Original Research

Assessment of Health-Related Quality of Life in a Greek Symptomatic Population with Atrial Fibrillation: Correlation with Functional Status and Echocardiographic Indices

Dimitrios Tsounis[1], Antonios Ioannidis[2], Georgios Bouras[1], Maria Raikou[3], Georgios Giannopoulos[1], Spyridon Deftereos[1], Charalampos Kossyvakis[1], Konstantinos Toutouzas[4], Dimitrios Tousoulis[4], Andreas Synetos[4], Vlasios Pyrgakis[1], Dimitrios Niakas[2], Christodoulos Stefanadis[4]

[1]Department of Cardiology, "G. Gennimatas" General Hospital, Athens, [2]Hellenic Open University, Faculty of Social Sciences, Patra, Greece; [3]LSE Health, London School of Economics, UK; [4]First University Department of Cardiology, Hippokration Hospital, Athens, Greece

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Introduction: Atrial fibrillation (AF) is known to have an unfavorable impact on quality of life. The purpose of this study was to assess the health-related quality of life (HRQOL) in a symptomatic population with AF seeking medical advice in a tertiary hospital, as well as to explore the relationship between HRQOL, functional status, and echocardiographic indices of left ventricular (LV) systolic and diastolic function.

Methods: The study sample consisted of 108 symptomatic patients suffering from AF who presented in the emergency department or were admitted to the cardiology department in an urban Greek tertiary hospital between January 1 and May 31, 2012. HRQOL was assessed using the SF-36 and EQ-5D instruments.

Results: In the study sample, AF was newly diagnosed in 16.5% of the patients, paroxysmal/persistent in 43.6% and permanent in 39.9%. The mean levels of physical and mental summary components of the SF-36 were 40.28 and 40.89, respectively. The EQ-VAS mean score was 59.63%, while the EQ-5D Europe VAS index and the York A1 Tariff index were 0.586 and 0.547, respectively. Reliability analysis found Cronbach's α to be 0.890 for the SF-36 and 0.701 for the EQ-5D. Convergent validity was proved to be at satisfactory levels. Impaired HRQOL was associated with worse NYHA class and echocardiographic indices of impaired LV systolic and diastolic function. Apart from higher NYHA class, other predisposing factors for lower HRQOL were female sex, advanced age, low physical activity, and higher levels of brain natriuretic peptide.

Conclusions: Symptomatic AF patients report impaired HRQOL. Functional status and echocardiographic indices of LV systolic and diastolic function appear to affect HRQOL significantly in these patients. The SF-36 and the EQ-5D are shown to be reliable and valid instruments in assessing HRQOL in patients with AF.

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Address:
Dimitrios Tsounis

Cardiology Department
"G. Gennimatas"
General Hospital
154 Mesogeion Ave.
115 27, Athens, Greece
tsounisd@gmail.com

The incidence of atrial fibrillation (AF), the most common clinically significant cardiac arrhythmia, has increased over the past 30 years as a result of population aging.[1,2] More than 2.3 million people in the United States and over 4.5 million Europeans suffer from the disease and AF has been shown to affect 1-2% of the general population and up to 7.3-13.7% of those older than 80 years.[3,4] Concerning the Greek population, recent publications estimate the overall AF prevalence to be up to 3.9%.[5] Moreover, as an increase of up to 2.5 fold in the incidence of the disease is expected over the next 50 years, due to population aging, AF is be-

coming a growing public health problem that is approaching epidemic proportions worldwide.[6]

The prevalence and incidence of AF are higher in men than in women, and the disease is associated with a variety of cardiovascular conditions, such as hypertension, symptomatic heart failure, valvular heart disease and cardiomyopathies, as well as thyroid dysfunction, obesity, sleep apnea, diabetes, chronic obstructive pulmonary disease and renal failure.[5,7-9] AF is also associated with increased mortality and morbidity, especially due to hemodynamic and thromboembolic complications.[10] The overall risk of stroke is increased five-fold in patients with AF, and AF is particularly related to severe stroke and subsequent disabilities.[11-13] Specifically in Greece, the prevalence of cardioembolic strokes is higher compared to other countries, varying from 23% to 38% among studies, and although the use of oral anticoagulants has increased over time, they are still underutilized by primary care physicians.[14,15] Additionally, the economic burden of the disease is enormous, given the severe complications and the increased hospitalization rates that are attributed to the disease. It is estimated that the annual AF-related direct and indirect cost in the USA reaches $6.65 billion.[16]

Moreover, patients with AF report impaired health-related quality of life (HRQOL) and functional status, with studies reporting lower levels of HRQOL in these patients, in comparison not only with the general population and healthy controls, but also with patients who have other major cardiovascular diseases (e.g. hypertension, coronary heart disease).[10,17-22]

The objective of this study was to assess HRQOL in a Greek symptomatic population with AF and to explore the relationship between HRQOL, functional status, as reflected by New York Heart Association (NYHA) functional classification, and echocardiographic indices of left ventricular systolic and diastolic function. Additionally, this study aimed to determine the demographic, social and clinical factors that affect HRQOL in this population with AF.

