

Factors associated with low health-related quality of life among younger and older Thai patients with non-valvular atrial fibrillation

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Abstract

Purpose The aim of this study was to investigate the factors associated with low health-related quality of life (HRQoL) compared between younger and older Thai patients with non-valvular atrial fibrillation (NVAF).

Methods This is a cross-sectional analysis of baseline data from a prospective NVAF registry from 24 hospitals located across Thailand. Patient demographic, clinical, lifestyle, and medication data were collected at baseline. EuroQOL/EQ-5D-3L was used to assess HRQoL. Health utility was calculated for the entire study population, and low HRQoL was defined as the lowest quartile. Multivariate logistic regression was used to identify factors that significantly predict low HRQoL among younger and older (≥ 65 years) patients with NVAF.

Results Among the 3218 participants that were enrolled, 61.0% were aged older than 65 years. Mean HRQoL was lower in older than in younger patients (0.72 ± 0.26 vs. 0.84 ± 0.20 ; p < 0.001). Factors associated with low HRQoL among younger NVAF patients were the treatment-related factors bleeding history (p = 0.006) and taking warfarin (p = 0.001). Among older patients, the NVAF-related complications ischemic stroke or TIA, heart failure (HF), and dementia (all p < 0.001) were all significantly associated with low HRQoL. Dementia is the factor that most adversely influences low HRQoL among older NVAF. Interestingly, symptomatic NVAF was found to be a protective factor for low HRQoL (p < 0.001).

Conclusions Bleeding history and taking warfarin among younger patients, and ischemic stroke/TIA, HF, and dementia among older patients are significant predictors of low HRQoL. These factors should be taken into consideration when selecting treatment options for patients with NVAF.

Keywords Atrial fibrillation · Health-related quality of life · Thai patients

COOL AF Investigators members of the group are listed in Acknowledgements.

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Introduction

Non-valvular atrial fibrillation (NVAF) is the most common cardiac arrhythmia, and it is associated with adverse consequences that lead to increased morbidity, mortality, and healthcare expenditure [1]. Associations between NVAF and several conditions that exert a high burden on patients and/ or society have been well documented. Apart from stroke, patients with NVAF are more likely to have higher rates of heart failure, hospitalization, cognitive impairment, and dementia [2]. Mainstay of treatment for patients with NVAF remains to anticoagulation (OAC) with vitamin K antagonists (VKAs) or non-vitamin K antagonist oral anticoagulants (NOACs) which could reduce stroke and mortality in AF patients. Other interventions have not demonstrated a long reduction in morbidity and mortality. Improvement in health-related quality of life (HRQoL) remains a primary aim in the management of patients with NVAF, as addressed in recent NVAF guidelines [2, 3].

HROoL in patients with NVAF has been widely studied, and the results have consistently shown HRQoL to be reduced in this group compared to healthy controls and patients with coronary heart disease [2, 4]. However, the factors that were reported to be significantly associated with reduced HRQoL varied among studies [5-7]. It was reported that Asian NVAF patients have a different risk profile from Caucasian studies [8]. Heart failure and hypertension are more common in non-Asians, whereas diabetes and history of stroke are more common in Asians [8]. Moreover, Asian NVAF patients pose a higher risk of developing warfarin-related bleeding complications than non-Asian NVAF patients [8, 9]. These findings may, therefore, suggest that Asian NVAF patients may have different disease burden and HRQoL than NVAF patients from Western countries. Data specific to the HRQoL of NVAF patients from low to middle-income countries (LMIC) are scarce. Studies on HRQoL of NVAF in patients from Asian countries were limited with small sample sizes [10, 11]. Investigators from Japan studied NVAF population and used the Atrial Fibrillation Effect on Quality of Life (AFEQT) Questionnaire which measured four aspects; symptom, daily activity, treatment concern, and satisfaction [12]. They aimed to study the effect on quality of life between rate control and rhythm control strategies. Data are lacking for the factors determining quality of life in NVAF especially among younger and older patients as defined by those < 65 and ≥ 65 years [7], respectively.

