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The Impact of Atrial Fibrillation Ablation on Quality of Life

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Abstract

Quality of life (QoL) is a very important endpoint in trials reporting the efficacy of catheter ablation in patients with atrial fibrillation (AF). It has been shown that AF ablation significantly improves the QoL, but recent studies question the usefulness of the most used generic QoL instrument in AF patients. The complexity of the disease makes it mandatory to employ disease specific instruments in the assessment of QoL. This paper reviews the current knowledge of various QoL instruments, including the limitations and pitfalls, and the impact of AF ablation on the QoL

Introduction

The cornerstone of treatment in patients with atrial fibrillation (AF) is to reduce symptoms and improve the quality of life (QoL).[1] The QoL is significantly reduced in AF patients, caused not only by symptoms related to the arrhythmia, but also the medication. Several trials have demonstrated that catheter ablation of AF improve the QoL significantly, [2-14] and QoL should be assessed and reported in every clinical trial with patients undergoing an intervention due to symptomatic AF.[15] However, concerns have been raised that the present QoL instruments are not sufficiently sensitive to detect changes in disease specific symptoms, such as those associated with AF. Several instruments to evaluate disease specific QoL exist [16-19] but there is a lack of consensus regarding how to evaulate the QoL in AF patients. This paper reviews the current knowledge of various QoL instruments, and the impact of AF ablation on the QoL.

QoL Assessment

QoL is a subjective phenomenon, and there is no consensus of how to define QoL. The World Health Organisation defined health as the absence of disease and the presence of physical, mental and social well-being. Hence, QoL is a complex and multidimensional quantity to measure, which explains why over 35 different QoL instruments have been reported.[15] Most instruments are not specific for AF patients, which has led to the development of new QoL instruments. Table 1 presents the most used QoL instruments.

Generally, the QoL assessment should include both a generic and symptom specific instrument. Generic instruments are used to evaluate the physical, mental and social well-being. The most used questionaire is the multi-purpose, short-form health survey with 36 questions (SF-36). The SF-36 form is very well-validated and has been applied in various types of patients and the general pop-

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Table 1 Quality of Life Measures Used in Atrial Fibrillation Studies

Generic measures	Disease specific measures
SF-36 (Short-Form health Survey)	Minnesota Living with Heart Failure Questionnaire
SF-12	Arrhythmia Symptoms Checklist: Frequency and Severity (AFSCL)
WHO-26	
EuroQOL (EQ-5D)	University of Toronto AF Severity Scale (AFSS)
SF-6	AF-QoL
Global Health Status Questionnaire	Atrial Fibrillation Effect on QualiTy of life (AFEQT)
Medical Outcomes Study	Mayo AF-Specific Symptom Inventory (MAFSI)
Depression Scale	Specific Symptoms Scale
Health Status Questionnaire	Specific Activity Scale
Assessment of Quality of Life	Quality of Life of Atrial Fibrillation
Instrument (AQoL)	
And many more	

ulation.[20] It yields an 8-scale profile of functional health and well-being scores including physical function (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role-emotional (RE) and mental health (MH). The scores in each of the eight subscales are standardized from 0 to 100, with the higher scores indicating better QoL. Several studies have compared the QoL in AF patients with the general population, and patients with other cardiac diseases.[1] The EuroQol (EQ-5D) is a well-validated, generic health-related quality-of-life measure.[21] It is self-administered and has 5 dimensions assessing mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It also includes a visual analog scale that asks respondents to rate their current health from 0 to 100, with 0 representing death and 100 indicating perfect health. The 5-item questionnaire can also be transformed to a societal-based utility score, ranging from 0 to 1, with higher scores reflecting better healthstatus.

