

Health-related quality of life among atrial fibrillation patients using warfarin therapy

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ABSTRACT

The current study aimed to assess health-related quality of life (HRQoL) among atrial fibrillation (AF) patients receiving chronic warfarin therapy, and to identify factors that may influence their HRQoL perceptions. A cross-sectional descriptive study with a representative cohort was undertaken at anticoagulation clinics within two public hospitals in Penang, Malaysia. Based on prevalence sampling techniques, a total of 339 patients were recruited. A specific bilingual instrument, the Duke Anticoagulation Satisfaction Scale (DASS), and a generic instrument, the European Quality of Life scale (EQ-5D-3L), were used. Generally, the quality of life perception of all participants was positive. Both instruments exhibited good average scores: mean \pm SD for DASS, 70.8 ± 19.8 , for the EQ-VAS, $69.3\% \pm 16.3\%$, and for the EQ-Index (TTO), $79.8\% \pm 26.5\%$. Younger patients (< 45 years old), patients with higher education levels, and employed patients, had significantly higher health perceptions ($p < 0.05$). On the other hand, women presented with a worse HRQoL evaluation compared to men. Further, a history of bleeding event, either major or minor, had a negative effect on health perception ($P < 0.05$). These findings could be helpful in clinical practice to enable clinicians to take preventive measures, especially with newly diagnosed patients in which improvement in quality of life is still possible.

Key words: Warfarin; Quality of life; DASS; Atrial fibrillation; EQ-5D

INTRODUCTION

Long-term treatment with oral anticoagulation is essential for prophylaxis of strokes and other thromboembolic events in patients diagnosed with atrial fibrillation (AF) [1,2]. However, treatment with warfarin is complicated due to variability in the biological response to the drug [3,4], its narrow therapeutic index (Ansell et al., 2008), its interactions with other drugs, alcohol, and

foods [5,6], and the potential occurrence of thrombotic or bleeding events. Thus, using warfarin therapy may cause changes in the lifestyle of warfarin users; these may include dietary restrictions to lower vitamin K intake, the fear of performance of physical activity, as well as the need to strictly adhere to the treatment regime. Moreover, the inconvenience of dosing adjustments and the need for regular blood tests to monitor INR levels, together with the fear of complications, such as the risk of minor or

major bleeding or stroke, may negatively effect patients' health-related quality of life (HRQoL) [7-9]. A perceived reduction in HRQoL is an important factor which may influence the physician's prescription and the patient's use of warfarin therapy [10].

HRQoL has been evaluated previously by many researchers; however, many authors have used a generic instrument to measure HRQoL, such as the Medical Outcomes Survey 36-item Short Form (SF-36) [7,11-13]. To study HRQoL among warfarin users, three valid and reliable instruments have been identified; the Sawicki instrument, the Duke Anticoagulation Satisfaction Scale (DASS), and the Deep Vein Thrombosis QoL (DVTQoL) [14]. The DASS is a specific instrument that was validated, and developed [13,15].

Since patients, clinicians, and health care providers are all keenly interested in the effects of medication on HRQoL [16], the aims of our study were: 1) to assess the impact of long-term use of warfarin on quality of life among AF patients, using two different tools, a specific instrument (DASS scale) and a generic tool (EQ-5D); and 2) to identify the factors influencing their health perceptions.

METHODS

Study design and setting

This cross-sectional descriptive study was undertaken among a representative cohort of AF patients undergoing anticoagulation therapy. It was conducted at the Cardiology Clinics and Anticoagulation Clinics in two tertiary hospitals; Hospital Pulau Pinang (HPP) and Seberang Jaya Hospital (SJH), Malaysia. Both of the institutes are teaching hospitals and are generalized in nature, currently providing services to about 90% of Penang state, Malaysia.

Participants and sampling criteria

A study conducted in Kuala Lumpur, Malaysia, suggested that the prevalence of AF in Malaysia was 2.8% [17,18]. According to a prevalence-based calculation, the appropriate sample size for this study is 106 AF patients [19]. Over a one year duration, 382 AF patients on warfarin therapy were conveniently recruited from the study hospitals. However, only 339 met the inclusion criteria. The inclusion criteria were as follows: 1) over 20 years of age, (2) diagnosed with AF at least one year prior, (3) use of warfarin for more than six months, and (4) able to communicate in the Malay language.

