

Effect Of Catheter Ablation On Quality Of Life In Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) is the most common sustained arrhythmia seen in clinical practice, affecting approximately 1% of the overall population. While rarely life-threatening, AF is almost universally associated with increased morbidity and mortality, predominantly through an increased risk of thromboembolic events, left ventricular dysfunction, as well as significant impairments in functional capacity and health-related quality of life (HRQOL).¹⁻⁸ Improvement in HRQOL, with a secondary reduction of disability and health-care resource utilization, is one of the major therapeutic goals in the management of AF.

Health-Related Quality Of Life

The Importance Of Assessing HRQOL In AF

The regular assessment of HRQOL with validated instruments has become an increasingly more common and widely accepted method for evaluating the impact of the disease and therapeutic interventions. In the case of AF traditional outcome parameters, such as arrhythmia-free survival, cardiac remodeling, and exercise tolerance are insufficient to evaluate the effects of different treatment approaches, and do not adequately correlate with the subjective assessment of the patients' symptoms or HRQOL. Moreover, the use of symptoms alone is particularly unreliable in AF, leading to an underestimate the overall AF burden.⁹⁻¹¹ As such, objective and valid assessment tools are necessary given the latent difficulty in determining the clinical impact of AF.

It is here where measures of HRQOL offer their greatest advantage. In considering multiple domains of wellness (i.e. pain, psychological, emotional, and physical disturbances), the HRQOL assessment tools are able to evaluate the degree of baseline disease-related impairment, as well as quantify the subjective improvements in well being (or conversely side-effects) resulting from therapeutic interventions. Specifically, these multi-dimensional HRQOL

instruments are able to determine if an intervention had a beneficial effect across all domains concurrently or if a benefit in one domain (i.e. physical health) was offset by a negative effect in another (i.e. mental health). As such, objective and valid HRQOL assessment tools represent increasingly important instruments in the clinical assessment of the impact of AF and its therapy on patients' functional status and health.

Definitions

Quality of life (QOL) is a subjective phenomenon and is defined as an "individuals' perception of their position in life in the context of the culture in which they live and in relation to their goals, expectations, standards and concerns."¹² While QOL is a global construct that includes domains such as job satisfaction and quality of housing, health-related quality of life (HRQOL) is narrower in scope, and can be conceptualized as a combination of symptoms, functional status and the patient's personal perception of health, which is in turn influenced by their beliefs, experiences, and expectations. However, it is important to note that while there is a significant interplay between each of these HRQOL factors the relationship between symptoms, disease recurrence, and HRQOL is not absolute. For example, while an intense symptom burden would be expected to adversely affect HRQOL, the absence of symptoms does not automatically correspond to an optimal HRQOL state. Likewise, a reduction in AF frequency and duration may not improve symptoms and HRQOL.¹³ Therefore, it is critically important to consider the individual contribution of each of these factors when assessing HRQOL, particularly in the face of the highly personal and multifaceted nature of AF.

Disclosures:
None.