Methods

The study sample consisted of 108 consecutive patients, who either presented to the emergency department with AF-related symptoms, such as palpitations, shortness of breath, fatigue, dizziness, chest pain and syncope, and had documented AF on their ECG, or were admitted to the cardiology department with the diagnosis of AF (ICD-10 code I48), at the "G. Gennimatas" General Hospital in Athens, between January 1 and May 31, 2012. Patients with AF and disabling stroke, acute stroke, acute heart failure, acute coronary syndromes, and pulmonary embolism were excluded from the study. Ethical approval for the study was obtained from the hospital's scientific committee, while patient consent was also acquired.

The Greek versions of two generic instruments were used to evaluate HRQOL, after the relevant license had been obtained: the SF-36 version 2.0 (QualityMetric) and the EQ-5D (EuroQol group). The SF-36 is a multi-purpose, 36-item, short-form, generic health survey that has been widely used and validated for the Greek population.[23] It yields an 8-scale profile of functional health and well-being scores, physical and social functioning (PF, SF), physical and emotional role (PR, RE), bodily pain (BP), general and mental health (GH, MH) and vitality (VT), as well as two psychometrically-based summary measures, those of physical (PCS) and mental (MCS) health.[24] The EQ-5D is a descriptive, generic instrument that has also been validated for the Greek population and consists of two parts.[25] The first part is a descriptive system of five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The second part consists of a visual analogue scale (VAS), the EQ-VAS, that asks respondents to self-rate themselves on a thermometer-like grading system in order to capture variations in health states. EQ-5D health state valuations may be converted into a single summary index by applying an algorithm that attaches values to each of the levels in each dimension. Value sets have been derived for the EQ-5D scores in several countries using either the VAS or the time trade-off (TTO) valuation technique. In this study, because of the lack of an available value set for the Greek population, two separate EQ-5D indices were utilized: one based on the VAS valuation technique applied to the European population and the other based on the TTO valuation technique applied to the UK population (York A1 Tariff).[26,27] Both instruments were completed by every patient at their discharge.

Data collected and analyzed for each patient included sociodemographic data (age, sex, marital status, occupation, education, smoking habits, physical activity, height, weight), type of AF (first diagnosed, paroxysmal/persistent or permanent), presenting symptom, presence of structural heart disease, concomitant diseases and medications, echocardiographic findings, laboratory test results, NYHA functional class, and therapeutic strategy (rate or rhythm control).

The echocardiographic evaluation was performed with a Vivid S6 device (General Electric Healthcare). The two-dimensional study involved the assessment of left ventricular end-diastolic diameter (LVEDd), left ventricular ejection fraction (LVEF), and left atrial diameter (LAd). The presence and the grade of valvular stenoses or regurgitations were assessed through Doppler analyses. The E/e´ ratio was assessed as an index of left ventricular diastolic function. Pulmonary artery systolic pressure (PASP) was evaluated using the maximum velocity of the tricuspid valve regurgitation jet. In addition, tricuspid annular plane systolic excursion (TAPSE) and pulsed wave tissue Doppler imaging of the systolic tricuspid annular motion at the lateral free wall of the right ventricle (s-TDI) were measured in order to assess right ventricular systolic function.

Blood samples were analyzed in the hospital's certified laboratory services department. Analyses consisted of hematological and chemistry tests, such as hematocrit, plasma creatinine, plasma lipids, troponin I, brain natriuretic peptide (BNP) and international normalized ratio (INR).

Statistical analysis

Descriptive statistics were produced to evaluate data completeness and to characterize the response distributions. Parametric (independent sample t-test, Pearson coefficient) methods were undertaken in normally distributed variables, whereas non-parametric tests (Mann–Whitney test, Spearman coefficient) were applied to non-normally distributed variables, in order to explore the statistical significance of the observed differences and the correlation between the variables of interest (deviation from the normal distribution was tested with the Kolmogorov–Smirnov test). Reliability was tested via Cronbach's coefficient α. Convergent validity was determined by the extent to which scores between the two instruments correlated with each other. Known-groups validity tests were performed to assess the ability of the questionnaires to distinguish between subgroups of respondents known to differ in key sociodemographic or clinical variables.

Results

Study population

Table 1 summarizes the major sociodemographic and clinical characteristics of the sample population. In total, 108 patients (mean age 65.4 ± 12.6 years) with AF, 69 men and 39 women, were enrolled in the study. Most of the patients were married, retired, and had received primary education. The mean body mass index (BMI) was 28.7 ± 4.9 kg/m^2, with 46.3% of the patients being overweight and 31.5% obese.

