Original Article

Association Between Functional Health Literacy and the Quality of Oral Anticogulation

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Abstract

Background: **Low functional health literacy in anticoagulated patients using warfarin has been widely discussed in medical literature.**

Objective: **To identify the quality of oral anticoagulation (QOA) over time and to analyze the association between this variable and functional health literacy.**

Methods: **Prospective cohort study conducted at an anticoagulation clinic (AC) in Minas Gerais, in a high-complexity hospital. The study included 81 patients, whose data were collected by direct consultation of medical records or by asking questions while patients were waiting for care. The QOA was assessed at 6, 9, 12, 15, and 18 months after the beginning of this study, and analyses of the association between this variable and functional health literacy were performed at the different time points. The QOA was identified by calculating the Therapeutic Time Range (TTR), with good quality being obtained with TTR values >59%. The incidence analysis of the TTR was performed for each of the five time points of the study through univariate Poisson regression. The significance level adopted in the statistical analysis was 5%.**

Results: **Throughout the study, inadequate control of oral anticoagulation was observed, with only 20% of the patients showing persistent improvement in TTR values. No statistically significant association was identified at the different measurement times between TTR and functional health literacy.**

Conclusion: **There was no direct association between the QOA and functional health literacy. However, the low incidence of persistent quality of anticoagulation in patients with low literacy suggests the development of specific educational actions for this subgroup of patients.**

Keywords: **Warfarin; Health Literacy; Health Care Evaluation Mechanisms; Anticoagulants.**

Introduction

Warfarin is an oral anticoagulant, a coumarin derivative, indicated for the prevention and treatment of thromboembolic disorders worldwide. Despite its benefits, this medication has a narrow therapeutic index, potential for interactions with an extensive list of medications and foods, and a wide variability in dose-response.[1,2] Inappropriate use increases the risk of adverse events, including thrombotic and hemorrhagic events, which can be serious, such as intracranial hemorrhages.[3] It is noteworthy that the risk of hemorrhagic events, such as hemorrhagic transformation associated with stroke,[4,5] increases when this medication is used incorrectly by patients.

Warfarin treatment is monitored using the International Normalized Ratio (INR) test,[4,6] calculated based on prothrombin activity. The quality of oral anticoagulation (QOA) can be assessed by calculating the Time in Therapeutic Range (TTR), which allows one to identify the proportion of time in which the patient presented INR values within the desired therapeutic range. TTR values below 60% are associated with a higher incidence of thromboembolic and hemorrhagic complications.[7]

The ability of patients to understand their health problems and treatment is a factor that interferes with the success of warfarin use. It has been identified that this is a complex process that requires patients not only to follow pharmacotherapy adherence, but also to adapt eating habits, self-medicate, perform frequent INR measurements, and periodically return to the health service to receive guidance.[8]

Despite the recommendation to use warfarin with caution in individuals with low socioeconomic and cultural conditions, in the practical context, this indication is often necessary.[4] The