Assessment of HRQoL

Generic EuroQoL (EQ-5D). EQ-5D is a generic

instrument consisting of a five-item descriptive system of health status (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a visual analogue scale (VAS) [20]. Each domain of the descriptive system has three levels of perceived problems (no problems/moderate problems/extreme problems), and their scores can be converted into a utility index score (EQ-INDEX) [21-23]. Higher utility index scores indicate better HRQoL. The EQ-VAS is a 20 cm health thermometer with two distinct end points; the best imaginable health state (score of 100) and the worst imaginable health state (score of 0). The English and Malay versions were used in this study.

Specific DASS. The DASS is specific scale for evaluating HRQoL among patients under treatment with oral anticoagulation [13]. It is composed of a 25-item scale which addresses limitations (e.g., physical activity limitations due to fear of bleeding and dietary restrictions), hassles and burdens (both daily hassles, such as difficulty in remembering to take the medicine, and occasional hassles because of regular visits and waits for blood tests results), and positive psychological impacts (e.g., feeling comfortable because of anticoagulation treatment). Each item has seven possible responses: "not at all", "a little", "somewhat", "moderately", "quite a bit", "a lot", and "very much". An extensive approach was undertaken to translate the questionnaire into Malay; this approach was in compliance with the standard procedure detailed in translation guidelines [14,24], where cultural and language equivalence, as well as psychometric properties, were checked. After translation of the DASS instrument, the reliability and validity of the newly translated version were shown to be maintained. The reliability of the DASS was confirmed using measures of internal consistency and test-retest reliability, and validity was examined through known group validity. The internal consistency reliability of the DASS was satisfactory, with a Cronbach's alpha of 0.758, and good test-retest reliability was observed ($p = 0.802$).

Data collection

A convenience sample of AF patients on warfarin therapy, who met the study criteria, was recruited from both hospitals. The medical records of all patients who attended the Cardiology clinics for follow up were reviewed to confirm the diagnosis and the use of warfarin. All cases that met the inclusion criteria for this study were invited to take part and sign the consent form. A socio-demographic questionnaire, the DASS, and the EQ-5D were administered in a face-to-face interview with each patient. After the interview, INR levels were recorded from INR booklets, and concurrent medications, medical history, and history of minor or major bleeding were confirmed by referring to the medical records.

Statistical analysis

All data entry and analyses were performed using the program Statistical Package for the Social Sciences (SPSS) version 19.0 (SPSS Inc., Chicago, IL). The significance level was set at $p < 0.05$. Descriptive statistics and frequencies were used to describe the categorical variables, while means and standard deviations (SDs) were calculated for continuous variables. The scores for the EQ-5D descriptive system were converted into a single utility index score²⁵, using values derived from the UK general population survey reported in 1995²⁶.

The scores from the DASS domains range from 9 to 63 for limitation, 8 to 56 for treatment inconvenience, and 8 to 56 for psychological impact, while the overall score varies from 25 to 175¹⁵. Lower DASS scores for all domains indicate higher satisfaction with QoL [13]. Analysis of the DASS was performed by summing the responses to each item (varying from 1 to 7 for each item; i.e., from "not at all" to "very much") to obtain a total score.

The data were further stratified by age, sex, race, education level, stroke risk as measured by the CHADS₂ score (age ≥ 75 years, hypertension, diabetes mellitus, heart failure, and prior stroke), and duration of warfarin use.

RESULTS

The mean age \pm SD of all participants ($n = 339$) was 60.4 ± 14.5 years, with 204 (60.2%) males participating in the study. The racial distribution of the sample was equivalent (30.1% of participants were Malay, 35.1% were Chinese, 34.8% were Indian). One-third of participants ($n = 127$) had a secondary school education, and 59% were employed or retired. The majority of patients (70%) were from a lower socioeconomic level.

