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Atrial fibrillation, oral anticoagulants and health related quality of life

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SOUHRN

Úvod: Fibrilace síní (FS) je porucha srdečního rytmu, která může ovlivnit kvalitu života v souvislosti se zdravím. Na kvalitu života v souvislosti se zdravím může působit i užívání perorálních antikoagulancií, jak z hlediska léčebného přínosu nebo komplikací, tak z hlediska jejich užívání jako takových, kdy ovlivňují způsob života daného pacienta, tedy nutnost pravidelných laboratorních vyšetření i různá omezení ve stravování.
Cíl: Určit a zjistit, zda existuje statisticky významný rozdíl při srovnání kvality života v souvislosti se zdravím osob užívajících antagonisty vitaminu K, warfarin a nová perorální antikoagulancia (novel oral anticoagulant, NOAC) rivaroxaban a dabigatran ve srovnání s pacienty neužívajícími žádné perorální antikoagulancium.
Materiály a metody: Výzkumný projekt s použitím průřezové analýzy byl proveden na Klinice kardiologie Fakultní nemocnice Pauls Stradins v litevské Rize v období od října 2016 do června 2017. Účast v tomto výzkumném projektu byla nabídnuta osobám s vysokým rizikem nevalvulární fibrilace síní. V případě souhlasu s účastí byl s pacientem proveden ústní pohovor s dotazy na osobní anamnézu, demografické údaje, výsledky laboratorních testů i výsledky echokardiografického vyšetření, výsledky modifikovaného dotazníku SF-36 a užívaný typ NOAC. Údaje byly ověřeny na základě informací osobní anamnézy účastníka výzkumu. Ke statistické analýze byl použit software SPSS.
Výsledky: Do výzkumu bylo zařazeno celkem 218 pacientů (56,9 % žen a 43,1 % mužů průměrného věku 70,4 roku s průměrnou hodnotu skóre CHA_2D_2-VASc 4,4. Warfarin užívalo 37,6 % pacientů, NOAC 33,0 %, žádná perorální antikoagulancia neužívalo 29,4 % účastníků výzkumu. Statisticky významný rozdíl byl zjištěn mezi průměrnými hodnotami dimenzí fyzického fungování při srovnání osob užívajících warfarin (průměr 95,85) nebo NOAC (průměr 124,57); $p = 0,012$. Statisticky významný rozdíl byl rovněž prokázán v dimenzi sociálního fungování při srovnání účastníků výzkumu užívajících warfarin (průměr 96,16) nebo NOAC (průměr 119,08); $p = 0,026$. Negativní korelace mezi věkem a fyzickým fungováním dosáhla nízké hodnoty (r = 0,23). Nebyla zjištěna žádná korelace mezi dobou od stanovení diagnózy fibrilace síní a výsledky.
Závěr: Užívání NOAC koreluje s nejvyššími hodnotami skóre kvality života v souvislosti se zdravím; byl nalezen statisticky významný rozdíl oproti osobám užívajícím warfarin v dimenzi fyzického fungování (warfarin 95,85; NOAC 124,57; $p = 0,012$) i sociálního fungování (warfarin 95,16; NOAC 119,08; $p = 0,026$). Negativní korelace se skóre fyzického fungování dosáhla nízkých hodnot.