AF was first-diagnosed in 16.7% of the patients, paroxysmal/persistent in 43.5% and permanent in 39.8%. The main presenting symptom in the emergency department was palpitations (49%), shortness of breath (20%), chest pain/discomfort (7%), or syncope (3%). The onset of AF was over a year before the start of the study in approximately half of the patients (50.9%), within 48 hours in 24.1%, while it could not be determined in 18.5%. In terms of functional status, as expressed by the New York Heart Association (NYHA) classification, 54.6% of patients were in class I and 22.2% in class II, while 23.2% were in higher classes (III & IV). Patients' mean CHA_2DS_2VASc score (Congestive heart failure, Hypertension, Age over 75 years, Diabetes Mellitus, prior Stroke or thromboembolism, Vascular disease, Age 65-74 years and Sex category) was 3.19 ± 1.86, with only 8.3% of patients having a low thromboembolic risk (score = 0) not requiring anticoagulation treatment. More than half of the patients (55.6%) were on rhythm control, with amiodarone being the major antiarrhythmic agent, while for the remaining patients a rate control strategy was chosen, with beta-blockers being the most common bradycardic agent (Table 2).

Table 3 summarizes the echocardiographic indices of the study population. Patients' mean LVEF was 44.8 ± 16.3% and their mean LVEDd and mean LAd were 54.93 ± 8.5 mm and 45.82 ± 6.83 mm, respectively. The mean value of the E/e´ ratio and the estimated PASP were 11.64 ± 5.24 and 39.46 ± 14.95 mmHg, respectively. Moderate or moderate-to-severe mitral valve regurgitation was present in 38% of the patients, while 15.7% had mild aortic valve regurgitation. The mean TAPSE was 1.96 ± 0.29 mm and the mean s-TDI was 10.35 ± 3.17 cm/s.

Quality of life

AF patients reported the lowest mean score in the GH scale (39.86 ± 23.68) of the SF-36 questionnaire and the highest mean score in the BP scale (64.58 ± 30.21). For the remaining scales of SF-36 the mean scores were 55.14 ± 31.50 for PF, 40.74 ± 43.17 for PR, 43.99 ± 23.43 for VT, 60.63 ± 28.16 for SF, 51.61 ± 43.37 for RE and 51.84 ± 21.58 for MH. The sum-

Table 1. Sociodemographic and clinical characteristics.

Age, years	65.4 ± 12.6
Sex n (%):	
Men	69 (64%)
Women	39 (36%)
Marital status, n (%):	
Single	11 (10.2%)
Married	76 (70.4%)
Divorced	4 (3.7%)
Widowed	17 (15.7%)
Occupation, n (%):	
Servant	15 (13.9%)
Freelance	12 (11.1%)
Farmer	5 (4.6%)
Retired	70 (64.8%)
Housewife	4 (3.7%)
Unemployed	2 (1.9%)
Education, n (%):	
Primary	46 (42.6%)
Secondary	41 (38.0 %)
Tertiary	21 (19.5%)
Somatometrics:	
Height, cm	168.8 ± 9.7
Weight, kg	82.1 ± 16.6
BMI, kg/m^2	28.7 ± 4.8
Normal weight, n (%)	24 (22.2%)
Overweight, n (%)	50 (46.3%)
Obese, n (%)	34 (31.5%)
Blood pressure, mmHg:	
Systolic	122.3 ± 15.4
Diastolic	72.8 ± 8.7
Heart rate, bpm	75.3 ± 14.1
ECG rhythm, n (%):	
Sinus rhythm	61 (56.5%)
Atrial fibrillation	47 (43.5%)
ECG conduction abnormalities, n (%):	
LBBB	18 (16.7%)
RBBB	14 (13.0%)
LAH	7 (6.5%)
Smoking habits, n (%):	
Current smoker	25 (23.1%)
Never/Former smoker	37 (34.3%)
Physical activity, n (%):	
Sedentary lifestyle	43 (39.8%)
Low (<20 min/day)	28 (25.9%)
Modest (20-60 min/day)	23 (21.3%)
High (>60 min/day)	14 (13.0%)
NYHA class, n (%):	
NYHA I	59 (54.6%)
NYHA II	24 (22.2%)
NYHA III	18 (16.7%)
NYHA IV	7 (6.5%)
Comorbidities, n (%):	
Hypertension	73 (67.6%)
Diabetes	30 (27.8%)
Dyslipidemia	42 (38.9%)
History of stroke	19 (17.6%)
Coronary heart disease	49 (45.4%)
PCI	15 (13.9%)
CABG	27 (25.0%)
Heart failure	54 (50.0%)
Valve disease	33 (30.6%)
Thyroid disease	23 (21.3%)
Anemia	14 (13.0%)
Antithrombotic therapy, n (%):	
Aspirin	22 (20.4%)
Vitamin K antagonists	59 (54.6%)
Clopidogrel	16 (14.8%)
Dabigatran	9 (8.3%)
LMWH	2 (1.9%)
Medications, n (%):	
b-blocker	63 (58.3%)
Digitalis	27 (25.0%)
Amiodarone	11 (10.2%)
Sotalol	10 (9.3%)
Propafenone	11 (10.2%)
ACE inhibitor	59 (54.6%)
Statin	52 (48.1%)
Diuretics	61 (56.5%)
Laboratory test results:	
Hematocrit, %	39.7 ± 5.1
Creatinine, mg/dL	1.06 ± 0.29
Troponin I, ng/mL	0.053 ± 0.137
Cholesterol, mg/mL	165.7 ± 43.1
Triglycerides, mg/mL	123.7 ± 61.7
High-density lipoprotein, mg/mL	39.8 ± 10.3
Low-density lipoprotein, mg/mL	104.6 ± 35.3
BNP, pg/mL	467.2 ± 548.9
INR (VKA receiving patients)	1.69 ± 0.68
eCrCl, mL/min	83.3 ± 38.6