Among the 339 AF patients recruited, 64% had hypertension, 39% had hyperlipidemia, and about one-third (33.6%) had diabetes mellitus. The prevalence of previous stroke among the cases was very low; less than 10%. Nearly half of the patients had used warfarin for less than two years, with a mean duration of warfarin use of 3.2 ± 2.4 years.

Regarding the clinical outcome of warfarin therapy, the study population showed moderate anticoagulation control with a mean \pm SD TTR% of 0.55 ± 0.25 , and 0.54 ± 0.24 for INR%. Fifty-five cases had suffered from major bleeding that required hospitalization (confirmed from their medical records); however, minor bleeding was more common, experienced by 83 patients. The most common site of bleeding was under the skin (bruises), followed by gum bleeding. The mean dose of warfarin used was 3.4 ± 1.6 mg. Table 1 summarizes the demographic and clinical characteristic of the study population.

Assessment of HRQoL amongst AF patients on anticoagulation therapy (Table 1)

DASS results

The overall DASS score was 70.8 ± 19.8 , which indicates that participants had a good perceived QoL, given that higher scores indicate lower QoL.

The mean score for limitation (range, 9-63) was 17.1 ± 8.9 for the whole sample. For the inconvenience subscale, the mean score was 19.3 ± 7.6 (range, 8-56). The mean score for psychological impacts was 34.4 ± 11.2 (range, 8-56).

EQ-5D results

The means \pm SD for the EQ-VAS among the whole sample was $69.3 \pm 16.3\%$, and for the EQ-Index (TTO) it was $79.8 \pm 26.5\%$. One-third (35.7%) of participants reported problems with mobility and approximately half of the participants (43.1%) suffered from pain. The frequency of reported problem in each domain is demonstrated in Table 2.

Effects of participant demographic and clinical characteristics on HRQoL

Regarding the generic instrument, there was a significant difference in the mean QoL score between males and females, among different age groups, and between patients with different educational levels, marital status, monthly income, and occupational status ($p < 0.05$) (Table 3). The younger age group (< 45 years old) reported better EQ-Index scores compared to older age groups; however, there was no significant difference in EQ-VAS score.

On the other hand, EQ-VAS scores differed significantly in terms of patient monthly income and marital status. Further, in terms of the specific measure of HRQoL (DASS), occupation status influenced scores; those who were employed had significantly higher DASS scores than those who were unemployed ($p < 0.05$).

Table 4 describes the mean reported HRQoL scores in relation to the clinical characteristics of the study population. The mean EQ-Index score was significantly lower in patients who had experienced minor or major bleeding ($p < 0.05$). Similarly, the mean DASS was significantly lower in those who had previous major bleeding ($p < 0.05$). A similar trend in DASS score was observed for participants who had experienced minor bleeding; however, this difference was not statistically significant. Further, there was an association between having a previous minor bleeding event and the reported EQ-VAS ($p < 0.05$).

TABLE 1. Demographic and clinical characteristics of study population (n=339)

DEMOGRAPHIC CHARACTERISTICS	n=339 n(%)	CLINICAL CHARACTERISTICS	n=339 n(%)
Age group (years) <45 45-64 >65	47(13.9) 159(46.9) 133 (39.2)	Duration of warfarin use < 2 years 2 years – 5 years > 5 years	151(44.5) 87(25.7) 101(29.8)
Sex Male Female	204(60.2) 135(39.8)	CHADS2 score 0-2 3 ≥4	270(79.6) 53(15.6) 16(4.7)
Ethnicity Malay Chinese Indian	102(30.1) 119(35.1) 118(34.8)	Medication number 1-3 4-6 ≥7	133(39.2) 182(53.7) 24(7.1)
Education No formal education Primary Secondary College/ University	52(15.3) 98(28.9) 127(37.5) 62(18.3)	Experience a previous minor bleeding Yes No	83(24.5) 256(75.5)
Occupation Unemployed Employed	131 (38.6) 208(61.4)	Hospitalized for major bleeding Yes No	55(16.2) 284(83.8)
Monthly income <RM 2000 RM2000- RM4000 >RM 4000	238(70.2) 68(20.1) 33(9.7)	Medical History Hypertension Diabetes Mellitus MI CHF CAD Previous stroke Hyperlipidemia Valve replacement	217(64.0) 114(33.6) 48(14.2) 82(24.2) 43(12.7) 30(8.8) 133(39.2) 33(9.7)
Marital Status Unmarried Married Widow/divorced	36 (10.6) 255(75.2) 48 (14.2)	Site of bleeding Gum Nose Bruises Coughing/vomited blood Stool Eye	25(7.4) 11(3.2) 35(10.3) 5(1.5) 7(2.1) 4(1.2)
Alcohol Yes	11(3.2)	Aspirin/ antiplatelet Use Yes	122(36.0)
Smoking Yes No	27(8.0) 318(92.0)	TTR% (mean ± SD) INR%(mean ± SD)	0.55±0.25 0.52±0.23

