker implantation,47–53 different pacing modalities,48,54–56 cardioversion,53–62 the Maze operation,59,63,64 percutaneous closure of the left atrial appendage,65 pharmacological therapies,51,53,66,67 and pulmonary vein isolation (PVI).68,69 Furthermore, the open-label nature of studies
investigating PVI may introduce a bias towards the intervention and may therefore influence QoL scores. A recent systematic review of randomized and non-randomized trials on QoL in elderly patients (mean age ≥ 65 years) with AF concluded that many pharmacological interventions may improve QoL in this patient population and recommended an algorithm to optimize QoL.67

The interpretation of data also presents a challenge. In a study investigating the impact of the control of symptomatic PAF on QoL, patients with uncontrolled symptomatic PAF at baseline had an inferior QoL compared with those with controlled symptomatic PAF. The QoL improved to a comparable level in controlled patients following treatment with controlled-release flecainide acetate.70 However, a discrepancy was found between patient-reported AF symptoms and physical functioning in the uncontrolled PAF group.71 While other studies have shown that symptoms in AF are inversely correlated to physical functioning, these results imply that uncontrolled PAF patients were not as physically impaired by their symptoms as predicted.72

Rate vs. rhythm control strategies
A number of randomized, controlled studies have investigated the effect of ‘rate vs. rhythm’ control strategies on QoL in patients with AF: the Strategies of Treatment of Atrial Fibrillation (STAF) study,41 the Pharmacological Intervention in Atrial Fibrillation (PIAF) study,42 the RAte Control versus Electrical cardioversion for persistent atrial fibrillation (RACE) study,43 the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study,70 and the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) study.72

Improvement in QoL during follow-up was observed in most of these studies, but with no difference between the rate vs. rhythm strategies.41–43 Similar improvements in QoL were observed between the rate and rhythm control arms of the AFFIRM and AF-CHF studies.73,74 Results from these studies indicate that a strategy of rate control can be at least as effective as efforts to control rhythm.41 However, a number of methodological weaknesses, including lack of control groups, short follow-up periods (<6 months), and the utilization of non-validated instruments for QoL assessment. With the exception of AFFIRM and AF-CHF, these studies were not powered to detect QoL differences between the two strategies. The patient cohorts were not highly symptomatic in terms of arrhythmia. Nevertheless, in general, rhythm did not perform better than rate control concerning changes in HRQoL.

Relationship between quality of life and disease states in atrial fibrillation
The relationships between QoL and different disease states in clinical AF are largely unexplored. In idiopathic AF, patients may not have symptoms between attacks, although the memory of the arrhythmia may have a negative impact on the patient’s activities and ambitions. The arrhythmia may be almost clinically silent in a large proportion of patients with persistent or permanent AF.75 Such types of arrhythmia may only be detected when a serious and often difficult-to-reverse condition occurs (e.g. stroke, decompensated heart failure), significantly reducing the patient’s QoL.

A recent study evaluated QoL in patients with persistent, paroxysmal, or permanent AF using the AF-QoL questionnaire.76 The HRQoL was influenced by clinical parameters but seemingly not affected by the type of AF, except in the psychological dimension. Patients with a long history of disease, specifically those with permanent AF, tended to have stable AF with fewer symptomatic episodes over the course of time. Therefore, they had better HRQoL in terms of psychological symptoms, due to a lessening of the anxiety associated with their condition.77 There is a correlation between the number of visits to the emergency department and the deterioration in HRQoL.78 Hence, it can be deduced that the greater the number of symptomatic episodes, as in patients with PAF, the greater the impact of the episodes on the patient. A high frequency of episodes will have a negative impact on the patient’s HRQoL, particularly in terms of psychological aspects of the AF-QoL scale.76

Relationship between achievement of sinus rhythm and quality of life
Despite the large number of studies conducted to date, there remains a lack of evidence of the relationship between achievement of sinus rhythm (SR) and QoL. In the SAFE-T study (n = 1180), patients with persistent AF, restoration, and maintenance of SR was associated with improvements in QoL measures.78 In the AF-CHF study, which is the largest study conducted to date (n = 1376), a higher proportion of time spent in SR was associated with a modestly greater improvement in QoL scores.79 Establishing such relationships presents a number of challenges. It is difficult to relate rhythm directly to complaints or formal assessment of QoL in clinical practice. Even if a relationship is established between rhythm and QoL, it may not be linear, i.e. an expected high QoL with chronic SR may be offset by the side effects of an antiarrhythmic drug such as amiodarone.79 Timing of assessment of QoL relative to the occurrence of the arrhythmia also seems to be important.11 Although this may be less important in patients with severe symptoms, QoL may be influenced by the memory of the symptoms, as well as anxiety about its recurrence.

Assessment of quality of life in asymptomatic patients
The assessment of QoL in patients who are largely asymptomatic presents a challenge. It is universally accepted that the reduced QoL associated with AF extends to patients with asymptomatic AF.11 Conversely, a significant proportion of ‘asymptomatic’ patients improve following restoration of SR, which suggests that they have been symptomatic without knowledge of the fact. In addition, these patients may benefit from the management of their underlying hypertension, angina, or heart failure. Nevertheless, the impact of rate or rhythm interventions on asymptomatic patients is not easily measurable. The EHRA score is not sensitive enough to measure QoL in this patient population, and the clinical usefulness of formal QoL measurement in asymptomatic patients needs to be investigated.
Unanswered questions in quality-of-life outcomes in atrial fibrillation

One of the least understood aspects of AF is the association between the disease and cognitive impairment; in particular, whether there is evidence of a causal link. Cognitive status in patients with AF has been assessed with the Mini Mental State Examination (MMSE) in several studies to date. A literature review showed that these data were somewhat unreliable, and a causal link between AF and cognitive impairment could not be established. However, in a recent study of subjects aged > 65 years with either SR or permanent AF, cognitive status was found to be significantly lower in the AF group (P < 0.05), as reflected by lower MMSE scores. Although cognitive impairment in older patients is multifactorial, permanent AF appeared to be one of the causes of low cognitive function in this study. Future prospective clinical trials may further elucidate the deterioration of cognitive function in AF patients.