BMI – body mass index; ECG – electrocardiogram; LBBB – left bundle branch block; RBBB – right bundle branch block; LAH – left anterior hemiblock; PCI – percutaneous coronary intervention; CABG – coronary artery bypass graft; LMWH – low molecular weight heparins; ACE – angiotensin-converting enzyme; BNP – brain natriuretic peptide; INR – international normalized ratio; eCrCl – estimated creatinine clearance.

mary component measures' mean scores were calculated to be 40.28 ± 11.98 for PCS and 40.89 ± 12.05 for MCS. The minimum score was 0 for PF, PR, GH, VT, SF, RE and 11 and 12 for BP and MH, respectively, whereas the maximum score was 100 for all the scales apart from MH, where it was 96. The minimum and maximum scores for the summary components were 15 and 67 for physical health and 18 and 69 for the mental health, respectively (Table 4).

The EQ-5D index mean summary score was 0.586 (SD: 0.231, min: 0.075, max: 1) and 0.547 (SD: 0.309, min: -0.181, max: 1) using the Europe VAS and the York A1 Tariff TTO valuation techniques, respectively. The mean VAS score was 59.63 (SD: 24.02, min: 3, max: 100). Among the different EQ-5D dimensions, the majority of the respondents had no problems with self-care (87%). By contrast, for the dimension of anxiety/depression 84.4% of the respondents reported having some/extreme problems. For the remaining dimensions of mobility, usual activities

Table 2. Atrial fibrillation: characteristics of the study population.

AF Type, n (%):			AF onset, n (%):		
First diagnosed	18	(16.7%)	<48 hours	26	(24.1%)
Paroxysmal/persistent	47	(43.5%)	48 hours - 7 days	4	(3.7%)
Permanent	43	(39.8%)	7 days - 1 year	3	(2.8%)
			>1 year	55	(50.9%)
			Unknown	20	(18.5%)
AF treatment strategy, n (%):					
Rhythm control	60	(55.6%)	CHA_2DS_2VASc, mean ± SD	3.19 ± 1.86	
Rate control	48	(44.4%)	CHA_2DS_2VASc = 0, n (%)	9	(8.3%)
Rhythm control drug, n (%):			Rate control drug, n (%):		
Propafenone	10	(9.3%)	b-blocker	21	(19.4%)
Amiodarone	34	(31.5%)	Diltiazem	6	(5.6%)
Ibutilide	2	(1.9%)	Digitalis	3	(2.8%)
b-blocker	7	(6.5%)	b-blocker + digitalis	18	(16.7%)
Vernakalant	5	(4.6%)			

AF – atrial fibrillation; CHA_2DS_2VASc – Congestive heart failure, Hypertension, Age over 75 years, Diabetes Mellitus, prior Stroke or thromboembolism, Vascular disease, Age 65-74 years and Sex category.

Table 3. Echocardiographic indices of the study population.

LVEF (%)	44.8 ± 16.3	
LVEDd, mm	54.9 ± 8.5	
AoRoot, mm	31.8 ± 3.4	
LAd, mm	45.8 ± 6.8	
E/e′	11.6 ± 5.2	
Mitral valve regurgitation, n (%):		
Mild	41	(38.0%)
Moderate	29	(26.9%)
Moderate-severe	12	(11.1%)
Aortic valve regurgitation, n (%):		
Mild	17	(15.7%)
Moderate	5	(4.6%)
TAPSE, mm	1.96 ± 0.29	
S-TDI, cm/s	10.3 ± 3.1	
PASP, mmHg	39.4 ± 14.9	

LVEF – left ventricular ejection fraction; LVEDd – left ventricular end-diastolic diameter; AoRoot – aortic root diameter; LAd – left atrial diameter; TAPSE – tricuspid annular plane systolic excursion; s-TDI – pulsed wave tissue Doppler imaging of the systolic tricuspid annular motion at the lateral free wall of the right ventricle; PASP – pulmonary artery systolic pressure.

and pain/discomfort, 50%, 36.8% and 58.3% of the respondents reported having some/extreme problems (Table 4).