Thailand is an LMIC country in Asia that has a rapidly growing older population, and the prevalence of AF and AF-related complications is, therefore, expected to increase commensurately. Population-specific data relating to the factors that affect HRQoL in this patient population would help to improve insight on factors that might potentially be modifiable and lead to better treatment strategies and patients' satisfactory. Accordingly, the aim of this study was to investigate the factors associated with low HRQoL compared between younger and older Thai patients with NVAF.

Methods

Study population

This is a cross-sectional analysis of baseline data from a prospective cohort. Subjects with NVAF were enrolled from 24 hospitals located across Thailand. Details relating to patient recruitment and data collection were previously published [13]. Briefly, patients aged \geq 18 years with NVAF diagnosed by standard ECG or ambulatory monitoring were eligible for inclusion. Patients having one or more of the following were excluded: (1) ischemic stroke within 3 months; (2) thrombocytopenia (<100,000/mm³), myeloproliferative disorders, hyperviscosity syndrome, or antiphospholipid syndrome; (3) prosthetic valve or valve repair; (4) rheumatic valve disease or significant valve disease; (5) atrial fibrillation from transient reversible cause; (6) ongoing participation in other clinical trial; (7) life expectancy less than 3 years; (8) pregnancy; (9) inability to attend scheduled follow-up appointments; and/or (10) current hospitalization or hospitalization within 1 month. The primary objective of the main study was to study the antithrombotic pattern and optimal INR levels in patients who were on warfarin. Analysis of HRQoL was the secondary objective of the main study.

After obtaining written informed consent, patients were interviewed and underwent physical examination for baseline assessment. Subsequent follow-up visits were scheduled at 6, 12, 18, 24, 30, and 36 months. Data relating to cardiovascular events, blood pressure, heart rate, and medications were collected at each follow-up visit. Protocols were established and followed by the data management team and the statisticians to ensure the integrity and quality of the data before final analysis. Patient enrollment began in May 2014 and ended in October 2017. The patient risk profiles and patterns of antithrombotic use were also previously reported [13]. The protocol for this study was approved by the institutional review boards of the Thailand Ministry of Public Health and all participating hospitals. All patients provided written informed consent prior to participation.

Data collection

The following data were collected from medical record and interview at baseline: (1) demographic information; (2) history of stroke and bleeding; (3) type and duration of atrial fibrillation; (4) component parameters of CHADS₂ score, CHA₂DS₂-VASc score for stroke risk, and HAS-BLED score for risk of bleeding; (5) history of medical and cardiovascular diseases; (6) antithrombotic medications; (7) reason for not using warfarin in those not taking warfarin; (8) concomitant medications; (9) twelve-lead ECG; and, (10) current INR. Reporting of any of the following symptoms; chest pain, discomfort, dizziness, fainting, irregular pulse, palpitations, tachycardia, shortness of breath, sweating, and tiredness were defined as symptomatic AF.

Regarding HRQoL, despite the fact that several different QoL instruments have been used in published NVAF studies [5], no recommendation has been made regarding the use of one questionnaire over another [14]. EuroQOL/ EQ-5D, which has been used in NVAF population [5] and validated in Thai population [15], was, therefore, selected to measure patient HRQoL in the present study. EuroQOL/ EQ-5D-3L was used to assess HRQoL. The EQ-5D-3L descriptive system comprises five dimensions of health, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension had three levels: no problem, some problems and extreme problems. It can be used as a health profile or converted into an index score representing a utility value for current health [16]. The level of problem reported on each of the EQ-5D dimensions determines a unique health state. Health states are converted into a weighted health state index by applying scores from the EQ-5D preference weights elicited from general population samples. Thai reference weights were used to convert EQ-5D health states into EQ-5D index scores [15] or health utility. These index scores lie on a scale from 0 to 1 for which full health has a value of 1 and dead a value of 0. The present study is a cross-sectional analysis utilizing the HRQoL recorded at the first visit at enrollment into the cohort.