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ABSTRACT

Introduction: Atrial fibrillation (AFib) is a disease that can influence the health related quality of life. Also oral anticoagulants can influence it both because of its therapeutic benefits or complications as well as how the anticoagulant usage influence the person's life style by regular laboratory test necessity or diet restrictions.
Aim: Determine and analyze whether there is a statistically significant difference comparing health related quality of life between K vitamin antagonist, warfarin, users, novel anticoagulant (NOAC), rivaroxaban, dabigatran, users and patients, who do not use any kind of oral anticoagulant.
Materials and methods: A cross-sectional analytic research was made in Pauls Stradins Clinical university hospital, Center of Cardiology in Riga, Latvia during the time period from October 2016 till June 2017. Persons with high-risk non-valvular atrial fibrillation were offered to participate in this research. If the person agreed, an oral interview with questions about disease anamnesis, demographic data, laboratory test results, echocardiography results, modified SF-36 survey, used oral anticoagulant type was held. Data were precised with the help of the case anamnesis information. For statistical data analysis were used SPSS Statistics database.
Results: Altogether 218 patients were enrolled, of which 56.9% were female and 43.1% – male, mean age – 70.4 years, mean CHA_2D_2-VASc score – 4.4. Warfarin used 37.6%, 33.0% – novel oral anticoagulants, but 29.4% did not use any kind of oral anticoagulant. A statistically significant difference was discovered between the mean ranks in physical functioning sections comparing warfarin (mean rank 95.85) with NOACs (mean rank 124.57); $p = 0.012$. Also a statistically significant difference was in social functioning comparing warfarin (mean rank 96.16) with NOACs (mean rank 119.08); $p = 0.026$. Age had low negative correlation ($r = –0.23$) with physical functioning. Duration of atrial fibrillation diagnosis did not have correlations with the results.
Conclusion: NOAC usage correlates with the best health related quality of life scores, gaining a statistically significant difference compared to warfarin users in physical functioning (warfarin – 95.85, NOACs – 124.57; $p = 0.012$) and social functioning mean ranks (warfarin – 95.16, NOACs – 119.08; $p = 0.026$). Age had low negative correlation with physical functioning scores.

Keywords:
Atrial fibrillation
Dabigatran
Oral anticoagulants
Quality of life
Rivaroxaban
Warfarin

Introduction

Atrial fibrillation is a disease that can negatively influence the quality of life [1]. In order to avoid new paroxysm patients have to try not to face provoking factors such as psychic stress, physical exertion, tiredness, coffee drinking, infections, alcohol consumption and many more [2]. Also these persons are in a higher risk group for developing thrombus in left atrial and therefor being predisposed for thromboembolism [3].

In 1954 warfarin was approved for medical usage [4] and new opportunities were opened for ischemic stroke prophylaxis for atrial fibrillation patients. Warfarin reduced the stroke risk by more than two thirds compared with no therapy or aspirin control group [5].

Nowadays it is calculated that in United Kingdom as much as estimate of 1% of all the population and 8% from all the persons over 80 years are using warfarin [4]. Warfarin is a K vitamin antagonist that inhibits the coagulation cascade in indirect path. Knowing that many of our daily used foods contain K vitamin, such as olive oil and many green leafy vegetables, oats and whole wheat [6], it is rather hard to precisely calculate how the coagulation cascade could be influenced by taking warfarin. For this reason, AFib patients that use warfarin daily are requested to make dietary limitations, excluding foods that contain large amounts of K vitamin. It is known that K vitamin intake lowering to 80% could increase the International Normalized Ratio (INR) by almost 30%. Respectively 100 microg increase of K vitamin daily can reduce INR by 0.2. [7]. Because of the narrow therapeutic range, and how easily diet can affect the INR warfarin may not reach its therapeutic range and predispose to thrombus development or, contrary, lead to warfarin overdose. For this reason, frequent INR monitoring is necessary.

For more than 50 years warfarin was the only used oral anticoagulant for atrial fibrillation therapy, when novel anticoagulants (NOACs) were introduced to society and new perspectives for atrial fibrillation treatment were found. In Latvia the most common ones that are used are dabigatran and rivaroxaban. Dabigatran received marketing authorization in Europe in March 2008 [8] and rivaroxaban that receive its marketing authorization in September 2008 [9]. In these nine years novel oral anticoagulants have gained good recognition and their use have increased from 0% in 2010 to 14.7% in 2016 among AFib patients [10]. NOAC users do not need regular anticoagulation monitoring [11], diet limitations and they have shown 10% lower mortality scores compared to warfarin [12]. But as a potential downside is the fact, that NOACs do not have an antidote, if the patient suffers from major bleeding event.

