International Journal Of Occupational Health and Public Health Nursing, vol.4, no. 1, 2017, 5-19
ISSN: 2053-2369 (print version), 2053-2377 (online)
Scienpress Ltd, 2017

The assessment of the Quality of Life in patients with atrial fibrillation, treated with dabigatran vs acenocoumarol; A prospective study

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Abstract

The comparison of the quality of life (QoL) between two different groups of patients with atrial fibrillation (AF) depending on their anticoagulant treatment; those that receive dabigatran (DB) and those who receive acenocoumarol (AC).Fifty patients received AC and 50 patients received DB. The Euro Quality of Life-15D (EQ-15D and the Atrial Fibrillation Effect on Quality-of-Life (AFEQT), where used to assess the quality of life of patients with AF. The statistical analysis was performed using the statistical software SPSS version 19.0. There was no significant difference at the total score of EQ-15D and AFEQT between the two groups of patients ($p>0.05$). The mean score of EQ-15D for AC was 60.6±9.6 vs. 62.7±9.5 for DB and the mean score of AFEQT for AC was 69.1 ±19.8 vs. 73.1±17.2 for DB. Despite the fact that AC is a treatment definitely more demanding than DB the quality of the patient's life in Greece is not affected by the different treatment.

Keywords: Atrial Fibrillation; anticoagulation therapy; Quality of Life; Dabigatran Etexilate; Acenocoumarol, Warfarin;Quality of Life questionnaires.

1 Introduction

Atrial fibrillation (AF) is the most common arhythm disturbance in the general population and is associated with increased morbidity and mortality, affecting approximately 2.2 million Americans in 2010 and may exceed 12 million people by 2050, according to the American Heart Association. AF is a disease that

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appears within a large population of Greek citizens. It mainly appears in elderly people but it also affects younger populations. Patients who suffer from AF have increased risk of clot formation, which in turn increases the risk of a stroke appearance [1,2]. Assuming that incidence and prevalence are expected to double in the next 20 years, it is important to set out the management strategy of rhythm and heart rate control therapy for atrial fibrillation [3].

The most common and probably the only medication of choice till nowadays for patients with AF was the anticoagulant agent acenocoumarol (AC) [4,5]. Recently new oral anticoagulant such as dabigatran have been developed and demonstrated for preventing cardiac thromboembolism (TE) in patients with AF [6-8].

According to World Health Organization (WHO), it is, predominantly, a concept mercurial and multidimensional, which, usually, includes subjective of individual ratings for both positive and negative aspects of life, compared with the value system, in which it lives and addresses concerns, but also, its standards, goals and expectations. Physical health, mental state, environment and interpersonal relationships develop personality of people and their Quality of Life [9].

The quality of life of patients with physical problems is related to the effectiveness of treatment. The evaluation or estimation is necessary to make appropriate interventions that would lead to improvement. It is proven that improvement of quality of life; it is very important indicator for assessing these interventions [10].

There are scales which assess the quality of life (QoL) for patients with cardiac diseases and have some advantages. The most important advantages could be the appropriate questions designed for the particular disease, high sensitivity to detect changes caused by the time or by the implementation of intervention programs and finally the largest rate of acceptance by patients, because of the association with their illness [10].

Some of these scales are the Quality of life index: Cardiac Version, Minnesota Living with Heart Failure Questionnaire, the Arrhythmia Syndromes Checklist: Frequency and Severity or the Quality of life of Atrial Fibrillation Scale [11].

The purpose of this study was to compare the quality of life for patients with AF receiving AC vs DB as anticoagulant for AF associated with their demographic characteristics. The main objective was to compare the daily activity of these patients with AF in relation to their anticoagulant. The secondary objectives were: a. the determination of factors that influence the quality of life of patients with AF and b. parameters that are influenced by AF and have an impact in QoL of patients.

2 Material and Method

The study was conducted with patients suffering from AF, with age 40-85 years old. The sample collection includes patients who were treated by physicians at public General District Hospital of Northern Greece and patients who were treated by physicians in private doctors' offices at various areas of Northern Greece.