Statistical analysis

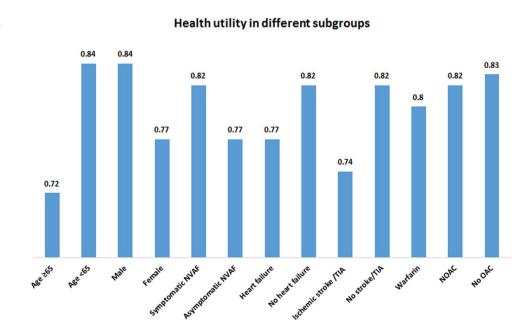
All data that we analyzed in this paper were from baseline data. Demographic and clinical data were interpreted using descriptive statistics. Continuous data are presented as mean±standard deviation, and categorical data are shown as number and percentage. The lowest quartile of health utility was used to define low HRQoL for which was at utility index of 0.645 in this study. This strategy of choosing the cutoff based on quartile has been used in a previous study [17]. All analysis was done using 65 years to define younger and older AF patients. Univariate and multivariate logistic regression models were used to identify factors significantly associated with low HRQoL in both age groups. All statistical analyses were performed using SPSS Statistics version 20 (SPSS,

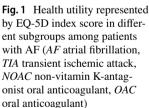
Inc., Chicago, IL, USA). A p value < 0.05 was regarded as being statistically significant for all tests.

Results

Among the 3218 subjects enrolled in this study, the mean age was 67.3 ± 11.3 years, and 61.0% were aged older than 65 years. Health utility in different subgroups is shown in Fig. 1. The mean HRQoL was significantly lower in older NVAF than in younger NVAF (0.72 ± 0.26 vs. 0.84 ± 0.20 , respectively; p < 0.001). Most common NVAF-related symptom was palpitation (57.5%) followed by shortness of breath (27.4%). People with symptomatic NVAF in both age group had a higher HRQoL than those in the asymptomatic group. Heart failure and stroke/transient ischemic attack (TIA) were found to significantly adversely influence quality of life in both age groups. However, taking oral anticoagulant (OAC) associated with lower HRQoL only in younger age group, with significant difference observed between patients taking warfarin and those taking no OAC.

The older age group had a higher proportion of females and cardiovascular comorbid diseases (including stroke), but a lower proportion of participants with symptomatic NVAF. Not surprisingly, the older group has higher thrombotic risk, higher warfarin use, and higher risk of bleeding. In both age groups, participants with low HRQoL were more likely to experience NVAF-related complications, such as ischemic stroke or TIA, heart failure, and dementia. The low HRQoL groups were more likely to have a higher rate of comorbid diseases and a higher CHA₂DS₂-VASc score. Bleeding tendency and taking warfarin were found to be significantly





higher only among younger patients with low HRQoL, as shown in Table 1.

Univariate and multivariate analyses were performed to investigate for factors associated with low HRQoL in the younger (Table 2) and older age (Table 3) groups. In the younger age group, some NVAF-related complications were significantly associated with low HRQoL in univariate, but not in multivariate analysis. In contrast, the treatment-related factors bleeding history and taking warfarin were found to be significantly associated with low HRQoL (odds ratio [OR] 2.07, 95% confidence interval [CI] 1.23–3.49 and OR 1.88, 95% CI 1.29–2.75, respectively). Among older aged patients, the NVAF-related complications ischemic stroke or TIA, heart failure, and dementia (all p < 0.001) were all significantly associated with low HRQoL in multivariate analysis. Dementia was shown to be the factor that most significantly influences low HRQoL (OR 6.41, 95% CI 2.29–17.94). Interestingly, symptomatic NVAF was found to be a protective factor for low HRQoL among older patients (OR 0.64, 95% CI 0.51–0.80). Warfarin was associated with low HRQoL in younger age group but not in older age group whereas NOAC had a trend toward a higher HRQoL in both younger and older patients.