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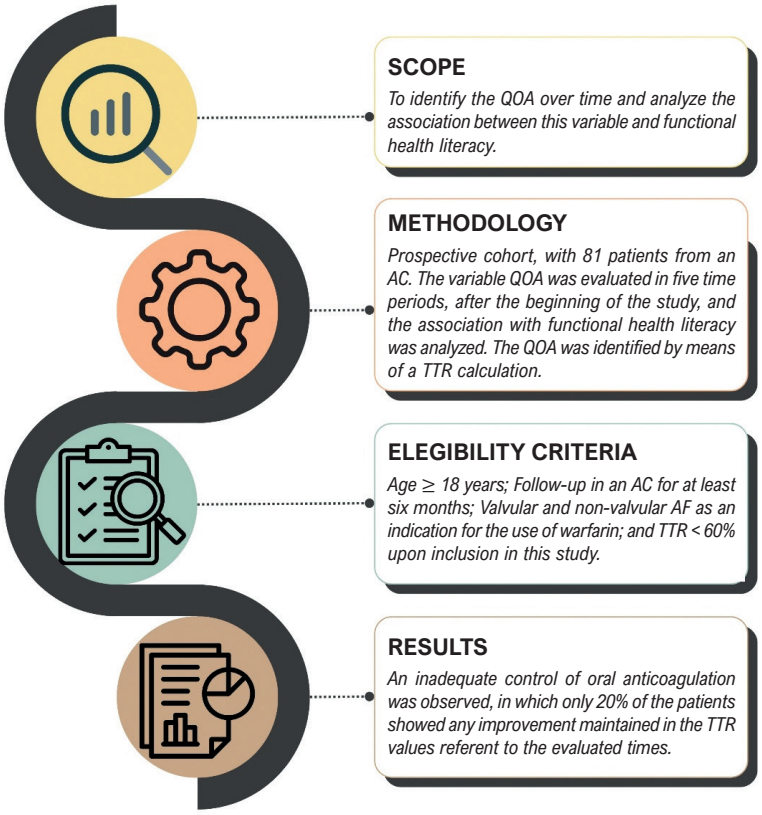
Central Illustration: Association Between Functional Health Literacy and the Quality of Oral Anticogulation



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Summary of the main points of the work. TTR: Therapeutic Time Range; AC: anticoagulation clinic; AF: atrial fibrillation; QOA: quality of oral anticoagulation.

use of warfarin in individuals with low functional health literacy has been increasingly discussed in medical literature, with the risk-benefit ratio still considered to be controversial.

Therefore, the present study aimed to identify the QOA over time and to analyze the association between this variable and functional health literacy.

Methods

This is a cohort study in which patients using warfarin were monitored over time. The individuals were divided into those with adequate and those with inadequate functional health literacy, with the QOA being calculated over time.

Participants were recruited from an anticoagulation clinic (AC) located in Belo Horizonte, Brazil. The AC is linked to a highly complex SUS hospital in Belo Horizonte, and is considered a reference in oral anticoagulation in the city of Belo Horizonte and surrounding areas. It is fully funded by SUS and provides care to outpatients who require periodic monitoring for the management of oral anticoagulation. The inclusion criteria were age 18 years of age or older, both sexes, outpatient follow-up in AC for at least six months, valvular or non-valvular atrial fibrillation (AF) as an indication for warfarin use, and TTR<60% at the time of inclusion in the study, considering the period between July and December 2018 for the calculation of TTR. This period was chosen considering the six months prior to the beginning of the research data collection.

Exclusion criteria included previous or concomitant participation in educational intervention groups related to warfarin use offered by other services, bedridden patients, people with total blindness or deafness; those with aphasia or speech difficulties that could impede communication; those with a diagnosis of dementia reported in medical records from previous hospitalizations or outpatient care, and those who requested discontinuation of the intervention.

The QOA was measured by calculating the TTR (Rosendaal method), which involves linear interpolation of a historical series of at least two INR results. The TTR is expressed as a percentage, and a minimum of two INR measurements are required. For participants who had INR intervals >56 days, the weighted average between the values with a temporal interval >56 days

was calculated. INR values were used to calculate the TTR for the valid intervals, and then each separate TTR value was used to calculate the weighted average, considered as the final TTR.[9]

Considering records in the literature that show that a follow-up time to identify improvements in TTR values usually occurs between three and six months, and that studies that aim to evaluate this impact over a longer period of time are considered to be of interest,[10,11] we decided to measure at times T1, T2, T3, T4, and T5, which corresponded to times 6, 9, 12, 15, and 18 months after inclusion in the study.

To calculate the TTR, reports with the INR values of all patients included in the study were generated in the institution's computerized system. In the case of specific failures in the system that occurred in the outpatient clinic between October 2018 and January 2020, a search for outpatient care records was carried out in physical medical records in order to supplement missing data in the system.

