Quality of life in nonpharmacologic treatment of atrial fibrillation

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The mainstay of treatment for atrial fibrillation, AF, remains pharmacologic control, either by maintaining sinus rhythm or by controlling the ventricular rate and allowing AF to continue. In patients where pharmacologic therapy is not effective, not tolerated or contraindicated, nonpharmacologic treatment may be beneficial. In the last two decades the number of nonpharmacologic treatment options (catheter ablation, cardiac pacing, internal defibrillation, and dysrhythmia surgery) for AF have markedly increased and the number of patients undergoing such treatment is steadily increasing. The most important reason for these treatment strategies is the hope of reducing symptoms, preventing complications and improving quality of life, QoL. However, the impact of nonpharmacologic therapy on QoL is far from established. Following a short presentation of the basic definitions and instruments used in QoL research the present paper reviews clinical studies that have assessed QoL in patients undergoing nonpharmacologic treatment of AF. Major limitations and methodological problems are emphasized. Among these are highly selected often-heterogenous patients groups, small size, lack of control group and the use of non-validated QoL instruments. Furthermore, in most studies antiarrhythmic medication have been discontinued at the time of the intervention and it is not clear to which degree the improvement in QoL is related solely to the nonpharmacologic treatment or to the removal of drug related adverse effects. Although the currently available data from adequately designed studies are sparse and further investigations are needed, it is noteworthy that the majority of patients undergoing nonpharmacologic treatment report enhanced QoL.

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KEYWORDS
Atrial fibrillation; Quality of life; Nonpharmacologic therapy; Maze procedure; Cardiac pacing; Catheter ablation

Introduction

Atrial fibrillation, AF, is the most common clinically significant cardiac rhythm disturbance and is associated with substantial complications and health care costs. The prevalence of AF is increasing with age and the reported prevalence of AF ranges from less than 0.5% in people 25 to 35 years of age, to 1.5% of people up to 60 years of age, to 9% in people older than 75 years of age.\textsuperscript{1} Furthermore reports from western populations concurrently indicate a significant increase in hospital incidence of AF\textsuperscript{2,3} often described as “the epidemic of AF”. An epidemic, which to some extent may be explained by the combination of improved diagnosis of the arrhythmia, increased awareness among referring physicians and increased longevity in the industrial societies.

In contrast to life-threatening arrhythmias, AF may appear benign but may reveal its detrimental effects only after many years. In the Framingham Study AF patients had a nearly two-fold increase in all-cause mortality and...
the management of AF is complex and richly faceted with antiarrhythmic therapy in combination with antiarhythmic drugs as the first-line treatment strategy and with the nonpharmacologic therapies (catheter ablation, cardiac pacing, internal defibrillation, and antiarrhythmic surgery) playing an increasingly important role. As the impact of these varying therapies on morbidity and mortality is unclear, the reduction in symptoms and an improvement in quality of life, QoL, are the most important reasons for treating the patients undergoing nonpharmacologic treatment of AF. Finally the third part sum up the methodological problems involved in the assessment of QoL in nonpharmacologic treatment of AF and proposes a set of eight criteria to be fulfilled when planning QoL studies in the future.

Definitions and descriptions of QoL

The evaluation of QoL is inherently subjective and no consensus on the definition exists. Most approaches used in medical contexts do not attempt to include more general notions such as life satisfaction or living standards and tend rather to concentrate on a multidimensional construct based on four components: physical condition, psychological well-being, social activities and everyday activities.

The lack of a clear definition of QoL is reflected in the many instruments that have been proposed to measure it. Indeed, a state of the art review identified some 150 different measures. However, there are two basic approaches to measure QoL: generic instruments and disease specific instruments.

Generic instruments are used in the general population to assess a wide range of domains applicable to a variety of health states, conditions, and diseases. They are usually not specific to any particular disease state or susceptible population of patients and are therefore most useful in conducting general survey research on health and making comparisons between disease states. The generic instruments facilitate comparisons among different disease groups, however, the broad approach may reduce responsiveness to effects of health care. Currently The Medical Outcome Study Short-Form Health Survey, SF-36, is the most widely validated generic instrument available.