Discussion

This is the first nationwide study of HRQoL among patients with NVAF in Thailand, which is an LMIC that is located in Southeast Asia. Most of the published studies in HRQoL among NVAF from high income and non-Asian countries [4, 5, 7] reported that patients with NVAF experienced reduced

Table 1 Baseline characteristics of the study population according to level of HRQoL compared between younger (<65) and older (\geq 65) aged patients

Characteristics	Age < 65			Age≥65		
	$\overline{\text{All}(n=1255)}$	Low QoL ^a $(n = 159)$ n (%)	High QoL $(n = 1096)$ n (%)	$\overline{\text{All}(n=1963)}$	Low QoL ^a ($n = 614$) n (%)	High QoL $(n = 1349)$ n (%)
Female gender	435 (34.7%)	65 (40.9%)	370 (33.8%)	909 (46.3%)	332 (54.1%)	577 (42.8%)
Symptomatic NVAF	1009 (80.4%)	118 (74.2%)	891 (81.3%)	1485 (75.6%)	429 (69.9%)	1056 (78.3%)
Type of NVAF						
Paroxysmal	456 (36.3%)	63 (39.6%)	393 (35.9%)	619 (31.5%)	188 (30.6%)	431 (31.9%)
Persistent	247 (19.7%)	34 (21.4%)	213 (19.4%)	376 (19.2%)	137 (22.3%)	239 (17.7%)
Permanent	552 (44.0%)	62 (39.0%)	490 (44.7%)	968 (49.3%)	289 (47.1%)	679 (50.3%)
Heart failure	358 (28.5%)	57 (35.8%)	301 (27.5%)	517 (26.3%)	216 (35.2%)	301 (22.3%)
CAD	152 (12.1%)	32 (20.1%)	120 (10.9%)	353 (18.0%)	126 (20.5%)	227 (16.8%)
Ischemic stroke or TIA	177 (14.1%)	35 (22.0%)	142 (13.0%)	378 (19.3%)	156 (25.4%)	222 (16.5%)
Hypertension	703 (56.0%)	102 (64.2%)	601 (54.8%)	1480 (75.4%)	487 (79.3%)	993 (73.6%)
Diabetes	290 (23.1%)	45 (28.3%)	245 (22.4%)	487 (24.8%)	170 (27.7%)	317 (23.5%)
Smoker	286 (22.8%)	41 (25.8%)	245 (22.4%)	364 (18.5%)	123 (20.0%)	241 (17.9%)
Dementia	4 (0.3%)	2 (1.3%)	2 (0.2%)	22 (1.1%)	17 (2.8%)	5 (0.4%)
Bleeding history	90 (7.2%)	22 (13.8%)	68 (6.2%)	218 (11.1%)	74 (12.1%)	144 (10.7%)
CHA2DS2-VASc sco	re					
0	207 (16.5%)	16 (10.1%)	191(17.4%)	_	-	_
1	366 (29.2%)	34 (21.4%)	332 (30.3%)	53 (2.7%)	9 (1.5%)	44 (3.3%)
2 or more	682 (54.3%)	109 (68.6%)	573 (52.3%)	1910 (97.3%)	608 (98.5%)	1305(96.7%)
HASBLED score						
0	452 (36.0%)	44 (27.7%)	408 (37.2%)	6 (0.3%)	1 (0.2%)	5 (0.4%)
1–2	756 (60.2%)	101 (63.5%)	655 (59.8%)	1501 (76.5%)	439 (71.5%)	1062 (78.7%)
≥3	47 (3.7%)	14 (8.8%)	33 (3.0%)	456 (23.2%)	174 (28.3%)	282 (20.9%)
Antiplatelet drugs	352 (28.0%)	46 (28.9%)	306 (27.9%)	502 (25.6%)	165 (26.9%)	337 (25.0%)
Anticoagulant	824 (65.7%)	124 (78.0%)	700 (63.9%)	1598 (81.4%)	496 (80.8%)	1102 (81.7%)
Warfarin	743 (59.2%)	117(73.6%)	626 (57.1%)	1461 (74.4%)	460 (74.9%)	1001 (74.2%)
NOAC	82 (6.5%)	7(4.4%)	75 (6.8%)	138 (7.0%)	36 (5.9%)	102 (7.6%)

^aUtility <0.645 was classified as low HRQoL

QoL quality of life, NVAF non-valvular atrial fibrillation, CAD coronary artery disease, TIA transient ischemic attack

