European Journal of Internal Medicine 25 (2014) 247–254

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

The quality of oral anticoagulation in general practice in patients with atrial fibrillation

Sabrina Mueller [a], Matthias Pfannkuche [b], Günter Breithardt [c], Rupert Bauersachs [d], Ulf Maywald [e], Thomas Kohlmann [f], Thomas Wilke [a,*]

[a] Institute for Pharmacoeconomics and Drug Logistics, University of Wismar (University of Applied Sciences), Germany
[b] Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
[c] Competence Network on Atrial Fibrillation (AFNET), Department of Cardiology and Angiology, University of Münster, Münster, Germany
[d] University Hospital Darmstadt, Germany
[e] AOK Plus, Dresden, Germany
[f] Institute for Community Medicine, Department for Methodology, University of Greifswald, Germany

ARTICLE INFO

Article history:
Received 10 June 2013
Received in revised form 10 December 2013
Accepted 27 December 2013
Available online 27 January 2014

Keywords:
Oral anticoagulation
Anticoagulation quality
VKA
Causes of poor anticoagulation quality

ABSTRACT

Background: The aims of this study were to evaluate the quality of oral anticoagulation (OAC) in AF patients in the practices of general practitioners (GPs) in Germany and to investigate possible causal factors which influence OAC quality.

Methods: We conducted a multi-center, non-interventional, prospective observational cohort study among general practitioners (GPs) in Germany. To assess the quality of OAC on the basis of the prospectively documented international normalized ratio (INR) values, the time in therapeutic range (TTR) was calculated using the Rosendaal linear trend method. The causes of poor OAC quality were identified by a multivariate analysis model (logistical regression; poor OAC quality: TTR <60%).

Results and conclusions: For 525 OAC patients (66.8%; patients with at least 2 prospectively documented INR values) the average TTR (target range of 2.0–3.0) was 67.6%. About 34.7% of the patients had a TTR <60%.

None of the variables representing characteristics of the medical practices were capable of explaining the occurrence of poor OAC quality. However, with regard to care provision-based variables, the existence of a brief discontinuation of medication was important. As the existence of adherence barriers increased, the probability of poor anticoagulation quality increased.

In conclusion, the provision of OAC in the German health care system is to be regarded as good, but far from ideal. Our causal analysis shows that patient-based factors should be addressed through the provision of improved training and that the rationale behind the interruption of OAC treatment should be critically examined.

1. Introduction

Atrial fibrillation (AF) is the most common significant cardiac rhythm disorder that is associated with substantial lethality from stroke and thromboembolism. Its incidence in the general population ranges from 0.85 to 4.1 per 1000 person-years [1–3]. According to current guidelines [4–6], oral anticoagulation (OAC) is recommended for AF patients with moderate/high risk of stroke, whereas abstention from antithrombotic therapy is preferred for AF patients at low stroke risk (<65 years and lone AF and/or CHA_2DS_2-VASc score = 0).

Along with OAC under-treatment, especially of moderate to high risk patients who need OAC [7,8], the quality of international normalized ratio (INR) adjustment is still a major challenge in OAC practice based on VKA [9]. INR values <2.0 are generally considered to be ineffective against stroke or thromboembolic events, whereas INR values >3.0 are associated with an increased risk of bleeding [5,10]. To obtain a benefit from OAC based on this medication class, a time in therapeutic range (TTR) cut-off of 60–70% has been suggested [11].

Even in clinical trials, it is difficult to achieve consistently high TTR values. In the RE-LY trial, in 16 out of 36 countries (44.4%) the warfarin-treated group achieved mean TTR rates below 60% [12].

Although there are numerous studies concerned with OAC quality based on VKA [13,14], two themes central to real-life VKA-based OAC quality have not been investigated in detail. First, a large number of the existing studies have been conducted in a hospital/outpatient cardiology setting or under the guidance of medical specialist [15,16]. Patients in specialized OAC-providing services are mostly better managed than patients treated by physicians not specializing in OAC [14,17,18]. In contrast, at least in Germany, most AF patients are treated by their general practitioner and/or specialist in internal medicine [7,19].

Second, care provision and patient-based causal factors influencing the quality of VKA-based OAC have not been sufficiently investigated.

* Corresponding author at: IPAM, Hochschule Wismar, PF 1210, 23952 Wismar, Germany. Tel.: +49 3841 753 504.
E-mail address: Thomas.wilke@hs-wismar.de (T. Wilke).

0953-6205/$ – see front matter © 2014 European Federation of Internal Medicine. Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.ejim.2013.12.013

International studies have shown differences in OAC quality between countries [20]. In addition, the age of a patient as a predictor of unstable INR values has been studied [21,22]. It has been suggested that the knowledge AF patients have about anticoagulation [23] and the non-adherence of such patients [9,24] are important influences on the TTR.

The aims of this study were, therefore, to evaluate the quality of VKA-based OAC in AF patients in the practices of general practitioners (GPs) in Germany and to investigate possible causal factors which influence OAC quality depending on the treating doctors (care provision based factors) or the patients (patient-based factors).