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Measuring HRQOL

To date a large number of instruments have been used in published research to evaluate HRQOL. In broad terms, these instruments can be classified into generic and disease specific questionnaires. Generic instruments assess valuations of health and functioning across a predefined set of health-related domains. A widely used generic instrument is the Medical Outcome Survey Short Form (SF-36), which assesses eight different health domains: physical functioning, role limitations due to physical health, bodily pain, and general health perception, which collectively comprise “Physical Health,” and vitality (energy and fatigue), social functioning, role limitations due to emotional health, and general mental health (psychological distress and well-being), which collectively comprise “Mental Health.” In addition to these eight subscales, the SF-36 also generates the physical health weighted composite score (PCS), and the mental health weighted composite scores (MCS). Other generic instruments include the Health Utilities Index Mark 2 and 3 (HUI2 and HUI3), the EuroQol-5D (EQ-5D). Generic instruments have the advantages of extensive validation across a wide range of populations and conditions, ease of use, and generalizability. Moreover the generic instruments are extremely useful for health economic evaluations. Through the use of a HRQOL weight (i.e. utility score) a Quality Adjusted Life Years (QALYs) score can be used as a summary measure of health outcome and to inform subsequent healthcare resource allocation decisions. Contrariwise, the main drawback of generic instruments being a disproportionate focus on general physical health and functioning, which may render it insensitive for measuring AF-specific HRQOL (i.e. the scores being more influenced by patient demographics and comorbidities rather than the impact of the disease or intervention itself). In response to these criticisms disease-specific instruments have been developed and validated. These instruments include symptom specific scales (the most widely used are the University of Toronto Atrial Fibrillation Severity Scale [AFSS] and the Symptom Checklist-Frequency and Severity Scale), and AFatrial fibrillation-specific QOL symptom scales (i.e. the Atrial Fibrillation Effect on Quality-of-Life questionnaire [AFEQT]). These instruments, while lacking the ability to compare between disease states (i.e. the HRQOL of AF patients to CHF patients), are more precise in measuring HRQOL domains directly-related to AF and therefore are more sensitive to changes in patients’ health status (either spontaneous or as a result of intervention). However, in comparison to the wealth of data behind the generic instruments, the use of disease-specific instruments is limited by lack of validation and generalizability. As such, a combination of both types of instruments represents the ideal method to balance the generalizability and extensive validation that comes with generic HRQOL measures with the relatively high sensitivity and precision associated with disease-specific HRQOL questionnaires.

HRQOL In Atrial Fibrillation

An understanding of the overall impact of AF on HRQOL is problematic owing to that the literature-base being derived from interventional studies (ie. examining the impact of cardioversion, various pharmacotherapies, pacemaker implantation and programming, and surgical or catheter-based ablation procedures), thus potentially biasing the assessment towards highly symptomatic patients. Within the context of these limitations the presence of AF is associated with significantly impaired functional capacity and

HRQOL across areas of physical and social functioning, mental and general health, and metrics of illness intrusiveness.¹⁴⁻¹⁸ These impairments are marked when compared to population norms, with a degree of impairment that is comparable or worse than in patients with heart failure or coronary disease (post-infarction or post-angioplasty), and as intrusive in their daily lives as chronic hemodialysis.¹⁴ In general older patients, women, and those with comorbidities (obesity, valvular heart disease, and chronic pulmonary disease) report lower HRQOL in relationship to AF.^{19,20} Interestingly, outside of the psychological dimension the subtype of AF (persistent, paroxysmal, or permanent AF) did not seem to have any relationship to HRQOL. This is postulated to relate to anxiety surrounding recurrences as the deterioration in HRQOL has been noted to parallel the number of symptomatic episodes, emergency department visits, and healthcare utilization.^{21,22} Lastly, it is important to note that patients with purported asymptomatic AF still express a lower HRQOL and reduced global life satisfaction compared to healthy controls in sinus rhythm.¹⁴