The internal consistency of the SF-36 instrument was assessed by Cronbach's coefficient α at 0.890, ranging from 0.854 (RE scale) to 0.941 (PF scale), exceeding in all cases the level of acceptance of 0.700 for group level comparisons. Cronbach's α coefficient for the EQ-5D was 0.701, also reaching the level of acceptance. Significant positive correlations were detected between the EQ-VAS, the EQ-5D Europe VAS (ϱ=0.628; p<0.001) and the EQ-5D York A1 Tariff (r=0.471; p<0.001) indices, and also between the EQ-5D Europe VAS and the EQ-5D York A1 Tariff indices (r=0.872; p<0.001).

Significant correlations were detected between the scales and the dimensions/indices of the two instruments. Specifically, dimensions and scales that assess the same aspect of quality of life demonstrated stronger negative correlations (e.g. mobility and PF, ϱ=-0.584; p<0.001) in contrast to less relevant ones (e.g. mobility and MH; ϱ=-0.182; p=0.063). On the whole, the EQ-VAS and the EQ-5D indices revealed significant positive correlations with most of the SF-36 scales.

Subgroup analysis showed that female patients reported statistically significant lower scores than male patients in 6 out of 10 scales (PF, PR, BP, SF, RE and PCS) of the SF-36 as well as in the EQ-VAS, EQ-5D indices and in the mobility dimension of the EQ-5D instrument. Similarly, older patients, those less physically active and those in a higher NYHA class reported lower levels of HRQOL in comparison to younger, more active and lower NYHA class patients. Specifically, patients over 65 years old reported statistically significantly lower scores in almost all scales, indices and dimensions of both instruments, except in the MH and MCS scales. Moreover, patients whose everyday physical activity exceeded 20 minutes reported statistically significantly higher scores in all scales, indices and dimensions, except in the BP scale and the pain/discomfort dimension. Patients with impaired functional status, as expressed by NYHA classes III and IV, also reported statistically significantly lower scores in 8 out of 10 scales (exclud-

Table 4. Distribution of SF-36 and EQ-5D scores and dimensions.

SF-36				EQ-5D			
	min	max	Mean ± SD		min	max	Mean ± SD
PF	0	100	55.14 ± 31.50	EQ-VAS (%)	3	100	59.63 ± 24.02
PR	0	100	40.74 ± 43.17	EQ-5D index			
BP	11	100	64.58 ± 30.21	Europe VAS	0.075	1	0.586 ± 0.231
GH	0	100	39.86 ± 23.68	York A1 Tariff	- 0.181	1	0.547 ± 0.309
VT	0	100	43.99 ± 23.43	EQ-5D dimensions	no	some	extreme
SF	0	100	60.63 ± 28.16	Mobility	54 (50.0%)	53 (49.1%)	1 (0.9%)
RE	0	100	51.61 ± 43.37	Self-care	94 (87.0%)	13 (12.0%)	1 (0.9%)
MH	12	96	51.84 ± 21.58	Usual activities	68 (63.0%)	37 (34.0%)	3 (2.8%)
MCS	18	69	40.89 ± 12.05	Pain/discomfort	45 (41.7%)	59 (54.6%)	4 (3.7%)
PCS	15	67	40.28 ± 11.98	Anxiety/depression	17 (15.7%)	50 (46.4%)	41 (38.0%)

PF – physical functioning; PR – physical role; BP – bodily pain; GH – general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health; MCS – mental component summary; PCS – physical component summary; VAS – visual analogue scale.

ing MH and MCS) of the SF-36, as well as in the EQ-VAS, EQ-5D indices and in 3 out 5 EQ-5D dimensions (mobility, usual activities, anxiety/depression).

Additionally, statistically significant negative correlations were detected between NYHA class and 8 out of 10 scales of the SF-36 (excluding MH and MCS), EQ-5D indices, and the EQ-VAS scale of the EQ-5D; there were also significant, positive correlations with 3 out of 5 dimensions (mobility, usual activity and anxiety/depression) of the EQ-5D.

Finally, statistically significant differences in HRQOL between the different AF types were detected in 5 out of 10 scales of the SF-36 (PF, GH, VT, PCS) and in the EQ-VAS scale of the EQ-5D. Specifically, patients with newly diagnosed AF reported higher scores in PF, GH, VT, PCS and EQ-VAS scales compared to those with permanent and higher scores in GH compared to those with paroxysmal/persistent. Patients with paroxysmal/persistent AF also reported higher scores in PF, GH, VT and EQ-VAS scales compared with those with permanent AF.