TTR%: Time within the normal range (Calculated by Rosendaal method), INR%: Percentage of INR readings within the normal range

TABLE 2. The frequency of reported problems in EQ-5D descriptive system (n=339)

	n	(%)
Mobility	121	35.7
Self care	32	9.4
Usual activities	85	25.0
Pain/Discomfort	146	43.1
Anxiety/depression	79	23.3

Table 5 shows the frequently reported problems from the EQ-Index domains (some/unable or moderately/extremely) for the groups that showed a significant difference in mean EQ-Index score. Mobility problems (physical problems) were

reported significantly more by the older age group. There were more complaints about pain and feeling discomfort among females than males, and among those who had a previous minor or major bleeding event, compared to those who had not. Moreover, lower educational level patients (without formal education) were more depressed and anxious.

Regarding the duration of warfarin use, the results were unpredictable and inconsistent. DASS scores were higher in participants who had used warfarin for 2-5 years, but then a deterioration in health was reported in the group who used warfarin for more than 5 years. The EQ-VAS and EQ-Index showed contradictory results; while EQ-Index scores decreased with longer duration of warfarin used, EQ-VAS showed an opposite trend. However, HRQoL was not significantly associated with the duration of warfarin use.

TABLE 3. Relationship between socio-demographic factors and HRQoL (n=339)

CHARACTERISTICS	N(%)	DASS SCORE	EQ-INDEX	EQ-VAS
Age group				
<45	47(13.9)	55.0±13.6	86.9±19.2*	67.9±15.0
45-64	159(46.9)	60.0±15.8	85.1±13.5	69.3±17.0
>65	133 (39.2)	59.1±20.5	74.7±31.0	66.2±16.1
Sex				
Male	204(60.2)	57.1±17.1	82.0±20.7*	69.5±16.5*
Female	135(39.8)	61.9±20.4	72.7±33.2	63.6±15.3
Ethnicity				
Malay	102(30.1)	57.3±16.8	78.7±23.9	69.8±16.4
Chinese	119(35.1)	59.6±19.4	79.2±29.3	64.6±17.2
Indian	118(34.8)	64.3±22.8	77.2±26.0	67.0±15.7
Education				
No formal education	52(15.3)	59.9±20.9	64.2±41.2*	66.7±17.7*
Primary	98(28.9)	59.8±19.1	80.6±25.9	61.9±14.7
Secondary	127(37.5)	58.3±16.9	81.3±17.0	68.8±16.9
College/ University	62(18.3)	57.7±20.1	85.4±21.1	70.5±15.8
Occupation				
Unemployed	131(38.6)	63.9±18.3*	70.6±35.2*	63.3±15.3*
Employed/ Retired	208(61.4)	55.9±18.3	84.0±17.7	69.7±16.4
Monthly income				
< RM2000	238(70.2)	59.3±17.9	78.5±27.7	66.6±16.3*
RM2000- RM4000	68(20.1)	57.4±18.9	78.3±21.7	70.7±16.2
>RM4000	33(9.7)	55.8±31.2	80.1±11.1	72.2±16.1
Marital Status				
Unmarried	36(10.6)	56.2±16.4	85.4±21.5	62.7±18.3*
Married	255(75.2)	58.9±18.6	79.3±26.8	68.4±16.1
Widow/ divorced	48(14.2)	61.0±20.8	71.7±26.9	62.8±15.3

ANOVA or Hest were applied whenever appropriate

*Significant difference at the level of 0.05

DISCUSSION

Patients on oral anticoagulation therapy often worry about complications, dietary limitations, less freedom when traveling, and frequent and regular visits to physicians and laboratories. These factors are likely to decrease quality of life.