Table 2 Factors associated withlow HRQoL in the younger

(age < 65) age group

Age < 65	Univariate	Multivariate		
	Unadjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Female gender	1.36 (0.97–1.91)	0.079		
Symptoms of NVAF	0.62 (0.45-0.98)	0.037		
Type of atrial fibrillation				
Paroxysmal	Ref.			
Persistent	1.00 (0.64–1.56)	0.985		
Permanent	0.79 (0.54–1.15)	0.216		
Heart failure	1.48 (1.04–2.10)	0.029		
Symptomatic CAD	2.05 (1.33-3.16)	0.001	1.80 (1.16-2.79)	0.009
Ischemic stroke or TIA	1.90 (1.25-2.87)	0.002		
Systemic embolization	3.48 (0.63–19.14)	0.152		
Hypertension	1.47 (1.04–2.08)	0.028		
Diabetes	1.37 (0.94–1.99)	0.097		
Smoker	1.21 (0.82–1.77)	0.336		
Dementia	6.97 (0.98-49.82)	0.053		
Bleeding history	2.43 (1.45-4.05)	0.001	2.07 (1.23-3.49)	0.006
CHA ₂ DS ₂ -VASc score				
0	Ref.			
1	1.22 (0.66–2.27)	0.526		
2 or more	2.27 (1.31-3.94)	0.003		
HASBLED score				
0	Ref			
1–2	1.43 (0.98–2.08)	0.062		
≥3	3.93 (1.96-7.91)	< 0.001		
Antiplatelet drugs	1.05 (0.73–1.52)	0.791		
Anticoagulant	2.00 (1.35-2.98)	0.001		
Warfarin	2.09 (1.44-3.04)	< 0.001	1.88 (1.29–2.75)	0.001
NOAC	0.63 (0.28–1.39)	0.249		
		<i></i>		

HRQoL health-related quality of life, OR odds ratio, CI confidence interval, NVAF non-valvular atrial fibrillation, CAD coronary artery disease, TIA transient ischemic attack

A p value < 0.05 indicates statistical significance (italics)

HRQoL and that the reduction was more pronounced among older persons [7]. Similarly, the findings of the current study revealed that older patients with NVAF had lower HRQoL than patients in the younger age group.

In the present study, patient factors associated with lower HRQoL showed some similarity and differences among the younger and older groups. In the older age group, NVAFrelated complications, such as stroke or TIA, heart failure, and dementia, were all significantly associated with low HRQoL, whereas treatment-related issues, such as history of bleeding and taking warfarin, were predominate factors in the younger age group. Most of the published HRQoL literature in NVAF do not directly compare patient factors between younger and older age groups, and few studies explored patient factors in detail [6, 7, 18; 7, 18]. In the ORBIT AF study [6], which had a mean age comparable to that of the older age group in the present study, heart failure was associated with low HRQoL, but not stroke or dementia. The RECORD AF study did not find any associations between these AF-related complications and HRQoL [18].

The factors associated with reduced HRQoL among the younger age group in the present study were unexpected. Specifically, we found treatment with warfarin to be significantly related to reduced HRQoL, while no significant associations with NVAF-related complications were observed. Subgroup analysis suggested that taking NOAC may not influence reduced HRQoL as much as warfarin does. Several previous studies [7, 14, 18, 19; 14, 18, 19] did not investigate HRQoL and treatment-related factors, such as bleeding history or OAC use, except one study [20]. That nationwide study from Turkey [20] reported that octogenarian AF patients experienced poorer quality of life compared to younger group when taking warfarin. This finding would require further qualitative study to explore the relationship between HRQoL and the effect of age on warfarin use. It