Echocardiographic indices and HRQOL

Statistically significant correlations were detected between LVEF and the SF-36 scales, as well as the EQ-VAS and EQ-5D indices. Specifically, weak positive correlations were detected between LVEF and the BP and the SF scales of the SF-36 and the EQ-VAS, while moderate to strong positive correlations were identified with the PF, PR, GH, VT, RE, and the summary component PCS of the SF-36 as well as EQ-5D indices. Moreover, LVEF was found to have weak to strong negative correlations with most of the dimensions of the EQ-5D (apart from the pain/discomfort dimension) (Table 5).

Conversely, LAd and PASP were found to be negatively correlated with 7 of the 10 SF-36 scales (PF, PR, GH, VT, SF, RE, PCS) and the EQ-VAS, EQ-5D indices, while positive correlations were detected with 4 out of 5 dimensions of EQ-5D (mobility, self-care, usual activities, anxiety/depression) (Table 5).

The E/e´ ratio, a widely used index of LV diastolic function, was shown to have weak to strong negative correlations with 8 out of 10 of the SF-36 scales (PF, PR, BP, GH, VT, SF, RE, PCS) and EQ-5D indices, and moderate positive correlations with 2 out of 5 the EQ-5D dimensions (mobility and anxiety/depression) (Table 5).

Subsequently, two groups of patients were formed according to LVEF: one with preserved ejection fraction (LVEF ≥45%, n=64) and one with reduced ejection fraction (LVEF <45%, n=44). Patients with preserved LVEF reported a higher HRQOL in 8 out of 10 of the SF-36 scales (excluding MH and MCS) and in the EQ-VAS and EQ-5D indices, whereas in the EQ-5D dimensions they reported fewer problems with mobility, usual activities and anxiety/depression (Table 6).

Additionally, two groups were formed according to the E/e´ ratio: those with E/e´ ratio <13 (n=70) and those with E/e´ ratio ≥13 (n=36). Patients with E/e´ ratio <13 reported better HRQOL in 6 out of 10 of the SF-36 scales (PF, PR, GH, SF, RE, PCS) and in the EQ-5D indices. Those patients also reported fewer problems in the mobility, self-care, usual activities and anxiety/depression dimensions of the EQ-5D (Table 6).

Table 5. Correlations of LVEF, LAd, E/e´ and PASP with SF-36 scales, EQ-VAS, EQ-5D indices and EQ-5D dimensions.

		LVEF		LAd		E/e´		PASP	
		n=106	p	n=106	p	n=106	p	n=106	p
Correlations	PF	0.422	<0.001	-0.406	<0.001	-0.304	0.002	-0.320	0.001
	PR	0.373	<0.001	-0.257	0.008	-0.315	0.001	-0.326	0.001
	BP	0.226	0.020	-0.142	0.147	-0.264	0.006	-0.091	0.357
	GH	0.520	<0.001	-0.447	<0.001	-0.354	<0.001	-0.415	<0.001
	VT	0.357	<0.001	-0.358	<0.001	-0.251	0.010	-0.310	0.001
	SF	0.253	0.009	-0.240	0.013	-0.294	0.002	-0.195	0.050
	RE	0.307	0.001	-0.266	0.006	-0.247	0.011	-0.237	0.015
	MH	0.102	0.299	-0.136	0.163	-0.051	0.603	-0.118	0.230
	PCS	0.400	<0.001	-0.268	0.005	-0.292	0.002	-0.320	0.001
	MCS	0.112	0.252	-0.127	0.196	-0.096	0.326	-0.151	0.124
	EQ-VAS	0.280	0.004	-0.196	0.044	-0.177	0.069	-0.351	<0.001
	EQ-5D (Europe VAS)	0.439	<0.001	-0.324	0.001	-0.345	<0.001	-0.414	<0.001
	EQ-5D (York A1 Tariff)	0.399	<0.001	-0.348	<0.001	-0.400	<0.001	-0.337	<0.001
	Mobility	-0.472	<0.001	0.406	<0.001	0.325	0.001	0.247	0.011
	Self-care	-0.192	0.048	0.254	0.009	0.128	0.192	0.210	0.032
	Usual activities	-0.288	0.003	0.287	0.003	0.186	0.056	0.242	0.013
	Pain/discomfort	-0.174	0.074	0.086	0.381	0.167	0.087	-0.110	0.265
	Anxiety/depression	-0.372	<0.001	0.327	0.001	0.393	<0.001	0.410	<0.001

LVEF – left ventricular ejection fraction; LAd – left atrial diameter; PASP – pulmonary artery systolic pressure; PF – physical functioning; PR – physical role; BP – bodily pain; GH – general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health – MCS – mental component summary; PCS – physical component summary; VAS – visual analogue scale.

BNP levels and HRQOL

Weak to strong negative correlations were identified between BNP levels and the EQ-VAS, EQ-5D indices and most SF-36 scales (except for the BP scale). Furthermore, weak to strong positive correlations were revealed between BNP levels and 4 out of 5 EQ-5D dimensions (with the exception of self-care dimension).