The TTR calculation was performed independently by two previously trained undergraduate students, using a Microsoft Excel® spreadsheet, in which the calculator proposed by Rosendaal[9] was inserted. The doctoral student responsible for this study was responsible for checking the discrepancies and performing the new calculation. Functional health literacy was identified using the Short Assessment of Health Literacy for Portuguese-speaking Adults (SAHLPA-18) test. This test is administered individually, and participants are asked to associate each medical term presented with one of two word options provided in the test. Compared to other methods, the SAHLPA-18, in addition to having similar psychometric properties, presents a lower risk of causing embarrassment to participants, since it uses isolated words and is a method previously validated in both Portugal and Brazil.[12,13] This test contains a total of 18 points, with patients who score between 15 and 18 points being considered adequately literate, and those who score between 1 and 14 points being considered inadequately literate.[13] In the present study, the examiner read the test, and patients were asked to choose the answers they considered most appropriate.

The following descriptive variables were collected: sex, age, self-reported skin color, educational level, reported ability to read, income, and municipality. These variables were collected by directly consulting patients' medical records and asking direct questions. The questions were asked at the time the patients were included in the study. They were approached at the anticoagulation outpatient clinic while they were waiting for their appointment. All participants received explanations about the study and, if they accepted, were invited to sign the free and informed consent form (FICF).

The data were analyzed using measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range, minimum and maximum values) in the case of interval or continuous variables; and by absolute and relative frequencies in the case of categorical variables. The variables were assessed for normality using the Shapiro-Wilk test. The stratification variable for the analyses was adequate literacy.

The comparison of means and medians was assessed using the Student's t-test and the Wilcoxon test, respectively, both for independent samples. Fisher's exact test was used to compare proportions for frequencies lower than five, and the Chi-square test was used for other comparisons. The incidence of TTR>60 was calculated at each level of the stratification variable and, subsequently, the incidence ratio - with the incidence of inadequate TTR as a reference - and its respective 95% confidence interval (95% CI) were obtained. This analysis was performed for each of the five time periods of the research.

The significance level adopted was 5%. The software used for the analyses was Stata/SE 12.0 for Mac.

This study is an excerpt from a clinical trial in which patients were characterized in relation to their literacy registered in the Brazilian Registry of Clinical Trials (*Registro Brasileiro de Ensaios Clínicos* – REBEC), logged under the code RBR-9cy6py and UTN U1111-1217-0151. The study protocol was published in the scientific journal *Medicine* (ISSN 0025-7974), in April 2019. The study was conducted in accordance with the terms of Resolution No. 466/2012 of the National Health Council, and the project was submitted for consideration by the Ethics Committee of the Federal University of Minas Gerais (UFMG) and approved under number CAAE 65928316.3.0000.5149

Results

Most individuals included in the study were male, non-white, with a mean age of 67.6 years, and a mean level of education of 4.3 years. Despite their low educational level, most reported being able to read. Regarding the QOA, inadequate control was evidenced by most participants. It is also important to note that only approximately 20% of the patients showed persistent improvement in TTR values over time. Further details on the sociodemographic and clinical variables are specified in Table 1, together with the main points of the article, explained in the Central Illustration of the study.

When analyzing the association of TTR with functional health literacy, no statistically significant association was identified at the different measurement times (Table 2).

Discussion

The high prevalence of elderly patients, identified by the mean age of 67.6 years, is expected, considering that AF is a sustained tachyarrhythmia, with a high prevalence in the elderly population.[4,13] Another interesting characteristic of the population is the low educational level and the low functional health literacy, which may suggest possible difficulties for patients in relation to self-care, understanding of treatment, and decision-making.