HRQOL With Medical Pharmacotherapy

In recent years a number of randomized, controlled studies have investigated the effect of ventricular rate control vs. a strategy of maintenance of sinus rhythm (rhythm control).²³⁻²⁷ While not a primary outcome, an improvement in HRQOL was observed in most of these studies over the early follow-up period (~12 month). Importantly, while similar improvements in HRQOL were observed between both the rate, and rhythm control arms at no point were significant differences observed between the randomized groups in any of the studies. As a result these studies have been interpreted to indicate that a strategy of rate control can be at least as effective as efforts to control rhythm with respect to HRQOL outcomes. However, there are several important limitations to consider. Firstly, with the exception of AFFIRM and AF-CHF, these studies were not powered to detect HRQOL differences. Second, it is possible that the antiarrhythmic drugs (AAD) utilized may have adversely impacted HRQOL due to side-effects or intolerance. In this regard the SAFE-T trial, which included a placebo group in addition to amiodarone and sotalol arms, did not note any significant difference in HRQOL between treatment groups.^{16,28} Likewise, the CTAF trial, which randomized patients to amiodarone, sotalol, or propafenone, reported improvements in all HRQOL measures from baseline to 3 months across all patients, however the magnitude of benefit was substantially lower than that observed post ablation (see below).²⁹ Lastly, it is important to note that none of these studies were comparisons of successful sinus rhythm maintenance versus permanent AF with ventricular rate control. This is particularly relevant as the ability to understand the true benefit of medical sinus rhythm maintenance on HRQOL is severely limited by the modest efficacy of AADs at maintaining sinus rhythm in these trials (9-58% 1 year success freedom from recurrent AF).³⁰⁻³⁹ Unfortunately attempts to examine the effect of “achieved rhythm” on HRQOL through post-hoc analyses is made even more difficult by the observation that the relationship between rhythm and HRQOL may be non-linear – i.e. HRQOL being influenced by severe but infrequent symptoms or drug side-effects. As such the results of these post-hoc analyses are somewhat contentious. In PIAF and AFFIRM there was no difference in HRQOL when patients were compared based on rhythm status.^{23,40} Conversely, RACE, SAFE-T and CTAF demonstrated that patients who remained in

sinus rhythm had an improved HRQOL compared to those with arrhythmia recurrence.^{16,26,29} Likewise AF-CHF demonstrated that a higher proportion of time spent in sinus rhythm was associated with a modestly greater improvement in HRQOL scores.⁴¹

HRQOL After An AF Ablation

Though AADs remain the first-line therapy for the maintenance of sinus rhythm, their use can be disappointingly ineffective and associated with significant cardiac and non-cardiac toxicities, the combination of which may limit the anticipated HRQOL benefit associated with sinus rhythm maintenance. Conversely, left atrial catheter ablation has been shown to be universally superior to AADs for the maintenance of sinus rhythm in multiple randomized controlled trials.^{31,33,39,42} Given this superior efficacy several studies have examined the effect of catheter ablation on quality of life (TABLE).

In general these studies included highly symptomatic patients who had previously failed one or more antiarrhythmic drugs, and thus preselected a fairly symptomatic subset of the AF population. Moreover the studies themselves are fairly heterogeneous in terms of: 1) the inclusion populations (varying degrees of both paroxysmal and persistent AF), 2) the ablation techniques and technologies, and 3) the HRQOL measure utilized (while almost all of the used the SF-36 questionnaire, many used a symptom checklist, with or without other HRQOL measures). However, despite these differences positive changes were near universally observed in almost all SF-36 subscales after catheter ablation (15-40 point improvement in individual SF-36 subscales; scored up to 100).^{31-33,39,43-48} Moreover, the extent of improvement in the Physical Health weighted composite score and the Mental Health weighted composite score were consistently in the range of 10-20 points (scored up to 50).^{31-33,39,43-48} In some cases the SF-36 PCS and MCS composite scores reached normative levels after an ablation procedure, while these scores remained impaired in the medical therapy group throughout the year of follow-up.³¹

In an elegant study Gerstenfeld et al. described 71 patients undergoing attempted ablation of focal PV ablation of AF triggers, with HRQOL prospectively assessed 1 month before and 6 months after the procedure.⁴⁵ While ablation was the intention for all patients, 23 patients underwent exclusive mapping due to insufficient or multifocal ectopy. When HRQOL was assessed 6 months post ablation a significant improvement was observed only in the subset of patients undergoing ablation (58 patients), with a significant improvement in all six HRQOL measures in the long-term successful ablation group, compared to four of the six measures in those undergoing ablation with AF recurrence.