However, generic QOL instruments may not be sufficiently sensitive or focused to detect changes in disease specific symptoms, such as those associated with AF. Several instruments to evaluate disease specific QoL exist. The most commonly used disease specific questionnaire is the AF Symptom Checklist (AFSCL), which measures frequency and severity of AF related symptoms.[22] The AFSCL is easy to use, and has been used in a high number of AF studies. The Atrial Fibrillation Severity Scale (AFSS) is a 19-item self administered questionnaire developed to capture subjective and objective ratings of AF related symptoms, health care utilization, and AF disease burden, including frequency, duration, and severity of episodes .[23] The AF symptom burden score is derived from the AFSS summary score that averages the frequency, duration, and patient perceived severity of AF episodes. A higher score indicates greater AF burden. Another QoL instrument is the Mayo AF-Specific Symptom Inventory (MAFSI) that was introduced to clinically follow AF-specific symptoms. Although it has some common elements with the AF Symptom Checklist, the MAFSI inventory monitors additional symptoms. Using a checklist of 12 symptoms, patients score the frequency of symptoms over 6 months as 0 (never), 1 (rarely), 2 (sometimes), 3 (often), and 4 (always). Total scores range from 0 to 48. It was recently used in a publication by Woklu et al., but has not yet been validated.[18]

The need for comprehensive, disease specific measurement tools, to quantify the effect of AF on patients QoL more accurately and reliably, has led to the development of new QoL instruments specific for AF patients.

The AF-QoL questionnaire was recently developed and validated in a Spanish population.[17] The AF-QoL instrument is an 18-item self-administered questionnaire with three domains: psychological, physical, and sexual activity. The psychological domain includes seven items, the physical domain includes eight items, and the sexual activity domain includes three items. The questions refer to the previous month. All domains have been standardized for a scoring between 0 (worst QoL) and 100 in order to facilitate interpretation and comprehension. The AF-QoL is able to discriminate between AF patients and patients with previous myocardial infarction in contrast to other questionnaires such as the AFSCL or the

SF-36. Additionally, AF patients with a higher percentage of clinical symptoms such as palpitations, chest discomfort, and dyspnea had lower scores demonstrating the discriminant validity of the questionnaire. In this context, the AF-QoL may be a necessary tool to evaluate the QoL and well-being in patients with intermittent AF who are in sinus rhythm at the time of evaluation and completely asymptomatic allthough severely affected by the disorder regardless the absence of symptoms at the moment of evaluation.

Another disease specific QoL instrument is the AFEQT questionnaire that has shown to be valid, reliable, and responsive to clinical change in AF patients.[16] It is a 20-item instrument including a 4-item Symptoms score, an 8-item Daily Activities score, a 6-item Treatment Concerns score, and a 2-item Treatment Satisfaction scale. The first 3 of these domains can be grouped to form an Overall score. This score was able to distinguish between patients with asymptomatic and symptomatic AF, but also between patients who had AF symptoms within 4 weeks versus 4 weeks from questionnaire completion. It was more responsive to changes in patients` QoL related to pharmacological therapy and ablation therapy as compared the generic SF-36 and EQ-5D questionnaires. The AFEQT was as responsive as the disease specific AFSCL and AFSS.

Other instruments used for quantifying the symptoms related to AF have been published.[1] The European Heart Rhythm Association (EHRA) AF classification and the Canadian Cardiovascular Society Severity in Atrial Fibrillation Scale (CCS-SAF) are instruments to quantify symptoms and functional capacity in patients with AF similar to the New York Heart Association (NYHA) functional class score in patients with heart failure.[19] Both instruments are easily applied and learned without the need for extensive training and experience. However, the CCS-SAF classification is the only one validated, and correlates highly with mental and physical aspects of QOL, patient-perceived severity of AF, the degree of symptoms judged from a validated questionnaire, and general well-being.