Disease-specific instruments focus on the domains most relevant to the disease or condition under study and on the characteristics of patients in whom the condition is most prevalent. Disease-specific instruments are most appropriate for clinical trials in which specific therapeutic interventions are being evaluated. Disease-specific instruments have several theoretical advantages. They reduce patient burden and increase acceptability by including only relevant dimensions. Disadvantages are the lack of comparability of results with those from other disease groups and the possibility of missing effects in dimensions that are not included. The Symptom Checklist: Frequency and Severity and The Modified Karolinska Questionnaire are both well-validated representatives of cardiac specific questionnaires.

Apart from being generic or disease-specific the instrument should possess several important psychometric properties, which includes coverage, reliability, validity, responsiveness, sensitivity, and practicality, see text Box 1.

### Basic requirements of quality of life assessments

- **multidimensional construct:** the instrument reflects several dimensions of QoL.
• coverage: the measurement of QoL should address each objective and subjective component (symptom, condition, or social role) that is important to members of the patient population and is susceptible to being affected, positively or negatively, by interventions.

• reliability: this concerns whether the measure produces the same results when repeated in the same population under the same conditions.

• validity: concerns whether the instrument measures what it is intended to measure, such as QoL.

• responsiveness: this is a measure of the association between the change in the observed score and the true value of the construct.11

• sensitivity: refers to the ability of a measurement to reflect true changes or differences in QoL.12

• practicality: for a measure to be useful in clinical practice it must not only be valid, appropriate, reliable, responsive and sensitive, but it must be simple, quick to complete, easy to score and provide useful clinical data.16

Studies of quality of life in nonpharmacologic treatment of atrial fibrillation

The mainstay of treatment for AF remains pharmacologic control, either by maintaining sinus rhythm or by controlling the ventricular rate and allowing AF to continue. However, both strategies have several limitations. Drug therapy to suppress atrial fibrillation and maintain sinus rhythm is often ineffective with a recurrence rate to AF in approximately 50% at 6 months during therapy with the best available drugs.6 Furthermore, both regimes are frequently poorly tolerated because of adverse effects and interactions with other drugs. A third limitation of pharmacologic therapy is the risk to the patient from the prescribed therapy. Indeed data are accumulating on increased mortality in patients receiving antiarrhythmic drug therapy.17–19 It is for the portion of patients who either remains symptomatic while receiving pharmacologic therapy or who experience adverse drug effects that nonpharmacologic options until now have been offered.

Surgical therapy

Operative treatment for the patient with refractory AF has been available since early 1980s. The Maze operation, designed by James L. Cox and co-workers, is clearly successful at restoring sinus rhythm, AV synchrony and atrial systole, and thereby diminish the risk of thromboembolism.20 It is an open-heart operation requiring cardiopulmonary bypass, and until now, usually reserved as a therapy of last resort for patients undergoing another clinically indicated surgical procedure, such as mitral valve repair or replacement.

However, in a longitudinal study by Lönnherholm et al.21 the indications for the Maze procedure were expanded to a group of patients with mostly (80%) lone AF, were AF was the primary indication for surgery in all patients. QoL was the primary endpoint in this study and was assessed before operation as well as 6 and 12 months after surgery using the SF-36 questionnaire.

Table 2  QoL before and 6 months after the maze operation21

<table>
<thead>
<tr>
<th>SF 36 variable</th>
<th>Baseline (n=30)</th>
<th>6 months follow-up (n=30)</th>
<th>p*</th>
</tr>
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<tbody>
<tr>
<td>Physical functioning</td>
<td>58.8±25.5</td>
<td>83.3±23.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Role limitation, physical</td>
<td>17.2±33.5</td>
<td>69.0±43.1</td>
<td>&lt;0.001</td>
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<tr>
<td>Bodily pain</td>
<td>70.2±29.8</td>
<td>82.7±28.3</td>
<td>0.07</td>
</tr>
<tr>
<td>General health</td>
<td>56.1±15.6</td>
<td>76.7±21.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Vitality</td>
<td>41.0±19.1</td>
<td>74.2±20.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social functioning</td>
<td>58.5±24.4</td>
<td>87.2±21.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Role limitation, emotional</td>
<td>36.8±42.9</td>
<td>88.9±28.1</td>
<td>0.001</td>
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<tr>
<td>Mental health</td>
<td>64.8±18.3</td>
<td>78.3±20.0</td>
<td>0.008</td>
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*p SF-36 score at 6 months follow-up vs. baseline. Values are mean±SD.