In this study, two tools (a specific and a generic tool) were used to obtain a comprehensive and clear estimation of AF patients' HRQoL. Using multiple types of measures in research gives additional information [27]. Furthermore, the DASS instrument addresses specific factors associated with anticoagulant treatment that may influence the treatment directly or indirectly, such as fear of bleeding, changes in behavior, and limitations towards treatment.

Based on both instruments, the quality of life perception of the studied patients was generally positive with regard to treatment with OAC. The average DASS score was 70.8 (\pm 19.8); the domain presenting with the greatest compromise was the one related to the psychological impact of treatment (what the patient knows and feels about their OAC treatment). On another study, the mean DASS was 58, which is lower than the value in our study, indicating that our participants perceived poorer quality of life related to warfarin use (lower scores represent higher satisfaction with OAT, less limitation, less hassle and

burden, and less psychological impact) [15]. In a previous study, study aimed to prospectively evaluate QoL in patients chronically anticoagulated, the DASS and SF-36 were administered, and QoL was found to be generally good [28]. In their study, the average DASS score was 67.1 (\pm 18.2); however, the domain presenting with the greatest compromise was the one related to treatment inconveniences (annoyances, burdens, and obligations) [28].

On the other hand, the average EQ-5D score was high (79.8 \pm 26.3%). Among the EQ-Index evaluated domains, the pain, discomfort, and mobility domains were the most compromised in terms of life quality perception. These findings add to the existing literature which suggests that the most impaired HRQoL domains are related to physical aspects and vitality [7,11,28], pain, physical functioning, and general health status [7].

Interestingly, out of the 339 participants, 36% believed that their health had improved since starting warfarin, 67-71% reported that warfarin did not restrict their physical activities, and only 14.5% reported that they were not confident while using warfarin. However, 52% of the patients believed that warfarin has no effect on their life, 10% reported worrying a lot about the bleeding side effect of warfarin, 58% reported being bothered by frequent blood tests as they are time-consuming, and 11% were not totally satisfied with warfarin.

TABLE 4. Relationship between patients' clinical characteristics and HRQoL (n=339)

CHARACTERISTICS	n(%)	DASS SCORE	EQ-INDEX	EQ-VAS
Duration of warfarin use				
< 2 years	151(44.5)	61.2±18.7	79.9±26.2	65.9±16.6
2 years – 5 years	87(25.7)	55.9±18.6	79.5±19.8	66.0±16.1
> 5 years	101(29.8)	58.2±18.5	77.3±30.7	69.8±15.9
CHADS2 score				
0-2	270(79.6)	59.9±19.0	79.6±25.6	67.6±16.5
3	53(15.6)	54.8±17.1	76.5±30.0	68.4±16.1
≥4	16(4.7)	53.0±14.8	71.5±31.7	59.3±10.7
Medication number				
1-3	133(39.2)	59.7±18.3	81.8±20.4	65.9±13.7
4-6	182(53.7)	57.5±18.2	75.1±31.0	68.1±17.5
≥7	24(7.1)	61.2±21.4	81.1±27.6	69.0±19.0
Previous minor bleeding				
Yes	83(24.5)	60.8±19.1	73.8±28.2*	62.2±16.4**
No	256(75.5)	58.2±18.5	81.9±25.6	68.2±16.2
Hospitalized for major bleeding				
Yes	55(16.2)	68.2±18.4**	70.4±27.7**	68.4±17.4
No	284(83.8)	56.4±17.9	81.2±25.8	67.0±16.0
Hypertension				
Yes	217(64)	58.9±19.9	77.8±28.4	66.8±16.9
No	122(36)	58.9±15.3	81.5±21.1	68.5±14.5
Diabetes Mellitus				
Yes	114(33.6)	59.3±19.8	77.2±32.6	67.1±16.6
No	225(66.4)	58.7±18.0	79.9±22.3	67.4±16.2
Congestive heart failure				
Yes	82(24.2)	60.7±18.0	82.0±25.4	68.3±18.4
No	257(75.8)	57.6±18.7	77.7±26.9	66.9±15.5
Valve replacement (VR)				
Yes	33(9.7)	63.2±18.2	80.8±21.5	72.5±11.4*
No	306(90.3)	58.4±18.7	78.6±27.2	66.6±16.5
PREVIOUS STROKE				
Yes	30(8.8)	58.6±21.2	72.7±31.7	72.7±31.7
No	309(91.2)	58.9±18.4	79.6±25.8	79.6±25.8