Limitations of QoL Instruments in AF Patients

AF is a very heterogenous disease making the QoL assessment in these patients difficult. Some studies have found that the impact is greater on the physical domain, and that QoL also depends on individual experiences, beliefs and expectations regarding the disease. Sociodemographic variables, like age and gender, also affect QoL, with female patients and those under the age of 69 obtaining the worst score.[15]

Studies show that QoL improve over time irrespective of rate- or rhythmcontrol,[1] which may relate to the low sensitivity of the generic instruments to changes in an AF patient. Furthermore, AF patients with paroxysmal AF may be in sinus rhythm at the time of evaluation or even asymptomatic during AF. The correlation between AF recurrence and subjective measurements like QoL is poor. This emphasizes the importance of symptom specific QoL assessment that allow a better assessment of the impact of this disease on patient's daily living while, in addition, other specific aspects of the disease can be identified. Most studies of AF ablation and QoL have been performed in patients with severe symptoms with a higher impact on the changes of the QoL. In a general population of patients undergoing AF ablation, the less symptomatic patients may reach scores of approximately 100 (ceiling effect) and subtle changes in the QoL cannot be evaluated. In this case, the disease specific QoL instruments seem more reliable.

Studies of changes in QoL in AF intervention should be performed prospectively. There might be some recall bias in retrospective studies overestimating the QoL scores before intervention.[15]

One limitation of studies assessing changes in QoL after ablation is the lack of details regarding how the QoL surveys were administered. Self-assessments of well-being by individuals can be biased by adaptation behaviour. Adaptation is aimed at reducing or eliminating psychological distress, and may explain why patients with health problems report higher levels of well-being than expected. Hence, adaptation behaviour may bias the answers to survey questions on subjective well-being or subjective quality of life which should be considered in trials reporting QoL. Patients may also respond more truthfully to self-administered questionnaires compared to interviewer-administered surveys. QoL surveys administered by a

nurse or physician involved in the study may be associated with report bias, since they may have an incentive to underestimate the QoL of patients before the treatment and to overestimate the QoL after the medical intervention.

Timing of the QoL surveys should also be considered. It might be speculated that patients may report a lower QoL before ablation biased by anxiety in the light of an upcoming invasive procedure.

Furthermore, the placebo effect is difficult to comprehend, and some trials suggest that the placebo effect is significant and may overestimate the QoL changes. The only way to objectively assess the impact of ablation on QoL would be a randomized trial with a sham ablation procedure but due to ethics, sham ablations have not yet been performed. Instead, researchers may theoretically minimize the placebo effect in AF trials by reporting long term QoL assessment after ablation.

Additionally, caution is needed when interpreting the results because the positive changes in QoL may not related to control of the rhythm. In fact, many patients with AF have periods of asymptomatic AF, so it is recommended to evaluate the rhythm outcome after AF ablation using long-term rhythm monitoring.[24]

Quality of Life After AF Ablation

The aim of catheter ablation in patients with AF is to reduce symptoms and improve the QoL. Several studies have shown that the QoL improve significantly after AF ablation assessed primarily by the generic SF-36 questionnaire as shown in Table 2. [2-11] Woklu and collegues recently published the long-term effect of AF ablation on outcome and QoL in 323 patients with AF (50% paroxysmal).[18] They used the SF-36 questionnaire and disease specific MAFSI instrument for QoL analysis. They found a marked and sustained improvement in QoL at 2 years of follow-up, but QoL improvement was not closely linked to overall ablative efficacy. Although the QoL improvement was high in patients with AF elimination, substantial QoL improvement was also seen in patients with AF control on anti-arrhythmic drugs and in patients with recurrent AF. In contrast, the MAFSI instrument was better to detect changes in AF-specific symptoms and was more strongly correlated to the efficacy of AF ablation.

Similar findings were reported by Fichter et al., who assessed the QoL after catheter ablation for symptomatic, drug-AF using 7 different validated generic and disease-specific instruments (AFSS, AFSCL, WHO-5-Well-Being-Index (WHO), Major Depression Inventory (MDI), Sleep and Vegetative disorder (SV), Vital Exhaustion (VE), and Illness intrusiveness(Ii).[25] During long-term follow-up, a highly significant improvement in all QoL questionnaires was found regardless of ablation success. Only the disease-specific questionnaires AFSS and AFSCL and the generic questionnaire MDI were able to detect a difference in improvement between patients with AF elimination or recurrences.