Of the 49 patients included 39 were men (80%) and 10 women (20%). QoL before surgery was significantly lower on all scales, except for bodily pain, than for the age matched general population. All patients underwent the Maze III operation and sinus rhythm was restored and maintained without antiarrhythmic medication in 90% of the 30 patients at 6 months follow-up. After surgery all scores were significantly improved except for bodily pain, which, was already normal before the operation, Table 2. Six months and 1 year after surgery QoL reached the levels of the age-matched general population. Lönnherholm et al. concluded that these results indicate...
that the Maze operation can be used in selected patients with drug-refractory paroxysmal or permanent AF as a primary indication for heart surgery.

Although the study provides important information, there are several limitations that must be recognised. Firstly, no disease specific QoL measure was used and the study was without a control and a placebo group. As mentioned by Lönnertom et al. a significant placebo effect of the surgical intervention is unlikely because the QoL at 1 year was essentially the same as that at 6 months. However, patients may be expected to be withdrawn from prestudy medication after surgery. It is unclear whether the marked improvements in measurement of QoL were related solely to the Maze operation. The removal of drug related adverse effects might have some effect. Secondly, the number of patients was very small with only 25 patients followed for 1-year. Thirdly, the study population was highly selected and severely impaired by their AF, which is evident from the low QoL scores before surgery. Furthermore, the included patients were heterogeneous in regard to the nature of the arrhythmia as well as to age (27 to 72 years). Finally, the fact that only 20% of the included patients were women in the present study cannot be ignored. This have become evident from other studies were QoL in AF have been assessed using the SF-36 questionnaire. 22-24 women have scored significantly worse than men indicating that the impact of AF on QoL is greater in women and findings obtained in a study population consisting of 80% men cannot be transferred to clinical settings with an even distribution of men and women.

In a study by Jessurun et al. 25 41 patients with long-standing symptomatic, drug-refractory, lone paroxysmal AF underwent Maze III surgery. The primary end-point was to establish the effectiveness and safety of the Maze III operation. However, QoL was assessed before surgery and at 3 and 12 months after surgery in 18 patients using the SF-36 questionnaire. 12 After surgery all SF-36 scores were significantly improved except for bodily pain and role limitation. In other words the QoL results as well as the limitations in this study are almost identical to the study by Lönnertom et al. 21 and indicates that the Maze operation has a positive effect on QoL in these highly selected patients groups.

Catheter ablation of atrial fibrillation

Two catheter ablation techniques to modify the substrate of AF are currently under investigation, linear atrial ablation and focal atrial ablation. In long-standing symptomatic, drug-refractory, lone paroxysmal AF underwent Maze III surgery. The primary end-point was to establish the effectiveness and safety of the Maze III operation. However, QoL was assessed before surgery and at 3 and 12 months after surgery in 18 patients using the SF-36 questionnaire. 12 After surgery all SF-36 scores were significantly improved except for bodily pain and role limitation. In other words the QoL results as well as the limitations in this study are almost identical to the study by Lönnertom et al. 21 and indicates that the Maze operation has a positive effect on QoL in these highly selected patients groups.

Catheter based ablation or modification of the AV node

Palliative ablation therapy for AF is well established for patients with disabling symptoms caused by a rapid ventricular rate who are refractory to or who do not tolerate pharmacologic therapy. The rationale for ablation of the AV conduction system with implantation of a pacemaker is that it is almost always easier to treat bradyarrhythmias than tachycardias. However, it must be emphasized that ablation of the AV node is permanent and irreversible. It renders the patient pacemaker dependent with the associated risk of pacemaker failure, lead malfunction, and need for re-implantation. Furthermore, the procedure has no impact on AF nor alter the thromboembolic risk.
AV node ablation and pacemaker implantation