The question of how early treatment intervention affects QoL outcomes should also be addressed. The administration of oral antiarrhythmic agents at the time of symptom onset has been shown to be safe and reduces the number of emergency room visits and hospital admissions. Therefore, it seems obvious that the earlier the AF can be treated, the higher the impact of treatment on QoL. However, asymptomatic AF can preclude its timely detection and early initiation of therapy; 30–45% of patients had an incidental diagnosis of AF after undergoing electrocardiogram for unrelated reasons. Asymptomatic AF may be more common than symptomatic AF in patients with PAF. Early treatment in addition to identification of patients at risk may help improve the impact of treatments on QoL.

It is well known that time-dependent atrial remodelling renders the arrhythmia unmanageable, leading to a decrease in QoL. The changes in atrial properties that cause AF result in contractile dysfunction and counter-regulatory processes, a cellular survival mechanism that attempts to prevent the death of myocardial cells due to cytosolic calcium overload. Although irreversible AF-induced atrial damage can occur within days of arrhythmia, this could be prevented by early restoration and maintenance of SR; clinical observations support this concept. Importantly, antiarrhythmic drugs are relatively effective in converting AF to SR when AF duration is short, but almost never effective when AF persists for > 2 weeks. Similarly, catheter ablation has a higher success rate in patients with PAF compared with patients with sustained forms of the arrhythmia. Therefore, rhythm control therapy may be more effective when it is initiated early.

Antiarrhythmic drug treatment is recommended only in patients with recurrent AF; current guidelines do not recommend treatment at the time of diagnosis. Although this strategy could be advantageous for delaying any potentially harmful effects of antiarrhythmic drugs until the second episode, it does not concur with the observation that AF is an arrhythmia that progresses chronically in most patients. Only a highly selected subgroup of patients will experience short, sporadic episodes of PAF over several decades. In fact, it is likely that many of the events contributing to AF occur before the first episode and before the disease is diagnosed. Delaying treatment may prevent effective prevention of AF recurrences.

The working group of the second AFNET/EHRA consensus meeting suggested that an early intervention with pharmacological rhythm control therapy and/or ablation should be tested in controlled trials in patients with a first documented episode. The pathophysiology of AF alludes to the idea that an early treatment strategy would be more successful, with fewer harmful effects than current practice. However, long-term follow-up would be required to detect any delay in AF progression, including long-term effects on left atrial mechanical function and the incidence of very late recurrence. Some of these issues will be addressed in the ongoing Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA), Early Treatment of Atrial Fibrillation for Stroke Prevention (EAST) trials, as well as in the Routine versus Aggressive upstream rhythm Control for prevention of Early atrial fibrillation in heart failure (RACE 3) study.

The impact of age on QoL in AF also merits discussion. The majority of older individuals with AF have comorbid conditions, such as CHD and diabetes, which affect treatment outcomes. However, this population may still benefit from interventions, such as electrical cardioversion and AF ablation therapy. One study compared 52 ‘elderly’ (mean age 77) patients with chronic AF with 48 age-matched controls in sinus rhythm. No differences were found in QoL, as assessed by the SF-36, between these groups. Older patients may have a lesser symptom burden specifically from AF than younger patients. Conversely, targeting the younger patient population for rhythm interventions is much more likely to result in positive outcomes for QoL, and the benefits of treatment are therefore likely to be much greater. This was observed in the RACE trial; age < 69 years was associated with a greater likelihood of QoL improving over time.

Conclusions

The management of AF is overshadowed by controversy and contradiction, and trials to date have failed to establish the ideal treatment strategy. Although medical advances will undoubtedly continue to reduce mortality rate, variations in QoL could be the most reliable way to differentiate between treatment regimens, given the currently available outcome measures. The assessment of QoL is still not standardized, and many assessment tools have shortcomings. However, the advent of new QoL scales with a greater focus on symptoms has increased the clinical utility of these instruments. The CCS-SAF and EHRA score could be valuable in the future, both for assessing the impact of symptoms on QoL and for assisting in the selection of appropriate treatment.

Rate and rhythm control studies have demonstrated a significant improvement in QoL among highly symptomatic patients. Future studies on AF should be conducted using large, randomized cohorts of a more ‘general’ population. The field would also benefit from studies measuring explicitly a range of QoL-specific endpoints in very symptomatic AF patients. Finally, the interventions tested should be comprehensive, including all aspects of AF. ‘Newer’ rhythm control strategies should be tested in conjunction with more traditional ones, as well as with rate control strategies, so that the best treatment option may be identified, not only in
terms of morbidity and mortality, but also in the context of QoL. Until all of these analyses are performed, there will be no change in treatment strategy.

Outcomes of future studies may support the development of new guidelines in favour of earlier intervention in the treatment of patients with AF. Future recommendations for AF should make provisions for the management of AF in terms of QoL in older as well as younger patients, in whom the QoL benefits may be much greater.

Acknowledgements
Editorial assistance was provided by Saira Ansari and Patricia Fonseca at Touch Medical Communications (UK).

Conflict of interest: Representatives of Meda Pharmaceuticals had no role in gathering, analysing, or interpreting the information presented. Otherwise, the authors have no other conflicts of interest to declare.

Funding
This work was supported by an educational grant from Meda Pharmaceuticals.

References
QoL in patients with AF


Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Europace 2006;8:651–745.