In a previous study, we found that patients who had asymptomatic AF recurrences one year after ablation showed improvement in the subscales of general health, vitality and role physical reflecting an improvement in the physical scores using the SF-36 questionnaire.[26] This improvement was obtained even though these patients often had persistent AF. Such transition to less severe or asymptomatic disease states could be due to direct ablation effects, secondary destruction of autonomic inputs to the atrium, or Woklu and collegues recently published the long-improved pharmacologic efficacy. Other explanations may be an overestimation of QoL improvement due to regression to the mean (less symptomatic on average than at presentation), placebo effects, or maybe the fact that the SF-36 questionnaire does not entirely describe the QoL burden that a complex disease such as AF imposes on the well-being of patients. The result underlines that a QoL assessment should include an AF-specific symptom instrument that reflect the efficacy of ablation more accurately.

Three randomized clinical trials compared catheter ablation to antiarrhythmic drug therapy in patients with paroxysmal AF, and also evaluated QOL as an outcome measure .[12,13,27] Catheter ablation was associated with significant improvement in SF-36 scores relative to baseline. QOL scores were significantly higher in patients undergoing ablation than in patients treated with drug therapy, in which there was little change from baseline scores. Similar significant trends were observed for the AFSCL scores. One randomized study examined QOL in 146 patients with persis-

Table 2 Studies with QoL assessment after AF ablation

Study	Population	Intervention	QOL Assessment	Results
Erdogan et al. 2003	Intervention • 30 pts with PAF • FU 36 months	Right atrial ablation (linear lesions)	• SF-36 • Symptom specific checklist (unvalidated)	• 30% in SR • Improvement in all SF-36 subscales in pts without AF
Pappone et al. 2003	• 33 pts with AF • FU 36 months	Ablation of focal triggers in right atrium and PVs	• SF-36	• 94% without AF recurrence (12% with AADs) • Improvement in all subscales except BP
Goldberg et al. 2003	• 211 pts with PAF • FU 12 months	109 pts circumferential ablation (109 pts) and treated medicine(102 pts)non- randomized.	• SF-36	• Physical and mental composite scores of the SF-36 increased significantly in AF ablation, no change in medically treated pts.
Hsu et al., 2004	• 58 pts with CHF and AF • 58 matched pts with AF without CHF	PVI + linear lesions	• SF-36 compared to matched healthy cohort • Symptom checklist	• Improvement in both groups
Chen et al., 2004	• 377 pts with AF (PAF?) • focus on 94 patients with CHF • FU 6 months	•PVI + CTI in 10% of pts	• SF-36	• Improvement in all subscales irrespective of LVEF
Weerasooriya et al., 2005	• 63 pts with PAF • FU 12 months	PVI + linear lesions	• SF-36	• Improvement in all subscales
Tondo et al., 2006	105 pts with PAF and persistent AF (75%) • CHF in 40 pts • FU 6 months	PV antrum ablation + linear lesions	• SF-36	• Improvement in >6 subscales. • Similar improvements in CHF pts.
Wazni et al., 2005	70 pts with PAF • FU 6 months	Randomisation to PVI or AADs.	• SF-36	• Improvement greater in PVI group than AAD in 5/8 subscales
Oral et al., 2006	46 pts with long-standing persistent AF • FU 12 months	• Symptom Severity Questionarie (locally derived	• Symptom Severity Questionarie (locally derived	• Significant QoL improvement in pts without AF recurrence compared to pts with AF recurrence. AF recurrence less common in pt undergoing AF blation