A number of longitudinal studies have evaluated the effect of AV node ablation and pacemaker implantation on QoL. Summaries of these studies appear in Tables 3 and 4. The studies summarised in Table 3 are purely descriptive with no control groups and no randomization. Only the studies by Bubien et al.14 and The Ablate and Pace trial, APT,33 have used validated QoL questionnaires. Bubien et al.14 used a battery of 4 QoL measures before ablation and 1 and 6 months after ablation. A generic instrument, the SF-36 questionnaire, and a disease-specific instrument The Symptom checklist: Frequency and Severity. The latter is intended to measure the patient’s perception of the frequency and severity of symptoms related to the arrhythmias. Furthermore Bubien et al. included two investigator developed non-validated instruments: Perceived Impact of the arrhythmia on Activities of Daily Living and Performance of Activities of Daily Living. A major limitation in this study is the heterogeneity of the arrhythmias included. Only 22 patients had AF and the nature of AF i.e. paroxysmatic, persistent or permanent is not specified.

The Ablate and Pace trial, APT (33) used tree validated self-administered questionnaires:

- Health Status Questionnaire is a generic instrument, nearly identical to the, SF-36.12
- Quality of Life Index, Version II is a disease-specific instrument designed to measure QoL in a population of individuals with cardiac disorders.
- The Symptom checklist: Frequency and Severity is a disease-specific instrument intended to measure the patient’s perception of the frequency and severity of symptoms related to arrhythmias.

After ablation and pacemaker implantation, significant improvements were seen in both the generic and the disease-specific QoL instruments as well as in arrhythmia related symptoms. However, the study was designed as a prospective registry rather than a controlled clinical trial. This makes it impossible to be certain that all of the changes in QoL were due to catheter ablation and pacemaker implantation. For example it is possible that some patients may have experienced improvements with continued medical treatment. In addition, patients included were highly selected, severely symptomatic patients where no distinction between paroxysmatic, recurrent and chronic AF were made. It is important to remember that these study results should not be generalized to less severely compromised patients most frequently seen.

AV node ablation versus medical treatment

The importance of medical ventricular rate control versus pacemaker mediated ventricular rhythm control have been evaluated in patients with persistent15 and permanent16–19 AF with normal25,35 and moderately impaired left ventricular function.36,37,39 These trials are summarised in Table 4. In a study by Brignole et al.37 QoL were assessed longitudinally at the time of enrolment and at the end of the 12 month study period using the following measurements:

- The Minnesota Living With Heart Failure Questionnaire,40 which is a well validated 21-item self-administered questionnaire that covers physical, socio-economic and psychological impairments. A score based on how each person ranks each item on a common scale is used to quantify the extent of impairment and how it is affected by therapeutic intervention.
- The Specific Symptom Scale is a disease-specific instrument used to measure the patient’s perception of the frequency and severity of arrhythmia related symptoms.

At the end of the 12 months study, the ablation- and pacemaker-treated group had significantly better scores in the disease-specific symptoms in comparison with the drug group. However, there were no significant differences in the generic Minnesota Living with Heart Failure Questionnaire scores, with both methods demonstrating improvement over baseline. Because of the controlled design, the study demonstrates that not all the benefits were due to ablation and pacemaker treatment per se, as some improvement occurred also in the conventional treatment group.

Levy et al.38 assessed QoL using the following two instruments:

- Modified Karolinska Questionnaire, KQ, is a cardiac specific questionnaire that has been validated for pacemaker patients.15
- The Nottingham health profile, NHP, is a general QoL instrument validated for cardiac patients.41,42 It is divided into two parts. The first consists of six dimensions: physical, mobility, pain, sleep, energy, social isolation, and emotional reaction. The second part lists aspects of life that may be affected by the patients’ health.

Both patient groups had significant improvement in total KQ scores and total NHP part 1 scores at all follow-ups. For inter-group comparison there was no significant difference in any baseline result or between groups in follow-up. For part 2 of the NHP there was no significant change from baseline in either group at any time or any difference between groups. Levy et al. conclude that in these patients improved rate control will lead to a significant improvement in exercise duration and QoL and that neither technique shows any significant advantage over the other.