The excluded criteria were bleeding or ecchymoses and the ability to understand the Greek language. The sample that included in research consisted of 100 patients. Fifty patients received AC and 50 received DB. The original sample included 133 individuals. From this sample, the 66 individuals were from the group of patients receiving AC and the 67 individuals were from the group of patients treated with DB. The 13 patients from the AC group, developed skin ecchymoses with overall diameter>10 cm or bleeding from the mucosals and were excluded from the study. For the same reasons, 12 patients from the DB group were also excluded from the study. At the final study groups, 2 patients from the AC group and 2 from the DB group were not included, because they developed bleeding from the stomach or cerebral hemorrhage. From the final sample, 3 patients refused to participate due to reservation reasons and 1 patient declined his participation due to serious health problems. From the patients who refused to answer the questionnaire, the 3 individuals were patients belonging to the DB group and the fourth individual was a patient from the AC group (response rate, RR=96.9%).

A written approval was granted by the Medical Ethics Committee of the General District Hospital in order to distribute questionnaires to hospitalized patients. In order to participate someone in the protocol, an informed consent was asked. A full respect of the confidentiality of information throughout the collection and procession of data was guaranteed. Seventy six percent (76%) of the data collection was acquired over the phone and approximately 23% after interview. The study was performed from November 2012 to January 2013.

The data collection was performed using two questionnaires. The EQ-15D (Euro quality of life-15D), which is a tool that evaluates the quality of life of patients in general, independently of their disease and the AFEQT (Atrial Fibrillation Effect on Quality-of-Life), which is a specific tool that assesses the QoL of patients with AF. Besides these two questionnaires, demographic data related to gender, age and education, profession, health insurance and family status.

The EQ-15D refers to the following 15 aspects of QoL. Each of these parameters can be assessed to a 5 levels scale. Level 5 reflects a patient's worse condition, while level 1 represents the best possible performance concerning very limited health problems [12,13].

The AFEQT was the second questionnaire and consists of 20 questions and evaluates the quality of life related to health evaluating three parameters [14,15]. It is a validated QoL instrument that assesses 4 conceptual domains in AF-related

QoL. AFEQT is the only validated instrument that assesses treatment, symptoms, QoL, physical limitations and abilities. The last two questions quantify the satisfaction of patients from their therapy, but not in accordance with the severity of their disease. Therefore, they were excluded from the questionnaire [16].
The statistical data process was carried out by SPSS 19.0 (IBM, SPSS Statistics, 2010 Chicago Illinois USA). The distribution normality of demographic data was preserved using the Kolmogorov-Smirnov criterion in significant level $p>0.05$. The QoL score according to AFECT was estimated using a five point Likert scale (1 to 5) was used. The reliability of scales used was affirmed using Crohnbach's a. The continuous variables of the study were shown as mean value and standard deviation. The comparison among the continuous variables was held by using Student's t criterion when 2 variables were involved and the ANOVA criterion when 3 or more were to be compared. Furthermore, the comparison among the categorical variables was performed by using x2 criterion or Fischer's exact test (if the expected value was <5). Finally, the correlation tracking among quantitative variables was achieved by using Pearson's r test.

3 Main Results

3.1 Demographic data

Demographic data of participants is shown in Table 1.

3.2 Questionnaire Weighting – Reliability of Internal Consistency

The Chronbach's α for AFEQT scale was $\alpha=0.911$ and for EQ15D showed Chronbach's $\alpha=0.897$. By examining the correlation of the score of AFEQT questionnaire with the EQ15D score for all participants, there was a strong correlation ($r=0.688$, $p<0.05$).

3.3 Comparison of AFEQT score between patients receiving dabigatran and those receiving acenocoumarol

The majority of patients were reported no or limited restraint from typical symptoms of AF (e.g. palpitations, dizziness etc.). Patients receiving DB presented an average AFEQT score 80.7±21.5 for symptoms, compared to 81.2±21.2 of those receiving AC, with a non-statistically important variance ($p=0.907$). (Figure 1)

Concerning the daily activities, the AFEQT score for the DB group was 61.6±26.5 compared to 57.4±29.1 of the AC group, p-value 0.451 (Figure 2). The third part of the AFEQT questionnaire (questions 13-18) refers to the anxiety of patients regarding the appearance of complications from the anticoagulation therapy. The differences that appear between the two groups are statistically not significant, except the level of anxiety of patients for the effect of the administered medication to their daily activities ($p=0.023$). in total, patients receiving DB had 83.4±16.8 AFEQT score for the anxiety related to the medication side effects in

comparison to 76.7±26.3 of the patients of the AC group, p=0.131. There was also no significant difference in the total AFEQT score between the two groups (AC group had 69.1±19.8 and DB 73.1±17.2, p=0.283).