Jais et al., 2008	• 112 pts with PAF • FU 12 months	Randomised to Lasso-guided circumferential PVI +linear lesion+CTI or medical treament (AADs)	• SF-36 • No AF-specific questionnaire	• AF freedom: 89% in ablation group, 23% in AAD group • Significantly higher PCS and MCS scores in the ablation group
Woklu et al., 2010	• 323 pts (50% PAF) • FU 24 months	Circumferential or lasso-guided PVI + linear lesion + CTI	Circumferential or lasso-guided PVI + linear lesion + CTI	• AF freedom: 69% after 24 months • Significant QoL (SF-36) improvement in pts with AF elimination • Substantial QoL improvement in pts with AF control on AADs and recurrent AF pts. • MAFSI was better to detect changes in AF specific symptoms and strongly correlated to the efficacy of AF ablation
Fichter et al., 2011	• 133 pts • 65 % PAF • FU median 4,3 years	PAF: PVI (+CFAEs) NPAF: circumferential PVI + linear lesions or ostial PVI + CFAEs.	• AFSS/AFSCL • WHO-5 • Major depression inventory (MDI) • Sleep and vegetative disorder • Vital exhaustion • Illness intrusiveness	• AF freedom: PAF 66%, NPAF 50% • Significant improvement in all QoL questionnaires regardless of AF ablation success. • Disease-specific instruments such as AFSS and AFSCL (and the generic MDI survey) could detect differences in symptom/ QoL improvement secondary to AF elimination
Mohanty et al, 2011	• 660 patients (PAF 27%) • High-BMI versus normal weight pts. • FU 12 months	PV antrum ablation + linear lesions + CFAEs in persistent AF	• SF-36 (self-adm) • Beck Depression Inventory (BDI) • Hospital anxiety and depression scale (HAD) • State-trait anxiety Inventory • No AF-specific questionnaire	• No differrence in procedural outcome between groups (AF freedom 63% (high- BMI) versus 69%) • Significant improvement in most QoL scales in high-BMI patients during FU • No improvement in normal weight pts.
Mohanty et al, 2012	• 1496 patients (PAF 29%) • Metabolic syndrome (MS) • FU 12 months	PV antrum ablation + linear lesions + CFAEs in persistent AF	• SF-36 (self-adm) • No AF-specific questionnaire	• MS was associated with higher AF recurrence rate, especially in pts with nonparoxysmal AF (46% vs. 35%) • AF type, female sex, and MS independent predictors of AF recurrence • Baseline QoL more impaired in MS pts, significant improvement during FU.

AF: atrial fibrillation, SR: sinus rhythm, QoL: quality of life, PAF: paroxysmal AF, FU: follow-up, PV: pulmonary vein, PVI: pulmonary vein isolation, CFAEs: complex fractionated atrial electrograms, CTI: cavotricuspid isthmus ablation, BMI: body mass index, AAD: anti-arrhythmic drug, CHF: congestive heart failure, LVEF: left ventricular ejection fraction, PCS:physical composite summary, MCS: mental composite summary, AFSS: AF Severity Scale, AFSCL: AF Symptom Checklist: Frequency and Severity, MAFSI: Mayo AF-Specific Symptom Inventory.mus or zotarolimus) and at least 6 months for a –taxel-eluting stent.

tent AF, randomized to catheter ablation or cardioversion alone.[28] This study demonstrated that catheter ablation was more effective in maintaining sinus rhythm, and patients who were in sinus rhythm demonstrated a greater improvement in the symptom severity score than those patients with recurrent AF or atrial flutter.

A non-randomized study showed that 58 patients with longstanding persistent AF and symptomatic heart failure improved both left ventricular ejection fraction (LVEF) and the QoL significantly after AF ablation compared to a control group evaluated by the SF-36 and AFSCL.[5] A randomized trial compared the effect between AF ablation and AV nodal ablation with CRT (cardiac resyncronization therapy) in 81 heart failure patients with symptomatic AF (50% paroxysmal). AF ablation increased the LVEF and the the 6-minutes walk test significantly compared to AV nodal ablation and resyncronization. The QoL after AF ablation was also higher reflected by the changes in the Minnesota Living with Heart Failure Questionaire.[29]