Table 3 Factors associated with low HROoL in the older $(age \ge 65)$ age group

$Age \ge 65$	Univariate		Multivariate		
	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value	
Female gender	1.57 (1.30–1.91)	< 0.001	1.87 (1.50–2.34)	< 0.001	
Symptoms of NVAF	0.64 (0.52-0.80)	< 0.001	0.64 (0.51-0.80)	< 0.001	
Type of atrial fibrillation					
Paroxysmal	Ref.	-			
Persistent*	1.31 (1.00–1.72)	0.048			
Permanent	0.98 (0.78-1.22)	0.827			
Heart failure	1.89 (1.53–2.33)	< 0.001	2.02 (1.62-2.51)	< 0.001	
Symptomatic CAD	1.28 (1.00-1.63)	0.049			
Ischemic stroke or TIA	1.73 (1.37–2.18)	< 0.001	1.68 (1.32-2.14)	< 0.001	
Systemic embolization	3.82 (1.50-9.76)	0.005			
Hypertension	1.38 (1.09–1.73)	0.007	1.32 (1.04–1.67)	0.021	
Diabetes	1.25 (1.00-1.55)	0.047			
Smoker	1.15 (0.90–1.47)	0.252	1.47 (1.12–1.95)	0.006	
Dementia	7.65 (2.81–20.84)	< 0.001	6.33 (2.25-17.80)	< 0.001	
Bleeding history	1.15 (0.85–1.55)	0.368			
CHA ₂ DS ₂ -VASc score					
0	-	_			
1	Ref.	_			
2 or more	2.27 (1.10-4.67)	0.027			
HASBLED score					
0	Ref.	_			
1–2	2.07 (0.24–17.74)	0.508			
≥3	3.09 (0.36-26.63)	0.306			
Antiplatelet drugs	1.10 (0.89–1.37)	0.373			
Anticoagulant	0.94 (0.74–1.20)	0.632			
Warfarin	1.04 (0.83–1.29)	0.736			
NOAC	0.76 (0.51-1.13)	0.174			

HRQoL health-related quality of life, OR odds ratio, CI confidence interval, NVAF non-valvular atrial fibrillation, CAD coronary artery disease, TIA transient ischemic attack

A *p* value < 0.05 indicates statistical significance (italics)

could be hypothesized that the quality of the medical services provided to different populations or differences in culture-related perceptions could influence reported differences among studies.

Further analyses have been conducted to explore the differences in younger group who taking warfarin and NOAC. We identified that younger group who took NOAC has significant lower proportion of heart failure and symptomatic CAD and nonsignificant lower rate of ischemic stroke and bleeding history. Those all might contribute to higher QOL in patients taking NOAC compared to taking warfarin. With the nature of data being cross-sectional, it prevents us to explore the causal relationship whether the finding of having lower complications is associated with taking NOAC or it occurs by the play of chance. Besides, NOACs are considered a safer drug compared to warfarin. This may affect the overall well-being and less anxiety in those taking NOAC as compared to warfarin.

The results of our study indicated that NVAF-related complications were not associated with QOL in younger patients. The reasons for this finding are unclear. It might be partly explained by the lower complication rate in younger age group as shown in Table 1 that younger patients had a lower rate of ischemic stroke/TIA compared to older patients. Moreover, brain of younger patients may have a better capacity foe recovery after stroke when compared to older patients.

The rate of anticoagulant use in our study was 65.7% in younger patients and 81.4% in older patients. Most physicians use anticoagulants according to the current practice guideline recommendation [2]. Since aging is an important factor in the CHA₂DS₂-VASc score, anticoagulants were used more in older adults. Among patients who received anticoagulants, NOACs were used in 9.9% in younger patients and 8.6% in older patients which was not statistical significance. Rate of NOAC prescription in our registry

had a trend toward an increasingly used among patients who were enrolled in the later phase compared to the initial phase [13]. There may be more chance to have older patients who were already used warfarin and physicians preferred to continue warfarin compared to younger patients.

Furthermore, patients with symptomatic AF in both age groups were less likely to have low HRQoL. Previous studies, including one systematic review [7, 21, 22], showed that symptomatic or uncontrolled AF associated with lower HROoL. This difference in findings compared to our study could be due the use of different tools to measure HRQoL. The fact that we found the same finding in both age groups in our study may suggest that culture may exert some influence that promotes greater tolerance of NVAF symptoms among Thai population. Asymptomatic AF are more common in elderly as shown in Table 1. We performed additional analysis and found that asymptomatic AF was significantly associated with a history of ischemic stroke/TIA in younger and older age group but it was significantly associated with dementia only in older age group. This finding may explain why asymptomatic AF is a predictor for low HRQoL in older age group.