All of these aspects have the potential to influence health related quality of life for high risk atrial fibrillation patients.

Aim

The aim of the study is to determine and analyze whether there is a statistically significant difference comparing health related quality of life sections between K vitamin antagonist, warfarin, users and NOAC, rivaroxaban, dabigatran, users.

Materials and methods

This cross-sectional analytic research was made in Pauls Stradins Clinical university hospital, Center of Cardiology

Table 1 – Gender distribution among study groups.		
	Women, %, n	Men, %, n
Warfarin users	57.3% (47)	42.7% (35)
NOAC users	51.4% (37)	48.6% (35)
None oral anticoagulants	62.5% (40)	37.5% (24)

Table 2 – Study group characteristics.	
Variables	No = 218
Female, n	124
Male, n	94
Mean age, years	70.4 (SD 9.8)
Hypertension, %	82.0
Chronic heart failure, %	64.0
Percutaneous coronary intervention, %	13.5
Cerebral infarction, %	14.6
Artificial cardiac pacemaker, %	21.9
Cardiomyopathy, %	45.6
Coronary heart disease, %	47.2
Paroxysmal AFib, %	22.1
Persistent AFib, %	45.0
Permanent AFib, %	32.9
LVEF, %	54.7 (SD 11.7)
LA, mm	45.6 (SD 8.1)
LAVI, ml/m^2	42.6 (SD 14.3)
CHA_2DS_2-VASc score	4.4 (SD 1.6)
HAS-BLED score	2.6 (SD 1.3)
ORBIT score	1.7 (SD 1.6)
ATRIA score	6.3 (2.6)

Table 3 – Mean laboratory test results.	
Leukocyte, × 10^9/L	8.2 (SD 5.11)
Erythrocyte, × 10^{12}/L	4.65 (SD 0.66)
Hemoglobin, g/L	128.22 (SD 27.40)
Hematocrit, %	40.42 (SD 5.38)
APTT, s	41.57 (SD 14.66)
INR	1.67 (SD 0.96)
ALAT U/L	29.99 (SD 19.27)
ASAT U/L	31.39 (SD 17.88)
Glucose, mmol/L	6.65 (SD 2.01)
Creatinine, mmol/L	96.96 (SD 47.02)
Potassium, mmol/L	4.44 (SD 0.56)
Triglycerides, mmol/L	1.42 (SD 0.70)
Cholesterol, mmol/L	4.39 (SD 1.41)
HDL, mmol/L	1.26 (SD 0.36)
LDL, mmol/L	2.53 (SD 1.05)
CRO, mg/L	13.03 (SD 38.16)

in Riga, Latvia during the time period from October 2016 till June 2017.

Inclusion criteria:

- person is at least 18 years old;
- person is a non-valvular (as defined by European Society of Cardiology [13]) high-risk atrial fibrillation patient at least in one of the risk evaluation scores (CHA_2D_2-VASc score for men more or equal to 2, for woman more or equal to 3; HAS-BLED score more or equal to 3, ORBIT score more or equal to 4, ATRIA score more or equal to 6);
- person agreed to participate in this research and confirmed it with signing the consent agreement;
- person during the questioning time is full conscious.

Exclusion criteria:

- patient use oral anticoagulants for any other reason that is not atrial fibrillation;
- person did not agree to participate in this research.

This research was made by selecting participants that meets the inclusion criteria in Latvia's Cardiology center during their hospitalization time.

Patients were asked whether they agree to participate in this research. If the answer was positive, the survey was collected with oral interview. Demographic data, disease anamnesis was obtained, laboratory test results, echocardiography results were specified. Patients were asked about the medication that they use daily and short form modified SF-36 questioner.

SF-36 is a health related patient-reported health survey that reviews the quality of life in different sections of functioning. In this research the SF-36 survey was modified for a better suitability for atrial fibrillation patients, excluding some of the sections. Final version of the modified SF-36 questioner included 16 questions that taps seven health concepts: physical functioning, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy-fatigue and general health perception. If some of the questions were not clear, the questions were explained and clarified, so that the patient would understand the meaning of these questions.