Two prospective trials by Mohanty et al. recently evaluated the effect of obesity and metabolic syndrome (MS) on outcome after AF ablation.[30,31] They found no significant difference in procedural outcome after AF ablation in high-BMI patients (Body Mass Index > 25) compared to normal-weight patients (AF freedom in 63% versus 69% of patients). High-BMI patients had significant improvement in the composite scales of QoL during follow-up, whereas normal-weight patients showed no improvement despite procedural success. In a prospective trial with 1496 patients, they found that patients with MS had a higher AF recurrence rate, especially in non-paroxysmal AF patients. AF type, female sex, and MS were independent predictors of AF recurrence. In MS patients, there were more impairment in baseline QoL and larger improvement in QoL during follow-up after AF ablation. Limitations to both studies were the lack of AF specific QoL assessment questionnaires.

Conclusions

QoL is a very important endpoint in trials reporting the effect of AF ablations. It has been shown that AF ablation significantly improve the QoL in AF patients, but recent studies question the usefulness of the most used generic QoL instrument in AF patients. The complexity of the disease makes it mandatory to employ disease specific instruments in the assessment of QoL. However, the new disease specific QoL instruments AF-QoL and AFEQT appear very promising and with further investigation may become a recommended tool for clinical research and clinical practice.

Disclosures

No disclosures relevant to this article were made by the authors.

References

1. A. John Camm et al. Guidelines for the management of atrial fibrillation. The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). European Heart Journal (2010) 31, 2369–2429

2. 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.

3. 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.

4. Pappone C, Rosanio S, Augello G, et al. Mortality, morbidity and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: outcomes form a controlled nonrandomized long-term study. J Am Coll Cardiol 2003;42:185–97.

5. 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.

6. Chen MS, Marrouche NF, Khaykin Y, et al. Pulmonary vein ablation for the treatment of atrial fibrillation in patient with impaired systolic function. J Am Coll Cardiol 2004;43:1004 –9.

7. WeerasooriyaR, Jais P, HociniM, ScaveeC,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.

8. Tondo C, Mantica M, Russo G, Avella A, De LL, Pappalardo A, Fagundes RL, Picchio E, Laurenzi F, Piazza V, Bisceglia 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.

10. Purerfellner H, Martinek M, Aichinger J, et al. Quality of life restored to normal in patients with atrial fibrillation after pulmonary vein ostial isolation. Am Heart J 2004;148:318 –25.

11. Tse HF, Sin PY, Siu CW, Tsang V, Lam CL, Lau CP: Successful pulmonary vein isolation using transvenous catheter cryoablation