ANOVA or *t* test were applied whenever appropriate

*Significant difference at the level of 0.05

** Significant difference at the level of 0.01

TABLE 5. Proportion of respondents reporting problems on each EQ-5D dimension in the significant groups

EQ-DOMAINS	AGE >65 YEARS N (133)	FEMALE N (135)	NO FORMAL EDUCATION N (52)	UNEMPLOYED N (131)	PREVIOUS MAJOR BLEEDING N (55)	PREVIOUS MINOR BLEEDING N (83)
Decreased mobility	61(45.9)	58(43.0)	28(53.8)	62(47.3)	21(38.2)	36(43.4)
Difficulty in self-care	15(11.3)	16(11.9)	10(19.2)	20(15.2)	4(7.2)	10(11.2)
Problems performing usual activities	36(27.0)	37(27.4)	25(48.0)	47(35.9)	9(16.4)	25(33.7)
Pain/discomfort	62(46.6)	64(47.4)	23(44.2)	62(47.3)	34(61.8)	56(67.4)
Anxious/Depressed	34(25.6)	37(27.4)	11(21.2)	34(25.9)	11(20.0)	22(26.5)

Bolded indicates significant at $P < 0.05$, Chi-square test was applied

Demographic factors influencing patients' QoL

Several studies have investigated the effect of OAC therapy on HRQoL. Regarding the generic instrument (EQ-5D), there was a significant difference between the three

patient age groups in terms of perceived QoL ($p < 0.01$). The correlation analysis showed that there was a negative correlation between age and EQ-Index ($r = -0.168$, $p = 0.028$). In consistent with Corbi et al. 10 study which found worse scores of HRQoL among elderly. Furthermore, other

studies found that age is a negative factor that impacts patient's QoL [7,29]; however, previous researcher found that middle aged patients (41 to 65 years old) had better QoL scores when compared to younger patients and older patients over 65 years [28].

When comparing the specific domains of HRQoL in relation to age, statistically significant differences were only found in the domain of mobility; the worst evaluation was obtained in participants aged above 65 years. This result verifies the common dictum that young individuals present with better physical functioning when compared to the elderly [7,10]. In addition to the age differences, women presented with worse HRQoL evaluations compared to men, with a statistically significant difference in the pain domain. Many previous studies reported worse HRQoL scores among women [7,10,29,30].

A greater tendency towards a positive perception of QoL as measured with the EQ-5D was observed in patients with higher education levels; patients with college education and above had the best perception of QoL, with the most significant deterioration observed in perceptions regarding the usual activities and the anxiety domains. Previous study observed that Warfarin-treated patients had higher levels of self-reported symptoms of depression and anxiety [31]. However, when examining the DASS, QoL was not associated with education level. On the contrary, positive perceptions were more predominant among patients with low educational levels (illiterates or those who only completed elementary school) [7,28]. Further, being employed or retired was related to high perceptions of QoL on both the EQ-5D and DASS.