There are several limitations in the present study. Firstly, the inherited limitation of cross-sectional analysis is that the causality of the associations identified could not be ascertained. Low HRQoL in for patients with NVAF in this study could be attributed by some known contributes such as comorbid diseases, gender or age. Some concurrent illnesses such as congestive heart failure, stroke and dementia also are multifactorial in nature, the reduced HRQoL in these groups might not be related to NVAF. Secondly, patients enrolled in the study are not newly diagnosed AF, symptoms related to AF might be under reported and misclassified resulting in the contrary finding to other studies that symptomatic AF was not related to reduced HRQoL. Lastly, there is no single universal accepted standard method to measure HRQoL in AF and to define 'low or reduced HRQoL' [5, 14]. Using different quartiles to compare HRQoL has been one among several methods that has been used including ORBIT-AF study [17]. The strength of this study is that it is a large nation-wide study that represent real-world practice in an Asian population with difference profile to previous western studies.

Conclusion

Multivariate analysis revealed the treatment-related factors bleeding history and taking warfarin among younger patients, and the NVAF-related complications ischemic stroke/TIA, heart failure, and dementia among older patients to be significant predictors of low HRQoL. These factors should be taken into consideration when selecting treatment options for patients with NVAF. For younger patients, bleeding history appears to be the strongest factor for reduce HROoL. Anticoagulant is usually indicated to reduce risk of ischemic stroke in patients with NVAF and additional risk factor. Choosing anticoagulant with lowest chance of bleeding complications might lead to better HROoL for younger AF patients. The fact that the findings of this study differed in some aspects from other investigations of HRQoL in NVAF strongly suggests the need for population-specific study and data.

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Compliance with ethical standards

Conflict of interest All authors declare no personal or professional conflicts of interest.

Ethical approval The protocol for this study was approved by the institutional review boards of the Thailand Ministry of Public Health and all participating hospitals. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent All patients provided written informed consent prior to participation.

References

- Zimetbaum, P. (2017). Atrial fibrillation. Annals of Internal Medicine, 166(5), Itc33–Itc48.
- Kirchhof, P., Benussi, S., Kotecha, D., Ahlsson, A., Atar, D., Casadei, B., et al. (2016). 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *European Heart Journal*, *37*(38), 2893–2962.
- Calkins, H., Kuck, K. H., Cappato, R., Brugada, J., Camm, A. J., Chen, S. A., et al. (2012). 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Journal of Interventional Car-diac Electrophysiology*, *33*(2), 171–257.
- Thrall, G., Lane, D., Carroll, D., & Lip, G. Y. (2006). Quality of life in patients with atrial fibrillation: A systematic review. *The American Journal of Medicine*, 119(5), 448.e441–448.e419.
- Reynolds, M. R., Ellis, E., & Zimetbaum, P. (2008). Quality of life in atrial fibrillation: Measurement tools and impact of interventions. *Journal of Cardiovascular Electrophysiology*, 19(7), 762–768.
- Randolph, T. C., Simon, D. N., Thomas, L., Allen, L. A., Fonarow, G. C., Gersh, B. J., et al. (2016). Patient factors associated with quality of life in atrial fibrillation. *American Heart Journal*, 182, 135–143.
- Zhang, L., Gallagher, R., & Neubeck, L. (2015). Health-related quality of life in atrial fibrillation patients over 65 years: A review. *European Journal of Preventive Cardiology*, 22(8), 987–1002.
- Chiang, C. E., Wang, K. L., & Lip, G. Y. (2014). Stroke prevention in atrial fibrillation: An Asian perspective. *Thrombosis and Haemostasis*, 111(5), 789–797.
- Tse, H. F., Wang, Y. J., Ai-Abdullah, M.A., Pizarro-Borromeo, A. B., Chiang, C. E., Krittayaphong, R., et al. (2013). Stroke prevention in atrial fibrillation—An Asian stroke perspective. *Heart Rhythm*, 10(7), 1082–1088.
- Hsu, N. W., Tsao, H. M., Chen, H. C., Lo, S. S., Chen, S. A., & Chou, P. (2016). Different impacts of atrial fibrillation and cardiac premature contractions on the health-related quality of life in elderly people: The Yilan Study. *The Tohoku Journal of Experimental Medicine*, 238(1), 75–83.
- Wang, K. L., Wu, C. H., Huang, C. C., Wu, T. C., Naditch-Brule, L., Steg, P. G., et al. (2014). Complexity of atrial fibrillation patients and management in Chinese ethnicity in routine daily practice: Insights from the RealiseAF Taiwanese cohort. *Journal* of Cardiology, 64(3), 211–217.
- 12. Inohara, T., Kimura, T., Ueda, I., Ikemura, N., Tanimoto, K., Nishiyama, N., et al. (2017). Effect of compliance to updated