Overall the studies suggest that ablation may be advantageous in patients with permanent AF when left ventricular function is moderately impaired. However, ablation offers no advantage in the presence of normal ventricular function if rate control can be achieved with AV blocking agents. The pragmatic clinical approach as proposed by Levy et al.38 may be medical treatment first in combination with a VVI-R pacemaker as it avoids initial...
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Intervention</th>
<th>Instrument(s)</th>
<th>QoL results</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Kay et al.,28 1988</td>
<td>Longitudinal (6 weeks) 12 patients with paroxysmal AF</td>
<td>AV junction ablation and VVI-R PM</td>
<td>McMaster Health Index Questionnaire, Physiological General Well-Being Index</td>
<td>Scores in both measures increased significantly from before ablation to 6 weeks after ablation</td>
<td>Small sample size, Short follow-up time, No control group, Highly selected severely symptomatic patients, The impact of drug-related adverse effects on QoL is unknown</td>
</tr>
<tr>
<td>Rosenqvist et al.,29 1990</td>
<td>Longitudinal (41±23 months) 47 patients, 29 with AF or atrial flutter</td>
<td>AV junction ablation and VVI, VVI-R, or DDD PM compared with direct current catheter ablation</td>
<td>Interview</td>
<td>83% of 42 patients reported improved activity level</td>
<td>No validated QoL instrument, No control group, Highly selected severely symptomatic patients, Heterogeneity of arrhythmias, Time of interview unknown, No information on interview method</td>
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<tr>
<td>Olgin and Scheinman,30 1993</td>
<td>Longitudinal (41±23 months). 103 patients, 73 with AF or atrial flutter</td>
<td>Radiofrequency AV junction ablation and VVI-R, DDI-R, or DDD PM compared with direct current catheter ablation</td>
<td>Interview</td>
<td>83% reported improved condition after ablation</td>
<td>No validated QoL instrument, No control group, Highly selected severely symptomatic patients, Heterogeneity of arrhythmias, Time of interview unknown, No information on interview method</td>
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<td>Fitzpatrick et al.,31 1996</td>
<td>Retrospective, cross-sectional review of patients medical cards and telephone survey, 90 patients with paroxysmal (n=36) and established (n=54) AF</td>
<td>AV junction ablation and DDD PM if paroxysmal AF and VVI PM if permanent AF</td>
<td>Semiquantitative questionnaire on QoL, symptoms and ADL, Registration of health care consumption</td>
<td>Significant improved QoL and reduced consumption of health care resources after AV junction ablation</td>
<td>No validated QoL instrument, Retrospective nature, No control group, Highly selected severely symptomatic patients</td>
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<tr>
<td>Bubien et al.,14 1996</td>
<td>Longitudinal (6 months). 161 patients with supraventricular or ventricular arrhythmia including 22 with AF</td>
<td>Radiofrequency catheter ablation</td>
<td>SF-36, Symptom checklist: frequency and severity, Perceived impact on ADL, Perceived effect on ADL</td>
<td>AF patients had poorer QoL at baseline than patients with other arrhythmias, Catheter ablation was associated with significant improvement in QoL</td>
<td>Heterogeneity of arrhythmias, No classification or description of AF, Small sample size, No control group, Highly symptomatic selected patients</td>
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</table>
| Natale et al., 32 | Longitudinal (12 months), 12 patients with chronic AF. | AV node ablation and VVI-R PM       | • Self-administered questionnaire on palpitations, rest dyspnea, effort dyspnea, exercise tolerance, weakness, and perception of well-being | • The perception of well-being increased significantly after ablation and persisted over time | • No randomization  
|                  | 1996                          |                                     |                                                                              |                                                                              | • No control group  
|                  |                               |                                     |                                                                              |                                                                              | • Small sample size  
|                  |                               |                                     |                                                                              |                                                                              | • No validated QoL instrument  
| Kay et al., 33    | Longitudinal (12 months), multicenter, 156 patients with paroxysmal, recurrent or chronic AF. | AV junction ablation and VVI or DDI PM | • Health Status Questionnaire (2.0)  
• Quality of Life Index, Version III  
• Symptom checklist: frequency and severity | • Significant improved QoL in all three measurements | • No randomization  
|                  | 1998                          |                                     |                                                                              |                                                                              | • No control group  
|                  |                               |                                     |                                                                              |                                                                              | • Highly selected severely symptomatic patients  
|                  |                               |                                     |                                                                              |                                                                              | • The impact of drug-related adverse effects on QoL is unknown  