The analysis of the answers, revealed that 70% of the patients receiving DB were 100% satisfied with the control of the AF whereas only 26% of the patients using AC had the same level of satisfaction (p<0.0005). Moreover, the percentage of the DB group that felt 100% satisfied with the decrease of symptoms of AF due to therapy was more than twofold compared with the percentage of the AC patients (68% of DB compared to 32% of the AC patients, p=0.001). (Figure 3)

3.4 Comparison of the EQ-15D scale results between patients receiving dabigatran and those receiving acenocoumarol

It was observed no statistically significant differences, in any aspect of daily living examined in EQ-15D, between the two groups. The participants gather the highest percentages of total satisfaction for activities such as meals, oral and mental function and the lowest percentage in the sexual activity, for both groups. The EQ-15D score for the AC group was 60.6±9.6 in comparison to 62.7±9.5 for the DB group (p=0.293) (Table 1).

3.5 Differences in results of AFEQT and EQ-15D scores depending on gender and age of the participants

Regardless, the medication received and since there were not important statistical differences in the rest of the demographic parameters, male patients presented better QoL compared to female, as it appears in AFEQT and ED-15D questionnaires. The male patients gathered 85.1±17.9 points in the AFEQT section referring to symptoms (questions 1-4) compared to women that had 76.2±23.9 (p=0.038). Moreover, the superiority of men was clear in the daily activities section of AFEQT where men had 65.4±26.4 whereas women had 76±24.7 (p=0.089). In the total grading of the questionnaires, male patients had better scores both in AFEQT (75.9±17.3 for men whereas 65.8±18.6 for women, p=0.006) and EQ-15D (men 63.8±10 and women 59.3±8.5, p=0.019).

The influence of age was also important in the completed questionnaires. Participants younger than 60 years (9 patients) gathered 81.8±9.9 points in total in AFEQT questionnaire, compared to 76.7±16.3 of the age group 60-68, 70±18.7 of age group 69-77 and 62.5±20 of the oldest group 79-85 years (p=0.015). Accordingly, in EQ-15D score, the lowest grading was achieved by the age group 79-85 years (54.4±10.5), followed by the group 69-77 years of age (61.7±8.4), the age group 60-68 scoring 65±8 and the highest score concerning QoL achieved by the youngest age group <60 years old, (p<0.0005) (Table 1).