Based on the plasma BNP cutoff level of 100 pg/mL, AF patients with BNP levels over 100 pg/mL reported lower HRQOL in all SF-36 scales and EQ-VAS, EQ-5D indices and EQ-5D dimensions, again with the exception of the self-care dimension (p=0.077).

Discussion

In this study, two discrete generic instruments, SF-36 and EQ-5D, were used to evaluate HRQOL in a Greek symptomatic population with AF. A total of 108 patients were included in the sample and they reported a mean score of 55.14 for PF, 40.74 for PR, 64.58 for BP, 39.86 for GH, 43.99 for VT, 60.63 for SF, 51.61 for RE and 51.84 for the MH scale of SF-36. The summary component measures' mean scores were 40.28 for PCS and 40.89 for MCS. These findings are consistent with the baseline scores of the reference multicenter AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study of 716 patients with AF (mean age 70 ± 9 years, 62% male), with limited exceptions in the mean scores of GH, SF and MH scales.[10] Other studies that assessed HRQOL in patients with AF using the SF-36 instrument also reported impaired HRQOL.[28-30]

The results derived from the EQ-5D also showed that the AF patients in this study reported impaired HRQOL. The mean EQ-VAS was 59.63%, the mean EQ-5D Europe VAS index was 0.586, and the mean EQ-5D York A1 Tariff index was 0.547. The EQ-VAS and the EQ-5D York A1 Tariff indices were lower than those reported at baseline by Berg et al, who studied 5050 patients with AF (mean age 66.4 ± 12.8 years, 58% male) in 35 European countries that were included in the Euro Heart Survey. Concerning EQ-5D dimension, this study's patients reported "no problems" as often as AF patients in the study from Berg et al in the mobility, self-care and usual activi-

Table 6. Correlations of LVEF and E/e´ with SF-36 scales, EQ-VAS, EQ-5D indices and EQ-5D dimensions.

	LVEF			E/e´		
	≥45% n=62	<45% n=42	p	≥13 n=36	<13 n=70	p
PF	65.87 ± 27.01	38.64 ± 25.32	<0.001	42.44 ± 26.85	60.43 ± 30.14	0.003
PR	53.65 ± 43.28	22.16 ± 33.76	<0.001	23.69 ± 36.58	49.00 ± 43.61	0.002
BP	69.10 ± 28.62	57.48 ± 31.79	0.050	58.92 ± 30.24	67.51 ± 30.42	0.140
GH	48.34 ± 20.11	25.98 ± 15.94	<0.001	31.94 ± 20.35	43.11 ± 23.11	0.010
VT	50.23 ± 20.64	32.11 ± 18.99	<0.001	37.56 ± 21.93	46.10 ± 22.22	0.092
SF	65.42 ± 29.74	52.70 ± 22.84	0.034	51.28 ± 23.08	64.70 ± 28.89	0.016
RE	64.03 ± 40.72	33.55 ± 40.75	<0.001	36.19 ± 40.20	59.93 ± 42.50	0.005
MH	53.42 ± 21.64	48.45 ± 20.43	0.198	50.89 ± 18.81	51.34 ± 22.64	0.769
PCS	43.71 ± 9.512	35.02 ± 13.24	<0.001	36.10 ± 9.66	42.15 ± 12.55	0.007
MCS	42.19 ± 12.15	38.65 ± 16.64	0.131	38.90 ± 11.78	41.66 ± 12.14	0.260
EQ-VAS	65.73 ± 21.63	51.02 ± 25.26	0.002	55.97 ± 25.55	61.50 ± 23.45	0.268
EQ-5D Index (Europe VAS)	0.676 ± 0.225	0.462 ± 0.177	<0.001	0.490 ± 0.208	0.637 ± 0.228	0.002
EQ-5D Index (York A1 Tariff)	0.658 ± 0.300	0.394 ± 0.254	<0.001	0.405 ± 0.288	0.623 ± 0.295	<0.001
Mobility:						
No problems	42 (67.7%)	11 (25%)	<0.001	9 (25%)	44 (62.9%)	0.001
Some problems	20 (32.3%)	32 (72.7%)		26 (72.2%)	26 (37.1%)	
Extreme problems	0	1 (2.3%)		1 (2.8%)	0	
Self-care:						
No problems	57 (91.9%)	35 (79.5%)	0.135	27 (75%)	65 (92.9%)	0.027
Some problems	5 (8.1%)	8 (18.2%)		8 (22.2%)	5 (7.1%)	
Extreme problems	0	1 (2.3%)		1 (2.8%)	0	
Usual activities:						
No problems	49 (79%)	18 (40.9%)	<0.001	17 (47.2%)	50 (71.4%)	0.040
Some problems	12 (19.4%)	24 (54.5%)		17 (47.2%)	19 (27.1%)	
Extreme problems	1 (1.6%)	2 (4.5%)		2 (5.6%)	1 (1.4%)	
Pain/discomfort:						
None	30 (48.4%)	15 (34.1%)	0.339	11 (30.6%)	34 (48.6%)	0.162
Moderate	30 (48.4%)	27 (61.4%)		24 (66.7%)	33 (47.1%)	
Extreme	2 (3.2%)	2 (4.5%)		1 (2.8%)	3 (4.3%)	
Anxiety/depression						
None	17 (27.4%)	0	<0.001	3 (8.3%)	14 (20%)	0.020
Moderate	29 (46.8%)	20 (45.5%)		13 (36.1%)	36 (51.4%)	
Extreme	16 (25.8%)	24 (54.5%)		20 (55.6%)	20 (28.6%)	