*a* QoL, quality of life.  
*b* AV, atrioventricular node.  
*c* VVI(-R), ventricular demand pacing.  
*d* PM, pacemaker.  
*e* AF, atrial fibrillation.  
*f* DDD, DDI(-R), dual chamber pacing.
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<tbody>
<tr>
<td>Brignole et al., 1994</td>
<td>Randomized, longitudinal. 23 patients with chronic AF or atrial flutter and moderately impaired left ventricular function (mean LVEF 46%).</td>
<td>Two-phase study 1. Randomized to AV junction ablation and VVI-R PM or VVI-R PM only. 15 days follow-up. 2. The remaining patients underwent AV junction ablation. 3 months follow-up.</td>
<td>Self-administered semiquantitative questionnaire on five symptoms (palpitations, rest dyspnea, effort dyspnea, exercise intolerance and asthenia.</td>
<td>After 15 days symptoms decreased more in patients undergoing ablation. After 3 months improvement in symptoms were associated with improvement in functional class (NYHA, exercise duration) No validated QoL instrument Small sample size Short follow-up Highly selected severely symptomatic patients The impact of drug-related adverse effects on QoL is unknown</td>
<td>Small sample size Short follow-up Highly selected severely symptomatic patients The impact of drug-related adverse effects on QoL is unknown</td>
</tr>
<tr>
<td>Brignole et al., 1997</td>
<td>Randomized, longitudinal (6 months), multicenter. 43 patients with paroxysmal AF.</td>
<td>Randomization to: AV junction ablation and DDD'-R PM or antiarrhythmic drug treatment</td>
<td>Minnesota Living With Heart Failure Questionnaire&lt;sup&gt;41&lt;/sup&gt; Specific Symptoms Scale</td>
<td>PM&lt;sup&gt;10&lt;/sup&gt; implantation was effective and superior to drug treatment in controlling symptoms and improving QoL</td>
<td>Highly selected severely symptomatic patients Small sample size Short follow-up The impact of drug-related adverse effects on QoL is unknown</td>
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<tr>
<td>Brignole et al., 1998</td>
<td>Randomized, longitudinal (12 months), multicenter. 60 patients with HF and chronic AF. Moderately impaired left ventricular function (mean LVEF 43%).</td>
<td>Randomization to: AV junction ablation and VVI-R PM or antiarrhythmic drug treatment</td>
<td>Minnesota Living With Heart Failure Questionnaire (LHQF)&lt;sup&gt;41&lt;/sup&gt; Specific Symptoms Scale</td>
<td>PM implantation was effective and superior to drug treatment in controlling symptoms No significant benefit on LHQF and NYHA</td>
<td>Highly selected severely symptomatic patients Crossover from drug treatment to PM (12%)</td>
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<tr>
<td>Study</td>
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<tr>
<td>Natale et al., 1999</td>
<td>Longitudinal consecutive (6 months), multicenter. 75 patients with chronic AF and moderately impaired left ventricular function (mean LVEF 40%).</td>
<td>Patients were assigned to one of three groups 1. AV ablation, VVIR PM and drug withdrawal 2. AV ablation, VVIR PM and continued medication 3. VVIR PM and continued medication</td>
<td>● Quality of Life Enjoyment and Satisfaction Questionnaire  ● Symptom score  ● Performance of specific activities  ● Perception of well-being</td>
<td>● Group 1: all variables assessed improved significantly  ● Group 2: all variables assessed improved, some significantly  ● Group 3: No change in the assessed variables</td>
<td>● Non-randomized  ● The questionnaires have not been validated in the present population  ● No placebo medication in group 1</td>
</tr>
<tr>
<td>Levy et al., 2001</td>
<td>Randomized, longitudinal (12 months) 36 patients with permanent AF and normal left ventricular function.</td>
<td>Randomization to: His ablation and VVI-R PM or AV modifying drugs and VVI PM</td>
<td>● Karolinska questionnaire  ● Nottingham health profile</td>
<td>● Similar QoL in the two groups.  ● Significant QoL improvement in both groups after treatment</td>
<td>● Small sample size.  ● No control group  ● Highly selected severely symptomatic patients</td>
</tr>
</tbody>
</table>

*QoL, quality of life.  
^AV, atrioventricular node.  
^LVEF, left ventricular ejection fraction.  
^VVI(-R), ventricular demand pacing.  
^NYHA, New York Heart Association functional class.  
^AF, atrial fibrillation.  
^DDD, DDI(-R), dual chamber pacing.  
^PM, pacemaker.  
^HF, heart failure.
irreversible ablation. Ablation can eventually be performed at a later stage in non-responders.