Three randomized trials of a pulmonary vein isolation (PVI) procedure vs. AADs for patients with paroxysmal AF have likewise showed significantly greater improvements in HRQOL following catheter ablation. Wazni et al. randomized 70 patients to PV ablation (33) vs. AADs (37).³² On follow-up the HRQOL was significantly improved in 5 subclasses of the SF-36 (general health, physical functioning, social functioning, role physical, and pain) in the ablation group, when compared to the AAD group. Jais et al. similarly randomized 112 patients to PV ablation (53) vs. AADs (59).³³ Significant improvements in symptom severity, physical composite scores, and mental health composite scores were observed in both groups, however the extent of benefit was more marked in the ablation group. Moreover, while, the largest magnitude of improvement was observed between baseline and day 91, the benefit

was maintained at day 365 where the physical and mental component summary scores remained significantly higher in the ablation group when compared to the AAD group. Wilber et al. randomized 167 patients to PV ablation (106) vs. AADs (61).³⁹ Similar to Jais et al., the SF-36 PCS and MCS were significant higher in the ablation group at 3 months post ablation, a difference that persisted without significant change at 6- and 9-months post ablation.

Similarly, significant changes in HRQOL have been observed after ablation of more persistent forms of AF. Oral et al. randomized 146 patients to amiodarone plus cardioversion (69 patients) versus catheter ablation (77 patients). Due to arrhythmia recurrence a significant proportion (77%) of the amiodarone group crossed over and underwent catheter ablation at a mean of 128±57 days after cardioversion, which limited the utility comparisons between groups. However, when all patients undergoing ablation were combined a significant improvement in the symptom severity score was observed at 12 months after ablation. While patients who remained in sinus rhythm had a greater improvement in the symptom severity score (10±5 vs. 5±7 in those with arrhythmia recurrence, P=0.002), significant improvements were noted at 12 months irrespective of arrhythmia recurrence. Fiala et al. prospectively examined 160 patients who were undergoing ablation of long-standing persistent AF (median AF duration of 28 months).⁴⁹ Quality of life was assessed using the European Quality of Life Group instrument. Compared with the baseline both HRQOL indices improved significantly at 1 year (EQ-5D: 68.8±12.5 to 75.4±14.4; EQ-VAS: 62.8±13.2 to 70.6±13.8) with a further slight increase at 2 years post ablation (EQ-5D: 77.1±15.5; EQ-VAS: 70.9±14.0). Similar to previous, the benefits in HRQOL were largely restricted to patients achieving sinus rhythm, as those who accepted permanent AF did not obtain any substantial benefit in HRQOL at 2 years. Further, restoration of sinus rhythm was associated with beneficial improvements in left atrial appendage outflow velocity, left ventricular ejection fraction, peak oxygen consumption, and NT-proBNP.

Hunter et al. examined the effect of a catheter ablation strategy geared towards sinus rhythm maintenance, with that of a medical rate control strategy in patients with persistent AF, symptomatic heart failure (HF), and an LVEF of <50%.⁴⁷ In total 50 patients were randomized to catheter ablation (26 patients) or medical rate control (24 patients). At 6 months post ablation freedom from AF was achieved in 21/26 (81%). Ablation was associated with an improved peak oxygen consumption (22±6 vs. 18±6 mL/kg/minute; P=0.01), improved LVEF (40±12% vs. 31±13%; P=0.015), and an improved HRQOL as measured by the Minnesota living with HF questionnaire score (23.7, 95%CI 14.6-32.8 vs. 47.0, 95%CI 36.5-57.6; P=0.001) and SF-36 (significantly improved domains of physical functioning, physical role functioning, bodily pain, and vitality). With respect to the MLWHF score the improvement was early (significantly lower scores at 1 month) and sustained to one year of follow-up.