improves quality-of-life in patients with atrial fibrillation. Pacing Clin Electrophysiol 2005;28:421-424.
12. Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs. antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA 2005;293:2634–40.
13. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. Circulation 2008;118:2498 –505.
14. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F Jr, Strickberger SA, Morady F: Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002;105:1077-1081.
15. Reynolds MR, Ellis E, Zimetbaum P: Quality of life in atrial fibrillation: Measurement tools and impact of interventions. J Cardiovasc Electrophysiol 2008;19:762-768.
16. John Spertus, Paul Dorian, Rosemary Bubien, Steve Lewis, Donna Godejohn, Matthew R. Reynolds, Dhanunjaya R. Lakkireddy, Alan P. Wimmer, Anil Bhandari and Caroline Burk. Development and Validation of the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire in Patients With Atrial Fibrillation Circ Arrhythm Electrophysiol 2011;4;15-25
17. Fernando Arribas, Jose´ Miguel Ormaetxe, Rafael Peinado, Nuria Perulero, Patricia Ramı´rez, and Xavier Badia. Validation of the AF-QoL, a disease-specific quality of life questionnaire for patients with atrial fibrillation. Europace (2010) 12, 364–370
18. Wokhlu A, Monahan KH, Hodge DO, Asirvatham SJ, Friedman PA, Munger TM, BradleyDJ, Bluhm CM,Haroldson JM, Packer DL: Longterm quality of life after ablation of atrial fibrillation the impact of recurrence, symptom relief, and placebo effect. J Am Coll Cardiol 2010;55:2308-2316.
19. Paul Dorian, Peter G. Guerra, Charles R. Kerr, Suzan S. O'Donnell, Eugene Crystal, Anne M. Gillis, L. Brent Mitchell, Denis Roy, Allan C. Skanes, M. Sarah Rose and D. George Wyse. Validation of a New Simple Scale to Measure Symptoms in Atrial Fibrillation: The Canadian Cardiovascular Society Severity in Atrial Fibrillation Scale. Circ Arrhythm Electrophysiol 2009;2;218-224
20. Ware JE Jr. SF-36 Health Survey. Manual and Interpretation Guide. Boston, MA: The Health Institute; 1993.
21. Ravens-Sieberer U, Wille N, Badia X, Bonsel G, Burstrom K, Cavrini G, Devlin N, EgmarAC, Gusi N, HerdmanM, Jelsma J, Kind P, Olivares PR, Scalone L, Greiner W: Feasibility, reliability, and validity of the EQ-5D-Y: Results from a multinational study. Qual Life Res;19:887- 897.
22. 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. JAmColl Cardiol 2000;36:1303-1309.
23. Bubien R, Kay G, Jenkins L. Test Specifications for Symptoms Checklist: Frequency and Severity. Milwaukee, WI: University of Wisconsin; 1993.
24. Hugh Calkins et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patient Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design. Europace (2012) 14, 528–606
25. Stephanie Fichtner, Isabel Deisenhofer, Sibylle Kindsmuller, Marijana Dzijan-Horn, Stylianos Tzeis, Tilko Reents, Jinjin Wu, Heidi Luise Estner, Clemens Jilek, Sonia Ammar, Susanne Kathan, Gabrielle Hessling, and Karl-Heinz Ladwig. Prospective Assessmment of Short- and Long-Term Quality of Life After Ablation for Atrial Fibrillation J Cardiovasc Electrophysiol, Vol. pp. 1-7
26. Pontoppidan J, Nielsen JC, Poulsen SH, Hansen PS. Symptomatic and asymptomatic atrial fibrillation after pulmonary vein ablation and the impact on quality of life. Pacing Clin Electrophysiol. 2009 Jun;32(6):717-26.
27. Wilber DJ, Pappone C, Neuzil P et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. Jama. Jan 27 2010;303(4): 333–340.
28. Oral H, Pappone C, Chugh A et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. N Engl J Med. Mar 2 2006;354(9):934–941.
29. Khan MN, Jaïs P, Cummings J, Di Biase L, Sanders P, Martin DO, Kautzner J, Hao S, Themistoclakis S, Fanelli R, Potenza D, Massaro R, Wazni O, Schweikert R, Saliba W, Wang P, Al-Ahmad A, Beheiry S, Santarelli P, Starling RC, Dello Russo A, Pelargonio G, Brachmann J, Schibgilla V, Bonso A, Casella M, Raviele A, Haïssaguerre M, Natale A; PABA-CHF Investigators. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. N Engl J Med 2008;359:1778-85
30. Sanghamitra Mohanty, Prasant Mohanty, Luigi Di Biase, Rong Bai, Amy Dixon, David Burkhardt, Joseph G. Gallinghouse, Rodney Horton, Javier E. Sanchez, Shane Bailey, Jason Zagrodzky, and Andrea Natale. Influence of body mass index on quality of life in atrial fibrillation patients underging catheter ablation. Heart Rhythm 2011;8:1847-1852
31. Sanghamitra Mohanty, Prasant Mohanty, Luigi Di Biase, Rong Bai, Agnes Pump, Pasquale Santangeli, David Burkhardt, Joseph G. Gallinghouse, Rodney Horton, Javier E. Sanchez, Shane Bailey, Jason Zagrodzky, and Andrea Natale. Impact of metabolic syndrome on procedural outcomes in patients with atrial fibrillation undergoing catheter ablation. JAm Coll Cardiol 2012;59:1295-301.