4 Labels of tables

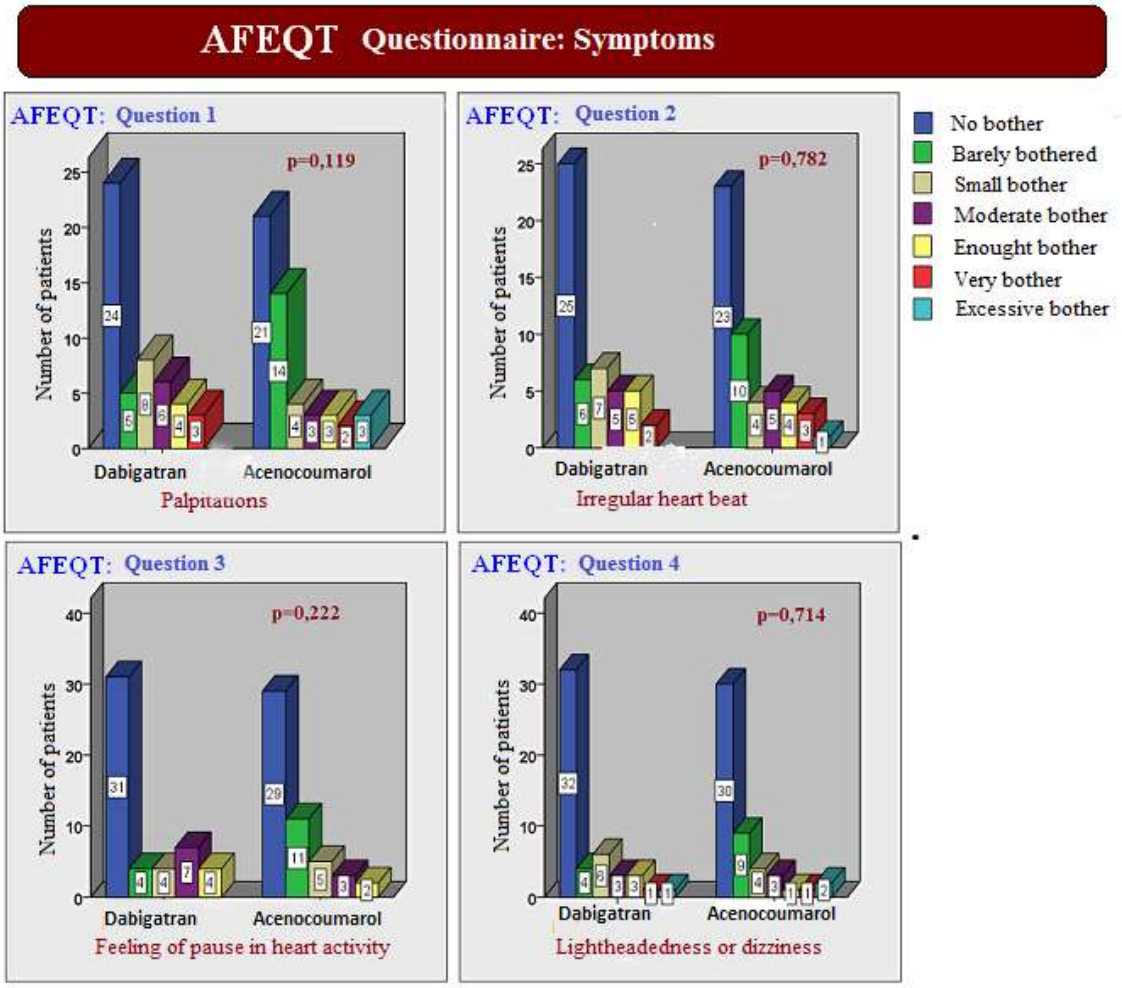

Figure 1. Answers segmentation in bar graphs for the first four questions of AFEQT questionnaire.