Three further observational studies of note examined the effect of catheter ablation on HRQOL in patients with impaired left ventricular (LV) function. Tondo et al. compared 40 patients with LV ejection fraction (EF) <40% (55% with known structural heart disease) to 65 control patients with normal ventricular function.⁴⁸ Seventy-six percent of patients had non-paroxysmal AF. After a mean follow-up of 14±2 months, 90% of patients were in sinus rhythm (87% with low EF, 92% with normal EF). Irrespective of baseline LV function all patients in sinus rhythm reported a considerable improvement in SF-

Table 1: Studies of AF ablation and HRQOL

	Type of Study	Population	Number of patients	Classification of AF	Male Gender %	Age	Ablation strategy	Follow-up	QOL tool	Time of QOL assessment	Findings
Pappone et al. ⁴⁴	Observational	1,171 patients. 589 patients in the ablation group were compared to 582 in the antiarrhythmic group. But only 211 completed the SF-36 (109 and 102 respectively).	1,171	Paroxysmal 70% "Chronic" 30%	59%	65 ± 10	PV isolation	900 days	SF-36	Every 3 m for 1 y	1) A significant time trend over one year was detected only in ablated patients, who reached normative levels at 6 months, with no further changes at one year 2) AF recurrence was independently associated with significant reductions in QOL
Hsu et al. ⁴⁶	Observational	58 patients with LVEF <45% (45% with structural heart disease) and 58 matched age, gender and type AF with normal LVEF.	116	Paroxysmal 9% Persistent 17% Permanent 74%	88%	56±10	PV isolation ± roof line or mitral isthmus	12 ± 7 months	SF-36, Symptom Checklist-Frequency and Severity Scale	At 3 and 12 months	1) QOL measures improved significantly in both groups 2) LVEF increased by a mean of 21±13 percent, with the greatest improvement within the first 3 months. Even in the presence of structural heart disease.
Oral et al. ³⁴	Randomized	146 patients randomized in two groups. 69 to amiodarone + CVE the first 3 months VS 77 to a circumferential pulmonary vein ablation.	146	"Chronic" 100%	88%	57±9	PV isolation ± roof line or mitral isthmus	1 y	Symptom Severity Questionnaire	At 12 months	1) If remained in sinus rhythm improvement from 17±4 at baseline to 6±2 points at 12 months (p < 0.001) 2) If AF recurrence smaller improvement from 17±4 at baseline to 12±4 points at 13 months (p = 0.002).
Wazni et al. ³²	Randomized	70 patients randomized in two groups. 37 to antiarrhythmic drugs treatment VS 33 to PV isolation. The patients had not been treated with AAD.	70	Paroxysmal 96% Persistent 4%	NA	53±8	PV isolation	1 y	SF-36	At 6 months	QOL was significantly better in 5 subclasses of the SF-36 in PV isolation group
Tondo et al. ⁴⁸	Observational	40 patients with LVEF < 40% (55% with structural heart disease) and 65 control patients with normal LVEF.	105	Paroxysmal 24% Persistent 76%	82%	57	PV isolation + mitral isthmus + cavotricuspid isthmus	14 ± 2 months	SF-36	At 6 months	All patients with sinus rhythm of both groups reported an improvement in general health, physical functioning and emotional well-being.
Chen et al. ⁴⁴	Observational	94 patients with LVEF < 40% (96% with structural heart disease) and 283 patients with normal LVEF. But only 193 completed the SF-36 questionnaire (43 in LVEF < 40% group, and 150 in the control group).	377	Paroxysmal 51% Persistent 13% Permanent 36 %	80%	55	PV isolation	14 ± 5 months	SF-36	At 6 months	1) Both groups reported an improvement in several areas, including general health, energy, physical functioning, and emotional well-being. 2) LVEF improved nonsignificantly, but 60% of the study group showed an increase of 7% in the LVEF.
Jais et al. ³³	Randomized	112 patients randomized in two groups. 53 to PV ablation VS 59 to antiarrhythmic drugs.	112	Paroxysmal 100%	84%	51.1 ± 11.	PV isolation ± roof line, mitral isthmus or cavotricuspid isthmus	1 y	SF-36, Symptom Checklist-Frequency and Severity Scale	At 3, 6 and 12 months	1) At 1-year the physical and mental component summary scores of the ablation group were significantly higher. 2) Both groups experienced a reduction in symptom severity, with a significantly greater effect favoring catheter ablation 3) The largest magnitude of improvement was observed between baseline and day 91, which was maintained at day 365.