One study points to several barriers related to anticoagulant treatment.[3] The authors discussed factors directly attributed to patients, such as health conditions, characteristics, and behaviors; those related to health service providers, such as attitudes and behaviors; and those related to the health system, such as patient expectations

Table 1 – Sociodemographic and clinical variables

Patient characteristics	Inaquequate Literacy n = 61	Adequate Literacy n = 20	Total n = 81	p value
Female n (%)	25 (41.0)	14 (70.0)	39 (48.2)	0.024
Age				
Average ± Standard Deviation	68.9 ± 11.6	63.7 ± 11.2	67.6 ± 11.6	0.084
Self-reported skin color n (%)				
White	15 (24.6)	6 (30.0)	21 (25.9)	0,632
Non-white	46 (75.4)	14 (70.0)	60 (74.1)	
Educational Level (in years)				
Median (Interquartile Range)	4 (1;5)	7 (4;8)	4 (4;8)	0.036
Reported knowing how to read n (%)	48 (78.7)	20 (100.0)	68 (84.0)	0.031
Income (in minimum salaries)				
Median (Interquartile Range)	2.0 (1.0)	1.2 (1.0)	1.5 (1.0)	0.467
Municipality n (%)				
Belo Horizonte	48 (78.7)	18 (90.0)	66 (81.5)	
Metropolitan Region of Belo Horizonte	12 (19.7)	2 (10.0)	14 (17.3)	0.502
Countryside	1 (1.6)	0 (0.0)	1 (1.2)	
TTR >60 n (%)				
Time 1	24 (39.3)	7 (35.0)	31 (38.3)	0.731
Time 2	20 (41.7)[1]	5 (31.3)[2]	25 (39.1)[7]	0.491
Time 3	21 (35.6)[3]	6 (30.0)	27 (34.2)[8]	0.717
Time 4	18 (31.6)[4]	6 (33.3)[5]	24 (32.0)[9]	0,969
Time 5	17 (37.0)[6]	6 (42.9)[4]	23 (38.3)[10]	0.857
TTR %[11]				
Time 1				
Average ± Standard Deviation	54.5 ± 34.9	50.1 ± 38.2	53.4 ± 35.6	0.630
Time 2				
Average ± Standard Deviation	52.6 ± 37.6	36.3 ± 33.8	48.5 ± 37.1	0.131
Time 3				
Average ± Standard Deviation	53.7 ± 29.3	43.5 ± 31.2	51.1 ± 30.0	0.187
Time 4				
Average ± Standard Deviation	53.2 ± 21.6	50.2 ± 24.8	52.5 ± 22.3	0.619
Time 5				
Average ± Standard Deviation	54.2 ± 19.1	56.4 ± 22.6	54.7 ± 19.8	0.719
Persistent improvement n (%)*	17 (27.9)	3 (15.0)	20 (24.7)	0.247

*Notes: [1] n=48; [2] n=16; [3] n=59; [4] n=57; [5] n=18; [6] n=46; [7] n=14; [8] n=64; [9] n=79; [10] n=75; [11] n=60 the sample sizes for calculating the TTR% estimators follow those in the notes;1-11 *TTR value greater than or equal to 60 continuously. TTR: Time in Therapeutic Range.*

Table 2 – TTR according to time

Time	TTR Incidence>60 in inadequate literacy	TTR Incidence>60 in adequate literacy	Calculation of the Ratio between incidences (RI)	RI (95% CI)	P-value
Time 1 (6 months)	0.39	0.35	1.12	1.12 (0.48; 2.61)	0.814
Time 2 (9 months)	0.42	0.31	1.33	1.33(0.50; 3.54)	0.592
Time 3 (12 months)	0.36	0.30	1.19	1.19 (0.48; 2.94)	0.742
Time 4 (15 months)	0.32	0.33	0.95	0.95 (0.38; 2.39)	0.881
Time 5 (18 months)	0.37	0.43	0.86	0.86 (0.34; 2.19)	0.734

TTR: Time in Therapeutic Range.

regarding the health system, communication within the health system itself, and clinical evidence.[3]