**AV node ablation versus AV node modification**

Partial AV node ablation, AV modification, has been tried as an alternative to AV node ablation. The objective of partial AV node ablation is to modify the conduction properties slowing the ventricular rate in AF without the need for pacemaker dependency. Unfortunately, AV node modification is technically difficult and long-term results often unpredictable. In contrast to the almost 100% success in AV node ablation, the success in AV node modification is approximately 70%. QoL in patients undergoing AV node ablation or AV node modification have been compared in a longitudinal study of 60 patients with medically refractory paroxysmal or chronic AF. The patients were randomly assigned to either complete AV nodal ablation with permanent VVI-R pacing or AV nodal modification. QoL was assessed before and at 1 and 6 months after ablation/modification using a QoL diary and a semiquantitative questionnaire.

Both treatments were associated with a significant improvement in general QoL. Patients who received AV nodal modification remained symptomatic, perhaps because of their irregular ventricular rhythm of AF. In other words AV nodal ablation with permanent pacing had a significantly greater effect than AV nodal modification in decreasing the frequency of attacks and extent of symptoms of AF, and the patients who received this procedure were more satisfied with their general well-being. A major limitation in this study was the use of non-validated QoL instruments. Furthermore, no control group was incorporated and the follow-up time period was only 6 months.

**Pacing management of atrial fibrillation**

Several investigators have reported an increased incidence of AF with the use of ventricular pacing as compared with atrial or dual-chamber pacing. These findings have led to newer pacing techniques for the prevention of AF in selected patients. The theoretical rationale for multisite atrial pacing is that pacing from a second site can achieve a more synchronous activation of the atria thus preventing the occurrence of reentrant circuits. Dual-site atrial pacing involves inserting one pacing lead in the right atrial appendage and the other pacing lead at the ostium of the coronary sinus. The impact of dual site atrial pacing on QoL has been tested in two prospective randomized crossover trials. Table 5.

Although both studies have used well-validated QoL instruments and both studies are randomized and prospective there are important limitations. First, the small number of patients, a much larger population would have been required to demonstrate differences in QoL because of large variability of the measured parameters. Second, the short follow-up periods. However, it is noteworthy that neither of the studies demonstrated a beneficial effect of multisite atrial pacing on QoL.

**Implantable atrial defibrillator**

In the currently used atrial defibrillator the shocks for AF can be activated by the patient or can be programmed to occur automatically in the early morning while the patient is asleep. Thus, this therapy provides some patient control over the treatment, which has lead to speculations concerning improved QoL. Newman et al. have evaluated the impact of QoL of patients implanted with atrial defibrillators. In the present study 144 patients with symptomatic AF or atrial tachycardia received an atrial defibrillator. QoL was assessed at baseline, 3 months post-implant, and 6 months post-implant using the SF-36 and The Symptom Checklist: Frequency and Severity.

QoL assessments were available at baseline, after 3 and 6 months. Two of the subscales in the SF-36 (role-physical and vitality) improved significantly after the implantation. The other 8 SF-36 scales showed no decrease from pre-implant over time. Furthermore, symptoms decreased significantly from baseline to 3 and 6 months without a change in symptom severity. In other words the implantation of an atrial defibrillator increased some domains of QoL and decreased the frequency of symptoms in a small subgroup of patients with symptomatic, drug-refractory AF. However, other investigators have not confirmed the results and the lack of a control group is a major limitation when interpreting these findings.

**Conclusion**

There is an increasing awareness that QoL is important and QoL has become a key issue in a growing number of clinical trials. However, despite the fact that AF is a very common disorder with profound impact in terms of morbidity and mortality, the currently available data from adequately designed studies are sparse. From the studies reviewed, the available data show that QoL is impaired in patients with AF and that the majority of patients after having undergone a nonpharmacologic treatment report enhanced QoL. There may be several reasons for these findings:

- Prior to the intervention all patients have been burdened by severe symptoms caused by AF and by side effects to antiarrhythmic drugs. Improvements in QoL are therefore more or less expected and similar improvements may not occur in less symptomatic populations.
- In most studies antiarrhythmic medication have been discontinued at the time of the intervention and it is not clear to which degree the improvement in QoL is related solely to the nonpharmacologic treatment or to the removal of drug related adverse effects.
- Participants who undergo an invasive procedure may report improvement in QoL simply as a result of being part of a treatment group.
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QoL: quality of life.
AF: atrial fibrillation.