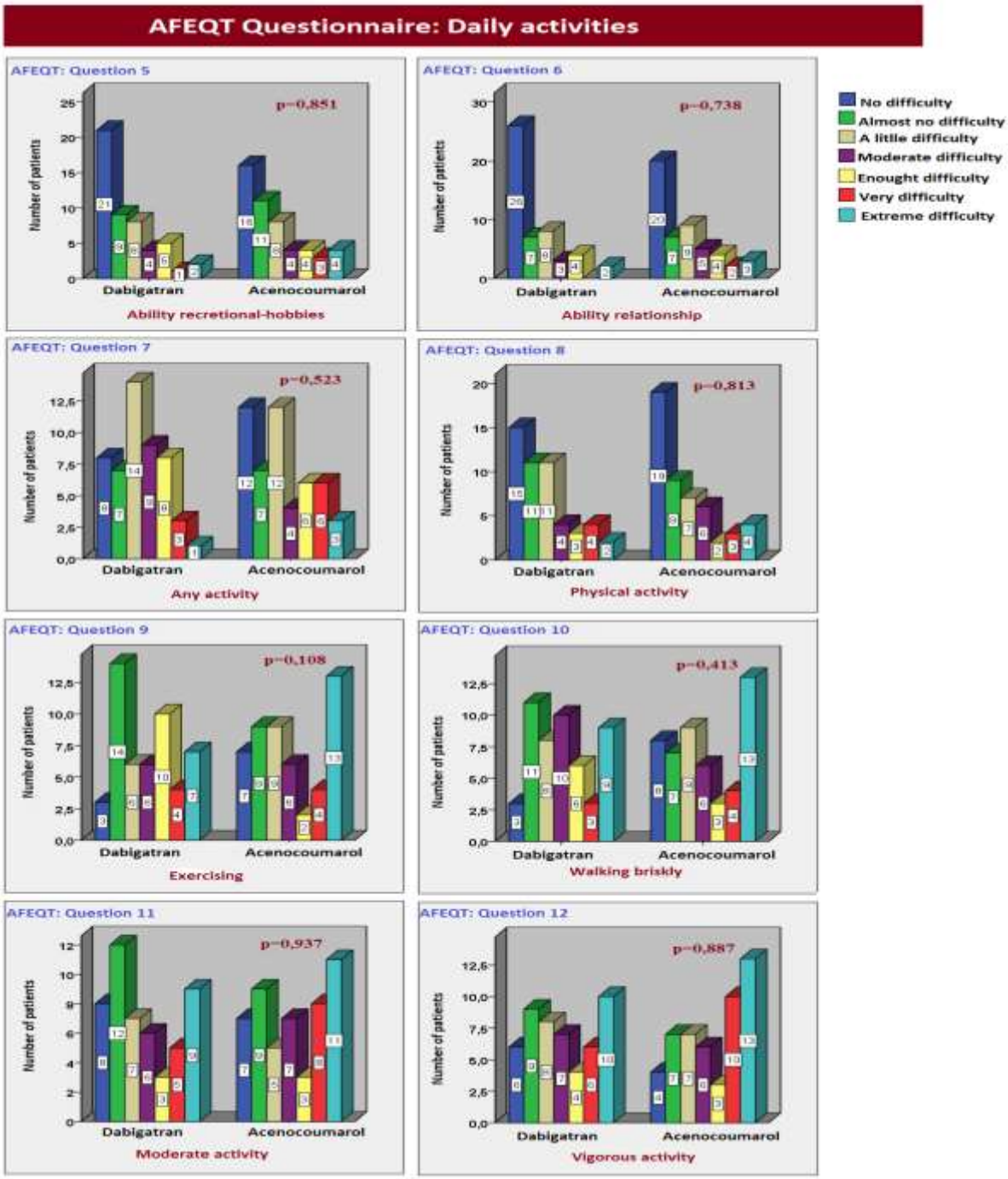

Figure 2. Distribution of answers in bar graphs for questions 5-12 of the AFEQT, discussing the daily activities of the participants.

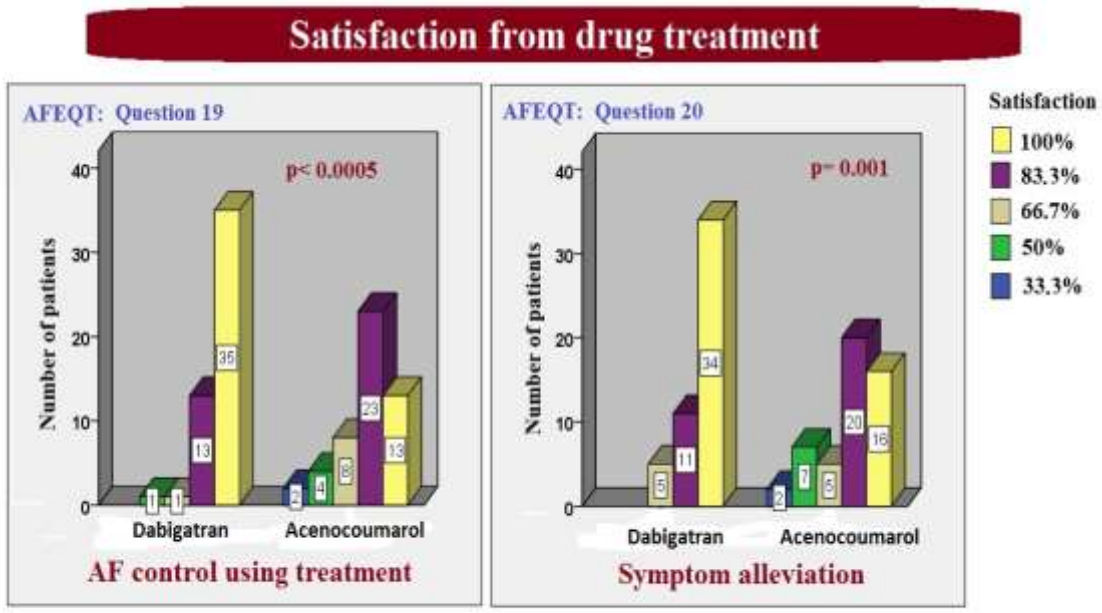

Figure 3. Distribution of answers in bar graphs, for questions 19, 20 of the AFEQT questionnaire, discussing patients' satisfaction from the received anticoagulation therapy.