Clinical factors influencing patients' QoL

An important issue with regard to the impact of warfarin on QoL relates to the rates of adverse outcomes, specifically hemorrhage. In the current study, a history of previous major bleeding event was associated with a significant reduction in patients' QoL, in both evaluation instruments. Lancaster et al. [8] observed no significant difference between warfarin-treated and control patients regarding HRQoL until a bleeding episode had occurred. They concluded that patients with bleeding episode had a significant decrease in perceived health. Another study had also shown that hemorrhagic events influence a more negative perception of QoL [28]. However, previous researcher found that hemorrhages (bleeding episodes) did not affect patients' perceptions of QoL, and negative perceptions related to anticoagulant treatment was more evident in patients worried about bleeding risks [7]. Additionally, Alegret et al. [32] observed higher minor bleeding events and worse HRQoL scores in the warfarin group when compared with new oral anticoagulant group.

In summary, the only modifiable factor affecting patients' HRQoL appears to be patients' education

level. This may be related to their better understanding of medication and disease control. Furthermore, there is a general consensus in the literature that improved medication knowledge improves the therapeutic outcome of warfarin. However, there is scarce data regarding the association between medication knowledge and HRQoL.

Considering the scarcity of studies involving HRQoL and oral anticoagulation, the present results can guide healthcare professionals to identify and direct resources towards those likely to present with worse HRQoL evaluations; that is, gender, education level, age, and a history of previous bleeding show associations with some HRQoL domains. This data may help in the prevention of events that may negatively affect QoL of these users.

CONCLUSION

Patients on warfarin therapy had good perceived QoL. However, this perception was influenced by demographic and clinical variables, which had either a positive effect (younger age, higher education level, and being employed or retired) or a negative effect (among women, and those who had experienced previous hemorrhagic events with either major or minor bleeding) on QoL perceptions. Studies evaluating medication knowledge and its relationship to HRQoL are highly recommended.

References

1. Mitine C, Leunens G, Verstraete J, et al. Is it necessary to repeat quality control procedures for head and neck patients? *Radiother Oncol.* 1991;21(3):201-210.
2. Ezekowitz MD, Bridgers SL, James KE, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med.* 1992;327(20):1406-1412.
3. Barcellona D, Contu P, Marongiu F. Patient education and oral anticoagulant therapy. *Haematologica.* 2002;87(10):1081-1086.
4. Taylor FC, Ramsay ME, Tan G, Gabbay J, Cohen H. Evaluation of patients' knowledge about anticoagulant treatment. *Quality and Safety in Health Care.* 1994;3(2):79-85.
5. Greenblatt DJ, Moltke LL. Interaction of warfarin with drugs, natural substances, and foods. *J. Clin. Pharmacol.* 2005;45(2):127-132.
6. Holbrook AM, Pereira JA, Labiris R, et al. Systematic overview of warfarin and its drug and food interactions. *Arch Intern Med.* 2005;165(10):1095-1106.
7. Casais P, Meschengieser S, Sanchez-Luceros A, Lazzari M. Patients' perceptions regarding oral anticoagulation therapy and its effect on quality of life. *Curr Med Res Opin.* 2005;21(7):1085-1090.
8. Lancaster TR, Singer DE, Sheehan MA, et al. The impact of long-term warfarin therapy on quality of life: Evidence from a randomized trial. *Arch Intern Med.* 1991;151(10):1944-1949.
9. McCahon D, Murray ET, Murray K, Holder RL, Fitzmaurice DA. Does self-management of oral anticoagulation therapy improve quality of life and anxiety? *Fam Pract.* 2010;28(2):134-140.
10. Corbi ISA, Dantas RAS, Pelegrino FM, Carvalho, Ariana Rodrigues