Type of Study	Population	Number of patients	Classification of AF	Male Gender %	Age	Ablation strategy	Follow-up	QOL tool	Time of QOL assessment	Findings
Wokhlu et al. ⁵³	Observational 502 patients prospectively followed post AF ablation. No control group.	502	Paroxysmal 51% Persistent 35% Long-standing 13%	82%	55.9±10.3	PV isolation + roof line, mitral isthmus and cavotricuspid isthmus	3.1 y	SF-36 in all the patients MAFSI in 103 patients	At 3 months and 1.2 and 3 years	1) Improvement in mental and physical component at 3 months, sustained at 12 and 24 months. 2) Improvement were noted across all ablations outcomes. 3) Patients who remained on warfarine had less improvement at 2 y. 4) Unlike changes in QoL, changes in AF symptoms differed significantly across the ablation outcomes (no AF no AAD < no AF with AAD < AF recurrence)
Hunter et al. ⁴⁷	Randomized 50 patients with symptomatic HF and LVEF < 50%. Randomized to AF ablation (26) VS rate control (24).	50	Persistent 100%	96%	55±12	PV isolation ± CFEs, mitral isthmus, roof line and cavotricuspid isthmus	1 y	SF-36 Minnesota Living with Heart Failure questionnaire (MLWHF)	6 months	1) Symptomatic improvement in the ablation group by the MLWHF questionnaire at 1 month sustained at 1 y
Wilber et al. ³⁹	Randomized 167 patients randomized (2:1) to AF ablation (106) VS antiarrhythmic drugs (61)	167	Paroxysmal 100%	66.5%	55.7	PV isolation ± CFEs, mitral isthmus, roof line, cavotricuspid isthmus, SVC and atrial foci	12.5 months	SF-36, Symptom Checklist-Frequency and Severity Scale	At 3, 6 and 9 months	1) At 3 months SF-36 physical and mental summary scores were significant higher in the ablation group. 2) The ablation group also reported significantly lower mean symptom frequency
Mantoan et al. ⁵⁴	Randomized 100 patients randomized 1:1:1 in 3 groups: 32 to PV isolation, 34 to CFEs; and 34 to PV isolation and CFEs.	100	"High burden" paroxysmal 64% Persistent 36%	74%	57 ±10	PV isolation or CFEs or both	1 y	SF-36	At 6 and 12 months	1) Significant improvement for the three ablation strategy, with and without recurrence 2) But patients with the highest quartile of symptomatic recurrence demonstrated no improvement and even decline in QoL scores at 12 months.
Fichtner et al. ⁵¹	Observational 133 patients prospectively followed post AF ablation. No control group. Evaluated by 7 different QOL questionnaires	133	Paroxysmal 65% Persistent 35%	74%	57 ±10	PV isolation ± CFEs ± roof line ± mitral isthmus	4.3± 0.5 y	WHO-5-Well-Being-Index, Major Depression Inventory, Vital Exhaustion, Sleep and Vegetative Disorder, AF Severity Scale, AF Symptom Checklist and Illness intrusiveness	At 3, 6 and 12 months, and yearly thereafter	1) Significant QOL improvement in all the 7 questionnaires at short and long term follow-up, regardless of ablation success. 2) Patients with a successful ablation had a significantly greater improvement of QoL during long-term follow-up.
Pontoppidan et al. ⁴⁸	Observational 149 patients prospectively followed post AF ablation. End point relation QoL and asymptomatic AF recurrences	149	Paroxysmal 54%	71%	56±8	PV isolation ± roof line, mitral isthmus	12 months	SF-36	At 12 months	1) Patients with asymptomatic AF recurrences showed significant improvement in role physical, general health and vitality scores at 12 months. 2) Patients with symptomatic AF recurrences showed unchanged or even worsened subscales compared to baseline.
Weera sooriya et al. ⁶⁶	Observational 63 patients prospectively followed post AF ablation. No control group	63	Paroxysmal 100%	78%	56±7	PV isolation + mitral isthmus + cavotricuspid isthmus	12 months	SF-36, Symptom Checklist-Frequency and Severity Scale	At 3 and 12 months	1) Significant improvement in all eight subscales of the SF-36 questionnaire, and this improvement was sustained at 12 months. 2) Significant improvement in the severity and frequency scores.