Table 1. Significant differences and demographic data of participants

		Group AC N=50	Group DB N=50	p-value
Gender	male	25 (50%)	28 (56%)	0.689
Age	<60 years old	5 (10%)	4 (8%)	0.557
	60-68 years old	10 (20%)	16 (32%)	
	69-77 years old	24 (48%)	19 (38%)	
	78-85 years old	11 (22%)	11 (22%)	
Education	Illiterate	5 (10%)	3(6%)	0.785
	Elementary	24 (48%)	24(48%)	
	High education	14 (28%)	13 (26%)	
	Higher education	7 (14%)	10 (20%)	
	MSc/PhD	-	-	
Insurance	Uninsured	1 (2%)	5 (10%)	**0.018**
Medicine administration	Alone	35 (70%)	40 (80%)	0.324
	His children	6 (12%)	6 (12%)	
	Someone else	9 (18%)	4 (8%)	
Transportation	On foot	15 (30%)	16 (32%)	0.572
	On his own car	13 (26%)	14 (28%)	
	His children	10 (20%)	12 (24%)	
	Bus	7 (14%)	7 (14%)	
	taxi	5 (%)	1 (2%)	
Distance	Inside town/village	28 (56%)	26 (52%)	0.481
	1-10 km	12 (24%)	17 (34%)	
	>10 Km	10 (20%)	7 (14%)	

	OGA	26 (52%)	12 (24%)	
	IKA	15 (30%)	16 (32%)	
	TEBE	4 (8%)	5 (10%)	
	Other	4 (8%)	12 (24%)	
Marital status	Single	3 (6%)	2 (4%)	0.620
	Married with children	0 (0%)	2 (4%)	
	Married with no children	40 (80%)	39(78%)	
	Divorced	1 (2%)	2 (4%)	
	Widow	6 (12%)	5 (10%)	
Children	Yes	46 (92%)	46 (92%)	1.0
Residence	Urban	27 (54%)	30 (60%)	0.688
	district	5 (10%)	6 (12%)	
	Rural region	18 (36%)	14 (28%)	
Profession	Unemployed	2 (4%)	5 (10%)	0.447
	Craftsman	0 (0%)	1 (2%)	
	Private employee	2 (4%)	4 (8%)	
	Public employee	1 (2%)	1 (2%)	
	Freelancer	1 (2%)	3 (6%)	
	Retired	44 (88%)	36 (72%)	
AF	Today	36 (72%)	35 (70%)	1.0
	Earlier today	1 (2%)	1 (2%)	0.305
	Before a week	1 (2%)	1 (2%)	
	Before a month	3 (6%)	1 (2%)	
	1 month-1year	4 (8%)	10 (20%)	
	>1 year	5 (10%)	2 (4%)	
	Not aware of AF	0 (0%)	0 (0%)	

5 Discussion

According to the results of our study, the QoL of patients with AF is influenced by the pharmaceutical treatment that they receive, but without any significant statistical difference between the two groups receiving different medication. Age, as well as sex, is determinant factors that influence patients' perception about their QoL. Many other studies as well as our one, show that AF is mostly appeared within elderly populations. Age possibly is an important factor that influences QoL of patients with AF [17-20].

In the systematic review of Reynolds et al., it is found that the QoL of patients with AF is notably influenced by their age [19]. Likewise, in another study, is mentioned that elderly patients present worse QoL, especially in the relation to their physical activity [21].

The percentages of male population (53%) did not appear to be higher than women's, according to the present study. In contrast to the majority of other studies which have shown elevated male rates suffering from AF, this study showed poorer QoL and higher symptoms charge in women [19, 23, 24].