AHA/acc performance and quality measures among patients with atrial fibrillation on outcome (from Japanese Multicenter Registry). *The American Journal of Cardiology, 120*(4), 595–600.

- Krittayaphong, R., Winijkul, A., Methavigul, K., Wongtheptien, W., Wongvipaporn, C., Wisaratapong, T., et al. (2018). Risk profiles and pattern of antithrombotic use in patients with nonvalvular atrial fibrillation in Thailand: A multicenter study. *BMC Cardiovascular Disorders*, 18(1), 174.
- Kotecha, D., Ahmed, A., Calvert, M., Lencioni, M., Terwee, C. B., & Lane, D. A. (2016). Patient-reported outcomes for quality of life assessment in atrial fibrillation: A systematic review of measurement properties. *PLoS ONE*, *11*(11), e0165790.
- Tongsiri, S., & Cairns, J. (2011). Estimating population-based values for EQ-5D health states in Thailand. *Value Health*, 14(8), 1142–1145.
- Rabin, R., & de Charro, F. (2001). EQ-5D: A measure of health status from the EuroQol Group. *Annals Medicine*, 33(5), 337–343.
- Piccini, J. P., Simon, D. N., Steinberg, B. A., Thomas, L., Allen, L. A., Fonarow, G. C., et al. (2016). Differences in clinical and functional outcomes of atrial fibrillation in women and men: Two-year results from the ORBIT-AF Registry. *JAMA Cardiology*, 1(3), 282–291.
- Ha, A. C., Breithardt, G., Camm, A. J., Crijns, H. J., Fitzmaurice, G. M., Kowey, P. R., et al. (2014). Health-related quality of life in patients with atrial fibrillation treated with rhythm control versus rate control: insights from a prospective international registry (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation: RECORD-AF). *Circulation: Cardiovascular Quality and Outcomes*, 7(6), 896–904.
- Freeman, J. V., Simon, D. N., Go, A. S., Spertus, J., Fonarow, G. C., Gersh, B. J., et al. (2015). Association between atrial fibrillation symptoms, quality of life, and patient outcomes: Results from the outcomes registry for better informed treatment of atrial fibrillation (ORBIT-AF). *Circulation: Cardiovascular Quality and Outcomes*, 8(4), 393–402.
- Biteker, M., Basaran, O., Dogan, V., Altun, I., Ozpamuk Karadeniz, F., Tekkesin, A. I., et al. (2017). Real-world clinical characteristics and treatment patterns of individuals aged 80 and older with nonvalvular atrial fibrillation: Results from the ReAllife Multicenter Survey Evaluating Stroke Study. *Journal of the American Geriatrics Society*, 65(8), 1684–1690.
- Tan, H. C., Koh, K. W. L., Wu, V. X., Lim, T. W., & Wang, W. (2018). Health-related quality of life, psychological distress, and symptom burden in an Asian population of outpatients with atrial fibrillation. *Heart and Lung*, 47(4), 322–328.
- Steg, P. G., Alam, S., Chiang, C.-E., Gamra, H., Goethals, M., Inoue, H., et al. (2012). Symptoms, functional status and quality of life in patients with controlled and uncontrolled atrial fibrillation: Data from the RealiseAF cross-sectional international registry. *Heart*, 98(3), 195–201.

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