2. Methods

2.1. Sample

We conducted a multi-center, non-interventional, prospective observational cohort study among general practitioners (GPs) in Germany. The whole study protocol was examined by the Ethics Commission of the University of Greifswald and fully approved. To recruit GPs, a database containing the names and addresses of 57,441 GPs in Germany (AdR; Ärzte der Region) was used to select 600 of them, who were then invited to participate in the study. This random selection was controlled for age, gender, type of specialization, and state of location to ensure German-wide representativeness of our GP sample. Therefore the proportion of the defined characteristics was identified within the database of all GPs in Germany. This proportion was used for the identification of 600 potential study investigators with the same distribution in respect to the characteristics mentioned above.

The participating GPs were asked to include into the study AF patients (ICD10 code I48; no further criteria) who were at least 18 years old and not participating in any other studies. No other inclusion/exclusion criteria were used. The first patient was included into the study at the 25th of May 2009; the last patient was excluded at the 12th of May 2011.

2.2. Documented variables

The baseline parameters documented in the study included the clinical and sociological background of each patient (Table 2). All INR values of the individual patient were included in a prospective observational period (up to 12 months). Besides the variables obtained from the individual GP's records, additional data with the potential to influence the OAC quality were collected, by contacting the patients via written questionnaires and phone interviews (Table A). The data collected about each participating patient at each visit made to their GP and based on the written questionnaires included (1) answers needed to calculate health related quality of life (HrQoL) [25,26], and (2) answers needed to evaluate AF symptoms as defined by the EHRA (European Heart Rhythm Association) questionnaire [4,27,28]. Data collected once by telephone interviews with patients included (1) answers needed to estimate the non-adherence of the patients, by using the adjusted Adherence to Refills and Medication Scale [29], (2) answers needed to assess patient-related problems with OAC management (self-developed Adherence Barriers Questionnaire [30], supplemented by the addition of new questions concerning anticoagulation), and (3) answers needed to assess the general level of knowledge the patients possessed about AF, the OAC/INR value management, and their individual risks of bleeding or stroke. To establish the feasibility of the modified questionnaire, a pilot test was conducted with 10 patients.

2.3. Assessment of anticoagulation quality

To assess the quality of OAC on the basis of the prospectively documented INR values, the TTR was calculated using the Rosendaal linear trend method [31]. In addition to the TTR range of 2.0–3.0 (or rather 2.5–3.5 for patients with mechanical heart valve) as suggested by present guidelines, a broader range of 1.8–3.2 as previously suggested [32] was calculated. All measured and documented INR values were included in the TTR calculation; this happened irrespective of any bridging/OAC interruption that took place during this observational period.

2.4. Identification of factors associated with poor anticoagulation quality

TTR cut-off points of between 60% and 70% are proposed in both the literature and the guidelines [4]. We decided to use the most conservative definition of poor OAC quality during the patient-specific observation period (dichotomous variable), by using TTR <60% as the cut-off point. The causes of poor OAC quality were identified by a multivariate analysis model (logistical regression). In principle, all the available information regarding patient/study center characteristics (Tables 1 and 2, and Table A) was included as independent variables. The data generated by the questionnaires addressed to the patients were used to calculate the following five scores: (1) HrQoL (EQ5-D score [25] and SF-36 sum scales [26]); (2) EHRA symptoms (severity from 0 to 3 multiplied with frequency from 1 to 3); (3) a non-adherence score [36] with a scale from 10 to 40 (higher score indicates higher non-adherence); (4) causes of the non-adherence score with range from 16 to 64 (higher score indicates higher adherence barriers as measured with the self-developed Adherence Barriers Questionnaire (ABQ)); and (5) a score representing the patients' anticoagulation knowledge (percentage of correctly answered questions).

Some of the patients were not able or willing to complete the questionnaires. Whenever a patient failed to answer more than 50% of the items, the entire data set of that patient was disregarded. In cases

Table 1
Characteristics of study centers (German general practitioners; GPs).

Parameter	Study center characteristics	
N	71	(100.0%)
Average age of GPs	49.4	(SD: 8.8)
Gender of GPs		
Female	23	(32.4%)
Male	48	(67.6%)
Type of GP (German classification)		
GP without any specification	52	(73.2%)
Practical doctor	2	(2.8%)
Internist working as GP	17	(24.0%)
Type of practice		
GP works for his or her own	32	(45.3%)
GP works with at least one colleague	37	(51.6%)
GP is employee in a medical center	2	(3.1%)
Region		
Town[a]	44	(62.0%)
Countryside	26	(36.6%)
Not available	1	(1.4%)
Number of patients in 3 months		
<1000	28	(39.7%)
1000–1500	18	(25.0%)
>1500	25	(35.3%)
Average number of patients with at least one GP's visit in the last quarter before study started	1426.8	(SD: 733.1)
Average number of AF patients in study centers with at least one GP visit in the quarter before the study started	53.5	(SD: 45.0)
Average number of AF patients with OAC in study centers with at least one GP visit in the quarter before the study started	42.9	(SD: 39.4)
Number of patients included in the study (patients/GP)		
Median	8	
Average	11.07	(SD: 8.0)
Minimum	1	
Maximum	25	

The table shows the main characteristics of the study centers. All centers were German GPs.

[a] More than 2000 inhabitants.