All of the answers were transformed in percentage terms, preferable being higher percentage score.

A part of the survey was filled by examining the patient's case history during his hospitalization time.

All obtained data were collected with MS Excel program and for statistical analysis SPSS Statistics was used. Collected data were processed, using the percentage frequency distributions, standard deviations, analysis of variance, x test, statistical reliability (p value) and Kruskall-Wallis H-test.

Results

A total of 218 patients were included in this study, of which 56.9% were female and 43.1% male, the average age was 70.4 (SD 9.8) years (Table 1). The main study group characteristics can be seen in Table 2 and 3. From

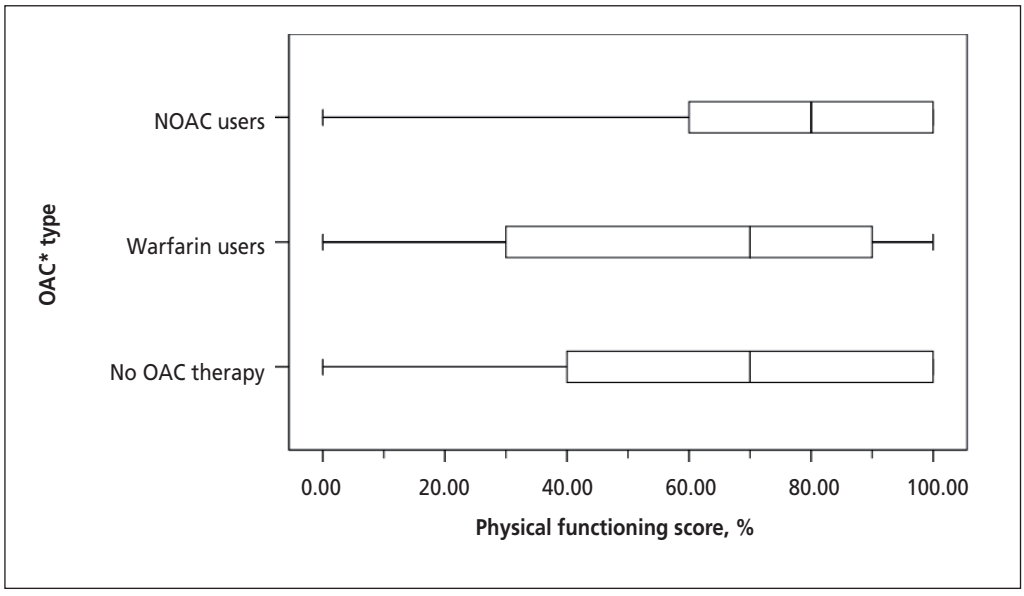

Fig. 1 – SF-36 survey's physical functioning score in all the study groups. * Oral anticoagulant.

all the patients the majority for ischemic stroke prophylaxis used warfarin (37.6%) with the mean age 71.1 (SD 9.4) years, 33.0% used NOACs with the mean age 67.9 (SD 11.1) years, but 29.4%, with the mean age 72.4 (SD 8.3), years did not use any kind of anticoagulant.

The mean scores of the modified SF-36 questioner are presented in Table 4.

For health related quality of life analysis between the groups Kruskall-Wallis H-test was performed, because the groups did not have standard normal distribution.

During the statistical analysis, it was discovered that there is a statistically significant difference between all three study groups comparing physical functioning (p = 0.016) and social functioning (p = 0.026) areas.

Examining closer physical functioning area, there was a statistically significant difference comparing warfarin users with NOAC users, warfarin users scoring mean rang of 95.85, but NOAC users scoring 124.57, p = 0.012 (Fig. 1).

Examining closer social functioning scores in all three study groups, there was a statistically significant difference also between warfarin and NOAC user group, where in warfarin group the mean rank was 95.16, but NOAC – 119.08, p = 0.026 (Fig. 2).