- da Silva. Health related quality of life of patients undergoing oral anticoagulation therapy. *Rev Lat Am*. 2011;19(4):865-873.
11. Howes CJ, Reid MC, Brandt C, et al. Exercise tolerance and quality of life in elderly patients with chronic atrial fibrillation. *J Cardiovasc Pharmacol Ther*. 2001;6(1):23-29.
 12. Matchar DB, Jacobson AK, Edson RG, et al. The impact of patient self-testing of prothrombin time for managing anticoagulation: Rationale and design of VA cooperative study# 481—the home INR study (THINRS). *J Thromb Thrombolysis*. 2005;19(3):163-172.
 13. Samsa G, Matchar DB, Dolor RJ, et al. A new instrument for measuring anticoagulation-related quality of life: Development and preliminary validation. *Health Qual Life Out*. 2004;2(1):22.
 14. Wild D, Grove A, Martin M, et al. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: Report of the ISPOR task force for translation and cultural adaptation. *Value health*. 2005;8(2):94-104.
 15. Pelegrino FM, Dantas RA, Corbi IS, da Silva Carvalho, Ariana R, Schmidt A. Cross-cultural adaptation and psychometric properties of the Brazilian-Portuguese version of the duke anticoagulation satisfaction scale. *J Clin Nurs*. 2012;21(17-18):2509-2517.
 16. Sawicki PT. A structured teaching and self-management program for patients receiving oral anticoagulation: A randomized controlled trial. *JAMA*. 1999;281(2):145-150.
 17. Freestone B, Rajaratnam R, Hussain N, Lip GYH. Admissions with atrial fibrillation in a multiracial population in kuala lumpur, malaysia. *Int J Cardiol*. 2003;91(2):233-238.
 18. Lim CW, Kasim S, Ismail JR, et al. Prevalence of atrial fibrillation in the malaysian communities. *Heart Asia*. 2016;8(2):62-66.
 19. Daniel WW, Cross CL. Biostatistics: Basic concepts and methodology for the health sciences. John Wiley & Sons New York; 2010.
 20. Group TE. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199-208.
 21. Cheung K, Oemar M, Oppe M, Rabin R. EQ-5D user guide: Basic information on how to use EQ-5D. Rotterdam: EuroQol Group. 2009.
 22. Szende A, Oppe M, Devlin N. EQ-5D value sets: Inventory, comparative review and user guide. Vol 2. Springer Science & Business Media; 2007.
 23. EuroQol Group. EuroQol - a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199-208.
 24. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: Literature review and proposed guidelines. *J Clin Epidemiol*. 1993;46(12):1417-1432.
 25. Rabin R, Oemar M, Oppe M, Janssen B, Herdman M. EQ-5D-3L user guide: Basic information on how to use the EQ-5D-3L instrument. Rotterdam: EuroQol Group. 2011;22.
 26. Dolan P, Gudex C, Kind P, Williams A. A social tariff for EuroQol: results from a UK general population survey. 1995.
 27. Matalqah IM, Radaideh KM, Yusoff ZM, Awaisu A. Health-related quality of life using EQ-5D among breast cancer survivors in comparison with age-matched peers from the general population in the state of penang, malaysia. *J. Public Health*. 2011;19(5):475-480.
 28. Almeida GdQ, Noblat, Lúcia de A C B., Passos LCS, do Nascimento HF. Quality of life analysis of patients in chronic use of oral anticoagulant: An observational study. *Health Qual Life Out*. 2011;9(1):91-91.
 29. Gadisseur A, Kaptein A, Breukink-Engbers W, Van Der Meer F, R Rosendaal F. Patient self-management of oral anticoagulant care vs. management by specialized anticoagulation clinics: Positive effects on quality of life. *J. Thromb Haemost*. 2004;2(4):584-591.
 30. Sprangers MA, de Regt EB, Andries F, et al. Which chronic conditions are associated with better or poorer quality of life? *J Clin Epidemiol*. 2000;53(9):895-907.
 31. Fumagalli S, Cardini F, Roberts AT, Boni S, Gabbai D, Calvani S, et al. Psychological effects of treatment with new oral anticoagulants in elderly patients with atrial fibrillation: a preliminary report. *Aging Clin Exp Res*. 2015;27:99-102.
 32. Alegret JM, Viñolas X, Arias MA, Martínez-Rubio A, Rebollo P, Ràfols C, et al. New oral anticoagulants vs. vitamin K antagonists: benefits for health-related quality of life in patients with atrial fibrillation. *Int J Med Sci*. 2014;11:680-4.