Quality of life in nonpharmacologic treatment of atrial fibrillation
• Underreporting of undesirable characteristics and over reporting of socially desirable characteristics might confound self-reporting methods.52

• In longitudinal study designs with variables containing random errors (short-term intra-individual variations and measurement errors) the computed relation is biased by the regression towards the mean phenomenon. Consequently, the observed improvement in QoL before and after nonpharmacologic intervention is not caused by the intervention alone but reflects the effect of repeated measurements and the regression towards the mean phenomenon as well.

Many of the methodological problems involved in the assessment of QoL have already been discussed in conjunction the relevant studies, however some of the major issues should be emphasized:

• Heterogeneity of study groups, which means that patients with different manifestations of AF as well as patients with different conduction disorders were analyzed together. As the impact of AF on QoL depends on the type of AF i.e. paroxysmal, persistent or permanent this heterogeneity is an important limitation when interpreting results.

• Many of the reviewed studies are descriptive with no control group and no blinding opening the door for possible investigator bias.

• The vast majority of the prospective studies have a short follow-up time and the long-term effects of any given pacemaker cannot be assessed. Short- and long-term results may very well differ which is apparent in the study by Lamas et al.53 where there were no significant differences in disease-specific QoL at either three or at nine months. However, there was a significant difference favouring dual chamber pacing at the 18 months visit, and longitudinal analysis demonstrated a significant difference favouring dual-chamber pacing. In addition longer follow-up would make it possible to determine whether pacemaker patient’s QoL changed over time in association with aging and the development of comorbid states.

• Small sample size is a general problem limiting the statistical power in the reports. Only a few authors have accounted for sample size calculations and power levels.

• Some investigators seem to substitute QoL for other terms such as ‘health status’ or ‘functional status.’ The investigators often do not define what they conceptualize as QoL and they do not identify the specific domains of measurements that are supposed to denote QoL.

Three randomised controlled trials have compared pharmacologic rate control therapy with pharmacologic rhythm control therapy using QoL as a secondary endpoint; The Pharmacological Intervention in Atrial Fibrillation (PIAF) study,54 The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trail,55 and the Rate Control versus Electrical Cardioversion (RACE) trail.56 The studies show that rate control is as efficacious as rhythm control in improving QoL and challenge the concept that restoration of sinus rhythm in patients with AF is always an important goal. At first glance these results may appear contradictory to the improvements in QoL obtained in studies on nonpharmacologic treatment. A discrepancy that is readily explained looking at the patients enrolled in the trials. Patients in the AFFIRM and the PIAF are representative of the majority of patients with AF being elderly often mildly symptomatic, where as patients undergoing nonpharmacologic treatment are severely symptomatic, often younger patients referred to tertiary care. However, these results underline the need for an individualised treatment strategy with careful assessment of symptoms and underlying cardiac disease. Patients in whom AF causes symptoms despite pharmacologic therapy or who experience adverse drug effects may be candidates for nonpharmacologic treatment strategies and can expect improved QoL following such treatment.

From the above reviewed studies it is apparent that the number of QoL instruments is overwhelming and that the wide variation in the instruments selected makes it difficult to compare QoL findings across studies. The following eight criteria may be useful when planning new studies as well as when evaluating the existing literature:

1 Having a conceptual definition of QoL
2 Identifying what dimensions of QoL are measured
3 Specifying the rationale for the choice of measures selected
4 Using at least one measure that is general in focus — i.e. a generic instrument
5 At least one measure that is specific to the population of interest — i.e. a disease-specific
6 Selecting measures with evidence of reliability and validity and reporting appropriately
7 If appropriate, collecting data at several points in the treatment process to consider any change over time
8 Asking patients to give an overall rating of their QoL

Hopefully these criteria may act as an inspiration for investigators planning future studies thus enhancing the quality of quality of life research in nonpharmacologic treatment of AF.

References