36 HRQOL measures including general health, physical functioning, and emotional well-being. There was no difference in the degree of improvement between those with a history of HF and those without. Chen et al. similarly compared 94 patients with LVEF < 40% (96% with structural heart disease) to 283 control patients with normal ventricular function.⁴⁴ Post ablation the LVEF non-significantly increased from 36% to 41% (LVEF improved by $7.2 \pm 3\%$ in 56/94 patients; LVEF unchanged in 31/94 patients). In the subset of patients that completed the SF-36 questionnaire (43 in low LVEF group, and 150 in the control group) HRQOL was significantly improved after catheter ablation. Specifically, six months post ablation patients with impaired LV function reported an improvement in general health, energy and fatigue, physical functioning, social functioning, pain, and emotional well-being. This improvement was similar to that observed in the group with preserved LV function. Hsu et al. compared 58 patients with congestive heart failure and a LVEF <45% with 58 controls without congestive heart failure who were undergoing ablation (matched according to age, sex, and classification of AF).⁴⁶ After a mean follow-up of 12 ± 7 months, 81% of patients were in sinus rhythm (78% with low EF, 84% with normal EF). Post ablation the LVEF significantly increased by $21 \pm 13\%$ in the impaired LV function group, which was irrespective of pre-ablation rate control adequacy and the presence/absence of structural heart disease. Post ablation the quality-of-life measures were significantly improved (SF-36 PCS and MCS improved by 24 ± 21 and 21 ± 19 points, respectively in the HF group; and 18 ± 17 and 14 ± 19 points, respectively in the control group). Concurrent to the improvement in HRQOL was a reduction in Symptom Checklist-Frequency and Severity scores, and a significant improvement in exercise time and capacity in both groups.

Arrhythmia Recurrence

Similar to studies of medical rhythm control the beneficial effect of ablation has been linked to an absence of arrhythmia recurrence, although there is some suggestion that an ablation procedure independently results in a significant improvement in HRQOL during short- and long-term follow-up irrespective of outcome.^{45,50-55} The reasons for the perceived disconnect between measured HRQOL improvement and objective arrhythmia recurrence is likely multifactorial, reflecting in part: 1) The difficulty in establishing a relationship between arrhythmia recurrence and HRQOL, as outlined above; 2) A relative transition from proportionally more symptomatic to proportionally more asymptomatic paroxysms of AF, which is known to occur after ablation⁹; 3) Placebo/nocebo effects surrounding ablation/AAD use, which given the lack of blinding may affect the results of short-term HRQOL questionnaires (although the effects should be minimal over long-term follow-up); and 4) An imprecise or inaccurate tool to measure HRQOL. Specifically, despite its widespread use, the generic SF-36 may not be sensitive enough to evaluate changes in HRQOL after catheter ablation, especially when arrhythmia recurrence needs to be considered. This was elegantly demonstrated by Wokhlu et al. who observed betterment in HRQOL, as assessed by SF-36, was not dependent on ablation efficacy.⁵³ Specifically when assessed by SF-36 catheter ablation produced a sustained improvement in HRQOL at 2 years irrespective of arrhythmia outcome. However, when they utilized a disease-specific symptom questionnaire (Mayo AF-specific Symptom Inventory - MAFSI), the HRQOL differed significantly among ablation efficacy outcomes suggesting that arrhythmia recurrence likely plays a larger

role in HRQOL than is appreciated on generic questionnaires. Similar results utilizing a disease-specific questionnaire have been observed in studies by Erdogan et al., Miyasaki et al., and Fichter et al.⁵⁰⁻⁵² As such, while catheter ablation may improve HRQOL irrespective of outcome, the degree of improvement appears to be linked to arrhythmia burden.