As far as concerning the symptoms (palpitations, light-headedness etc), there hasn't been great intensity on both groups. This could probably be explained by the fact that the majority of the patients lived with permanent or persistent AF while receiving the optimal treatment (usually a combination of anti-arrhythmic and b-blocker drugs) which possibly helps to the restriction of the symptoms. Also, some of these patients, during the specific period of the study, didn't appear with AF, so the symptoms were not obvious. On the other hand, AF sometimes appears to be asymptomatic. Some studies don't refer to any symptoms at all [21, 23].

Conversely, other studies have shown that patients with permanent AF turned up in smaller rates and seemed to have intense symptoms, especially palpitations [13, 23, 24]. It is observed, that independently of the anticoagulant treatment, the majority of the patients during intense physical activity present with excess difficulty. This is possibly observed due to their increased age and the coexistence of other diseases (cardiological, orthopedical, stroke disabilities etc) which, a prior worsen, mobility and QoL. Also, light and medium strength demanding exercises are executed without limitations from both studied groups.

One of the largest studies that has been conducted to evaluate the QoL of patients with AF receiving specific anticoagulant treatment (RE-LY study) found that one third of these patients had some mobility difficulties (results similar to ours). In the RE-LY study, the patients appear to have difficulties in everyday activities, something that had not been found in our study [23].

The participants in both studies demonstrate no or almost no problems in everyday activities, such as speaking, eating and intellectual functions providing them a good QoL, in contrast with their sexual activity that presented lower potency in both groups of anticoagulant treatment. Lower potency of sexual activity possibly comes from the elevated age average of these patients, the symptoms of the disease (dyspnoea, palpitations, fatigue etc) and the coexistent

diseases.

In the study of Fernando Arribas et al. the results showed that the lower potency in psychological, physical and sexual activities is due to the symptoms of the disease [22]. In our study, it is depicted that the reduced sexual activity existed even when the symptoms were not present.

A statistical significant difference between the two anticoagulant drugs has arisen is the degree of concern of the patients about the effect of the drugs in their everyday activities. The patients of the group receiving DB have had bigger concern (83.4±16.8) than those receiving AC (76.7±26.3). This is possibly happening because DB is a new drug, recently released in Greece which results in being encountered by the patients with reservations. Statistically significant differences between the two drugs are depicted regarding to the level of satisfaction of the patients from their treatment and to the level of symptoms recession. The group of DB appears to be more satisfied than this of AC. This result is, possibly, due to the easily handled medication and to the lack of interaction with other drugs or food in relation with AC which poses a lot of restrictions, further costs due to the laboratory examinations for frequent control of blood coagulation and forced locomotion.

Last but not least, the economic impact of drug administration in Greece of economic crisis is major. In a study of Andrikopoulos et al. is shown that the cost per quality-adjusted life year of dabigatran 150 mg twice daily relative to other therapies which is varied from €5547 to €11762. Also, dabigatran etexilate may represent a cost-effective option with grant role in the prevention of thromboembolic events in AF patients, as concerned the moderate-to-high risk of stroke or systemic embolism [25]. Furthermore, recent studies have noted that oral direct thrombin inhibitor such as dabigatran, given in fixed doses, requires no routine coagulation monitoring and is effective in preventing embolic events [26].

6 Study limits

Although this research was carefully prepared, we are still aware of its limitations and shortcomings. First of all, the research was conducted in only one region of Greece. It is not enough for the researcher to observe all the AF patients QoL, the factors that influence it and their perception on it. It would be better if it was done in many other Greek regions. Secondly, the population of the participants is small, and might not represent the majority of AF patients. In addition, extended research should be done, so as to have enough population from different regions and the health professionals would have the opportunity to intervene and support patients suffering from AF to receive the appropriate treatment.

7 Conclusion

Nowadays, it has shown that the new oral anticoagulants are effective and safe than warfarin for the prevention of stroke and systemic embolism in patients with AF [27]. AC outbalances longevity and validity as anticoagulant treatment but this is compensated by the advantage of DB, where the cost is almost prohibiting for some patients in Greece. Regarding to the health system, measuring the life quality of a specific group of patients will help monitor the progress concerning the achievement of the targets for health, including the reduction of costs for its preservation.

ACKNOWLEDGEMENTS. The authors have no funding or conflicts of interest to disclose.

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