In the rest 5 areas there was not found a statistically significant difference between the groups, although in the examined areas NOAC users scored the best scores, following with the study group of patients, who did not use any kind of oral anticoagulant for ischemic stroke prophylaxis and the least scores showing warfarin users (Table 4).

It was found that the age had a low negative correlation with the physical functioning (r = –0.23; p = 0.001). There was no correlation with the AFib diagnosis duration with the health related quality of life scores.

Considering that majority of Afib patients are polymorbid, we aimed to establish whether the study groups have differences in the baseline parameters of other comorbidities. It was concluded that the only diagnosis prevalence that had a statistically significant difference among groups was anamnesis of old myocardial infarction. Thus, the presence of this diagnosis did not have influence on the answers given for HRQOL evaluation questions.

All other diagnosis between the groups had similar prevalence among all study groups without a statistically significant difference, yet there was found that some of these diagnoses did influence the HRQOL. It was conclu-

Table 4 – The modified SF-36 quality of life scores across all study groups.

SF-36 scale	NOAC users (n = 71)	Warfarin users (n = 72)	No OAC therapy (n = 63)
General health, %	45 ± 25	37 ± 25	46 ± 29
Physical functioning, %	75 ± 26	59 ± 35	65 ± 35
Role limitations due to physical health problems, %	65 ± 48	46 ± 50	51 ± 50
Emotional well-being, %	76 ± 15	73 ± 18	74 ± 21
Social functioning, %	79 ± 24	66 ± 31	75 ± 30
Role limitations due to personal or emotional problems, %	68 ± 47	52 ± 50	58 ± 50
Energy-fatigue, %	57 ± 22	49 ± 25	53 ± 25

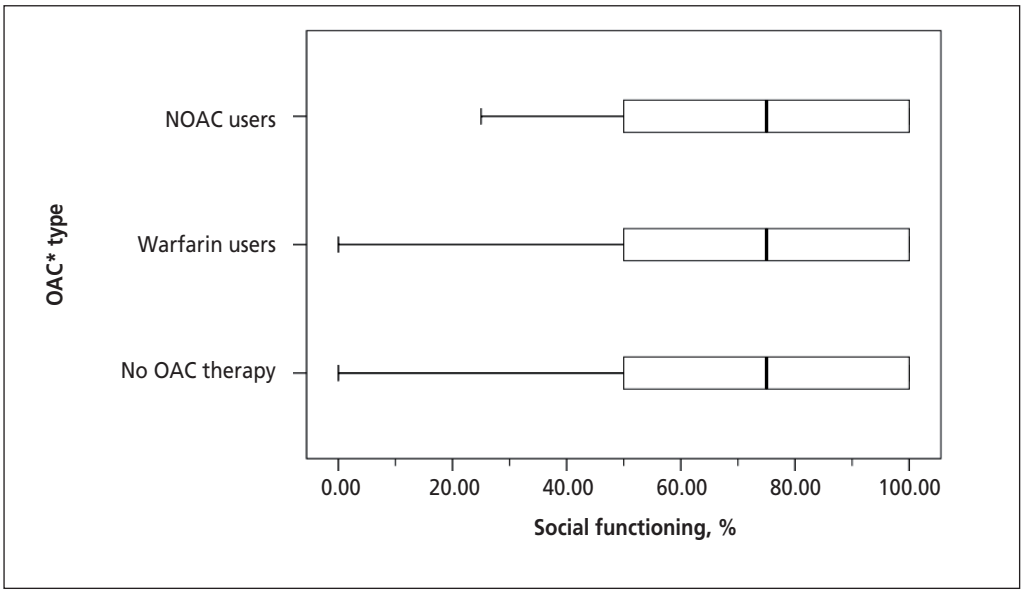

Fig. 2 – SF-36 survey's social functioning score in all the study group. * Oral anticoagulant.

ded that anamnesis of cerebral infarction had low negative correlation with physical function scores (r = –0.27) and energy-fatigue (r = –0.28). Chronic heart failure had low negative influence on the scores of role limitations due to physical health problems (r = –0.21). Cardiomyopathy had low negative correlation on role limitations due to personal or emotional problems (r = –0.22) and emotional well-being (r = –0.24). This information is valuable from the aspect of how separate diseases influence the HRQOL, but taking into count that the distribution of these diagnosis were equally among the groups, it should have not influence the acquired results.