HRQOL After AV Node Ablation

Multiple large randomised controlled trials have demonstrated that a strategy of ventricular rate control is not inferior to restoration of sinus rhythm in appropriately selected patients.²³ For those who are unable to achieve adequate control of ventricular rate with pharmacologic agents, a strategy of AV junction ablation followed by permanent right ventricular pacing is an established therapeutic strategy. While preformed less frequently than previous, there is a wealth of evidence demonstrating that AV junction ablation is a safe and highly efficient means to control ventricular rate, with consequent improvements in symptoms, exercise capacity, quality of life, and healthcare resource utilization.^{26,56-60} One of the largest prospective studies, the Ablate and Pace Trial (APT) evaluated the effect of AV junction ablation and permanent pacemaker implantation on quality of life, and exercise capacity in 156 patients with symptomatic AF.⁵⁸ At twelve months of follow-up they demonstrated a significant improvement in HRQOL scores across: 1) all 8 subscales of the Health Status Questionnaire (HSQ), 2) the overall rating of the Quality of Life Index, and 3) the Health and Function subscales. Additionally there was a significant reduction (>30%) in arrhythmia-related symptoms (Symptom Checklist: Frequency and Severity scale). Interestingly, this was despite no significant changes in treadmill exercise duration (10.0 ± 4.3 min at baseline and 11.6 ± 3.6 min at 12 months) or VO2 max (1467 ± 681 ml O2/min baseline and 1629 ± 739 ml O2/min at 12 months). The AIRCRAFT study randomized 99 patients with permanent AF and mild to moderate symptoms to AV junction ablation and permanent pacemaker implantation vs. pharmacologic rate control.⁶¹ Using a disease-specific instrument (CAST QOL) they demonstrated an 18% relative improvement in QOL, however no difference was observed with generic QOL instruments. To evaluate the effect of placebo Natale et al. divided patients into three treatment groups: Group 1 undergoing AV junction ablation and pacemaker implantation as well as discontinuation of rate-control medications, Group 2 undergoing AV node ablation and pacemaker implantation without discontinuation of rate-control medications, and Group 3 undergoing pacemaker implantation with continued rate-control medical therapy but without AV node ablation.⁶⁰ At 6 months of follow-up they observed a significant improvement in HRQOL and activity scores in the groups undergoing AV junction ablation, an effect that was most marked in the group that concomitantly withdrew rate-limiting pharmacotherapy. Similar to previous, the improvement in HRQOL was independent of exercise duration and the maximal VO2 consumption, which did not change significantly. Moreover, the effects of AV junction ablation appear to be long-lasting. Tan et al demonstrated that AV junction ablation and permanent right ventricular pacing, after a mean follow-up of 4.3 ± 3.3 years, resulted in comparable quality of life scores in seven of the eight scales of the SF-36 questionnaire when compared to age- and sex-matched healthy controls.⁶² While in agreement with previous studies of AV junction ablation^{58,63} this is in stark contrast to a pharmacologic approach of ventricular rate-control, which is

unable to improve HRQOL of patients with permanent AF to the level of healthy controls.²⁶

Conclusions:

Atrial Fibrillation is associated with an adverse impact on HRQOL. Improvement in HRQOL, with a secondary reduction of disability and health-care resource utilization, is one of the major therapeutic goals in the management of AF. Successful AF ablation is associated with significant long-term improvement in HRQOL irrespective of the type of AF, however those with lower baseline HRQOL derive a greater and more robust improvement in HRQOL after catheter ablation.

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