Even if the patient wishes to make a greater investment in the self-care process, the needs for practices that involve skills and cognition go beyond knowledge. Going to the supermarket to buy leafy greens, cooking skills, and choosing ideal foods are examples of actions that can be compromised by low cognition. Associated with these are the management of other medications in use (which often constitute polypharmacy and interact with warfarin), in addition to the skills required for the use of warfarin (which often requires the ability to understand the constant adjustments in doses, in addition to the need to break the pill). The impact of low functional health literacy on skills related to the use of medications, as well as other self-care practices, has been previously pointed out in the literature.[14]

The poor QOA was a characteristic presented by a significant portion of the patients, showing with a persistent low improvement in TTR values. Although the poor QOA was a criterion for the inclusion of participants in this study, an increase in TTR was expected over time considering the multidisciplinary approach of the AC and the large investment in educational interventions.

A recent study suggests that the provision of oral anticoagulation for AF has been insufficient and inefficient. The data indicated a greater need for consultations with specialists, in addition to demonstrating an underuse of oral anticoagulants in patients with AF, given that only 9.3% of patients with a high risk of stroke were using oral anticoagulant therapy.[15]

The existence of patients with low functional health literacy using anticoagulants in Brazil is a reality. One study carried out in an AC in Minas Gerais identified that the subgroup of patients with inadequate anticoagulation control was comprised of both patients with good functional health literacy and those with inadequate functional literacy.[16]

A prospective observational Italian study involved 1,341 patients with non-valvular AF and followed the patients for 37.7 months. The authors calculated the TTR for each year of anticoagulant therapy for each patient, and a reduction in TTR to values <70% over time was observed in 20% of the patients, with this reduction being associated with a higher risk of cardiovascular events.[17]

The literature has shown that approximately 60% of all patients using warfarin had low functional health literacy.[14] Hence, there is a need for scientific studies with educational interventions aimed at patients using oral anticoagulants and who are in vulnerable conditions, especially those with low functional health literacy.[18]

Regarding the association between TTR and literacy, no statistically significant association was identified. The association between low literacy and a low QOA is still controversial information in the literature. Studies have suggested that increased patient knowledge regarding oral anticoagulant therapy may significantly impact the measurement of TTR,[19,20] although there are limitations regarding correlation methodologies.[10]

The literature has reported an inverse association between age and knowledge about warfarin, which may be associated with the lack of clear information conveyed to this population.[21] This information highlights the need to invest in educational practices aimed at the study population, which is mostly made up of elderly patients with low educational levels, with a significant percentage of patients having low functional health literacy.

Elderly people may present physiological and cognitive changes inherent to senescence, which may compromise the effectiveness of certain drugs, as well as their understanding and ability to exercise self-care in health.[22] In addition, the participants have AF, which reflects a greater need for care due to the risk of thromboembolic events.[4,13]

The present study has the limitation of including patients with low TTR, and the inclusion of patients with adequate and inadequate TTR would enable a monitoring over time of groups with different profiles. The impossibility of extrapolating the data is also seen as a limitation.

As strengths, the study reflects the profile and seeks to identify impacting associations for clinical outcomes of a vulnerable population, in a real-world context, in a middle-income country. It is recommended that larger studies be conducted, exploring the interference of health literacy in

the control of oral anticoagulation among patients treated in Brazil.

Conclusions

No direct association was identified between the variables of adequate and inadequate functional health literacy and the QOA. More extensive studies on the topic in question are recommended.

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Author Contributions

Conception and design of the research, analysis and interpretation of the data: Souza GC, Costa JM, Machado CJ, Martins MAP; acquisition of data: Souza GC, Costa JM, Martins MAP; Statistical analysis: Souza GC, Costa JM, Machado CJ; writing of the manuscript and critical revision of the manuscript for intellectual content: Souza GC, Costa JM, Ortiz MCO, Lima PDA, Nogueira PEF, Machado CJ, Martins MAP.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the UFMG under the protocol number 2.018.850 CAAE 65928316.3.0000.5149. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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