Examining whether other cardiovascular drug usage, such as antiarrhythmics, antihypertensive drugs, cholesterol-lowering medication and other types, had influence on quality of life it was found that diuretic usage had a low negative correlation with energy-fatigue level (r = –0.25), but among all three studies groups the frequencies for diuretic usage were similar without a statistically significant difference.

Discussion

Quality of life is a very significant factor that also influences the choice of the most suitable medication together with other benefits that a medication can offer. Although it is known that NOACs have many benefits over warfarin, for example, they reduce stroke and systemic embolic event rate by 19% compared to warfarin [12], they also have shown themselves as oral anticoagulants, that does influence most positively the health related quality. In recent years researchers have started to draw more attention to this aspect, evaluating the potential benefits on health related quality of life for AFib patients that use oral anticoagulants. Comparing our results to other preexisted researches, the results were similar. There have been researches where the results have been almost the same as in this study. Both researches state that at baseline NOAC users score better results than warfarin users [14]. But in this research we have found statistically significant difference in separate section. Also there have been studies, where warfarin was compared with dabigatran separately, but in those studies was not found any statistically significant difference [15]. It has also been showed that rivaroxaban usage does improve the quality of life over the period of 12 months [16].

If we look separately at warfarin users and patients that did not use any kind of oral anticoagulants the results were the same as in other researches. Neither do older studies [17] nor the newer ones [18] show statistically significant difference between the groups.

We can conclude that in this research the results are similar to other researches, but in separate sections it shows a statistically significant difference between warfarin users and NOAC users.

All this knowledge opens new opportunities for the most suitable medication selection, so the patient could gain the most of it. In other words, the chosen therapy would not only have the best therapeutic results, but also would offer a better quality of life.

The fact that age had a low negative correlation with physical functioning have been the same as in other similar researches, where cardiologic patients with cardiac pacemaker were studied, where age negatively correlated with functional capacity [19].

Although we know that usage of the majority of other cardiac medication groups does not correlate with a change in HRQOL in this study, we cannot exclude the possibility, that if looked on each group and the drugs, that are included in these groups, separately, there could be an impact on the quality of life evaluations.

We can conclude that the health-related quality of life for AFib patients is influenced by many factors and one of them is also the oral anticoagulant type.

Conclusion

NOAC usage correlates with the best health related quality of life scores, gaining a statistically significant difference compared to warfarin users in physical functioning (warfarin – 95.85, NOACs – 124.57; p =0.012) and social functioning mean ranks (warfarin – 95.16, NOACs – 119.08; p = 0.026). There is a low negative statistically significant correlation (r = –0.23) with age for physical functioning scores. Diuretic usage had a low negative correlation with energy-fatigue level (r = –0.25).

Authors' contribution

Ketija Apsite – the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be submitted.
Baiba Lurina – the conception and design of the study, analysis and interpretation of data, drafting the article, final approval of the version to be submitted.
Andris Tupahins – acquisition of data, drafting the article, final approval of the version to be submitted.
Vladimirs Voicehovskis – the conception and design of the study and interpretation of data, revising article critically for important intellectual content, final approval of the version to be submitted.
Tarass Ivascenko – analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be submitted.
Oskars Kalejs – the conception and design of the study and interpretation of data, revising article critically for important intellectual content, final approval of the version to be submitted.
Aivars Lejnieks – the conception and design of the study, interpretation of data, revising article critically for important intellectual content, final approval of the version to be submitted.

Conflict of interest

None declared.

Funding body

None.

Ethical statement

Authors state that the research was conducted according to ethical standards.

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