LVEF – left ventricular ejection fraction; PF – physical functioning; PR – physical role; BP – bodily pain; GH – general health; VT – vitality; SF – social functioning; RE – role emotional; MH – mental health; MCS – mental component summary; PCS – physical component summary; VAS – visual analogue scale.

ties, and less often in the pain/discomfort and anxiety/depression dimensions.[31] Notwithstanding some differences in the HRQOL instruments and patient populations, the results of the present study provide further support for the existing evidence concerning HRQOL in patients with AF.

Both HRQOL instruments presented satisfactory levels of acceptance, sensitivity, reliability, and validity. The response rate was 100% and there were no missing data. Moreover, a satisfactory response distribution was observed for both instruments. Internal consistency for both instruments, as measured by Cronbach's coefficient α, was found to be greater than the level of acceptance of 0.700.[23] In addition, convergent validity was thoroughly examined, revealing, as expected, weak to strong correlations between similar items.

Female sex, advanced age, low physical activity, and higher NYHA class were shown to be associated with impaired HRQOL. Women have consistently reported lower levels of HRQOL globally, even in general population studies.[17,32] Age is another crucial factor that affects physical health more than mental health.[33] Moreover, physical activity has been repeatedly confirmed by many studies to be a positive predictor of well-being and is associated with higher

HRQOL, whereas functional capacity deficiencies have been shown to have a negative impact on physical aspects of HRQOL.[34,35]

Functional capacity in particular, as expressed by NYHA class, seems to have a strong association with HRQOL in patients with heart failure, as many studies have shown.[36-39] As the present study shows, NYHA class is also associated with HRQOL in patients with AF, as AF patients with a higher NYHA class (II-IV) reported worse scores in most of the scales and dimensions of both HRQOL instruments. These results are consistent with the findings of a study by Arribas et al, which also reported lower HRQOL scores in patients with AF who had worse NYHA functional class.[40]

Furthermore, in this study the echocardiographic indices associated with lower reported HRQOL included impaired LVEF, elevated E/e´, a dilated left atrium, and increased PASP. Studies of AF patients, and even healthy adults, have shown impaired HRQOL to be related to the above mentioned indices.[41-44] Notably, Punjani et al, in a study involving ambulatory men with AF, concluded that the E/e´ ratio is independently related to HRQOL.[42]

An interesting finding of this study is the differences in the HRQOL that were detected among patients with different types of AF. Taking into account the more severe symptoms in the paroxysmal/persistent types of AF, one would expect lower HRQOL scores. In contrast, this study's patients with newly diagnosed or paroxysmal/persistent AF reported higher scores in both HRQOL instruments compared to those with permanent AF. This could be attributed to the fact that patients with permanent AF are older, with more comorbidities such as hypertension, heart failure and diabetes, and with more impaired functional status—factors that seem to affect their HRQOL.

Finally, BNP, a marker of increased left ventricular filling pressures and left ventricular dysfunction, was associated with worse reported HRQOL in patients with AF, in the expected manner.[45,46] Hoekstra et al also suggest that increased BNP levels are responsible for a comparably low HRQOL and well-being.[41] Furthermore, not only are elevated BNP levels associated with left ventricular function, but they can also significantly predict the recurrence and the outcome of AF.[46-49]

Study limitations

One limitation of this study is that it was a single-center study, in patients seeking medical assistance for AF-related symptoms in a tertiary hospital, with a relatively small sample size. Moreover, asymptomatic AF patients were not included and only a limited number of patients with AF who had been treated interventionally or had received recently approved antiarrhythmic and/or antithrombotic agents were included. Additionally, this study did not examine the repeatability of the HRQOL measurement as assessed by the two generic instruments, or the change in HRQOL over time as the disease progressed.

Conclusions

Patients with AF who seek medical advice for AF-related symptoms have impaired HRQOL, as assessed by both the SF-36 and the EQ-5D generic instruments, and a number of contributing factors seem to significantly affect it. Furthermore, both generic instruments used in this study, SF-36 and EQ-5D, appear to be well accepted, reliable, and valid in assessing the HRQOL in patients with AF.

Finally, a suggestion for future research into the HRQOL in patients with AF would be the simultaneous administration of an AF-specific instrument, along with the two generic instruments, to a national representative sample of a Greek AF patient population, and an investigation of the changes in HRQOL over time as the disease evolves.

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