Good quality of oral anticoagulation treatment in general practice using international normalised ratio point of care testing

Thomas Løkkegaard[1], Tina Heidi Pedersen[1], Bent Lind[2], Volkert Siersma[1] & Frans Boch Waldorff[1]

ABSTRACT

INTRODUCTION: Oral anticoagulation treatment (OACT) with warfarin is common in general practice. Increasingly, international normalised ratio (INR) point of care testing (POCT) is being used to manage patients. The aim of this study was to describe and analyse the quality of OACT with warfarin in general practice in the Capital Region of Denmark using INR POCT.

METHODS: A total of 20 general practices, ten single-handed and ten group practices using INR POCT, were randomly selected to participate in the study. Practice organisation and patient characteristics were recorded. INR measurements were collected retrospectively for a period of six months. For each patient, time in therapeutic range (TTR) was calculated and correlated with practice and patient characteristics using multilevel linear regression models.

RESULTS: We identified 447 patients in warfarin treatment in the 20 practices using POCT (median: 19 patients; range: 6-55). The mean TTR for all patients was 69.3% (standard deviation (SD) = 24%), and for all practices the mean TTR was 67.3% (SD = 6.7%). The TTR in single-handed practices was lower than in group practices, 64.6% (SD = 8.0%) and 70.0% (SD = 3.6%), respectively; but the difference was not significant (4.2 percentage points (pp); 95% confidence interval (CI): –0.8-9.2). Short sampling intervals, e.g. 10-20 days (–11 pp, 95% CI: –16-–6)) and lack of diagnostic coding (–11.8 pp; 95% CI: –19.9-–3.7) were correlated with a low TTR.

CONCLUSION: In our study most of the general practices using INR POCT in the management of patients in warfarin treatment provided good quality of care. Sampling interval and diagnostic coding were significantly correlated with treatment quality.

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Oral anticoagulation treatment (OACT) with warfarin is commonly used for patients with atrial fibrillation, deep venous thrombosis, pulmonary embolism and mechanical heart valves to prevent thrombo-embolic complications [1]. The quality of OACT with warfarin is primarily measured by the percentage of time the patients´ INR measurements (INRs) lie within a well-defined target interval; also referred to as the time in therapeutic range (TTR) [2]. With the introduction of the new oral anticoagulants (NOACs), the importance of maintaining a high quality OACT with warfarin has again been emphasised [3]. According to recently published Danish guidelines, if a TTR of more than 70% cannot be maintained, treatment with NOACs should be considered [4].

In Denmark, general practitioners (GPs) are responsible for up to 80% of patients treated with warfarin [5], but only few studies have documented the quality of this treatment [6-8]. Since the publication of these studies, there has been a development towards an increase in the use of INR point of care testing (POCT) with concurrent involvement of practice staff in management decisions.

To our knowledge, no studies have addressed the consequences of these changes in the management strategy on OACT with warfarin. The purpose of the present study was to describe and analyse the quality of OACT with warfarin among randomly selected general practices in the Capital Region of Denmark using POCT.

METHODS

The study design is retrospective and the study was conducted in a primary care setting during a 6-month period from 15 December 2012 to 30 June 2013. Data sources were general practice, the regional health authorities of the Capital Region of Denmark, and the Elective Laboratory of the Capital Region of Denmark (ELCR).

Eligible for the study were general practices that used the reimbursement code for INR POCT more than three times per month in the 6-month study period as identified using data from the Regional Health Authorities. The practices were divided into two groups: single-handed practices and group practices (**Figure 1**). Within each of these groups, a random sample of practices was invited to participate in the study. The sampling was done independently from the study group. Due to limited resources, a pre-set target of 20 practices

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1) The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen
2) Elective Laboratory of the Capital Region of Denmark (ECLR), Copenhagen

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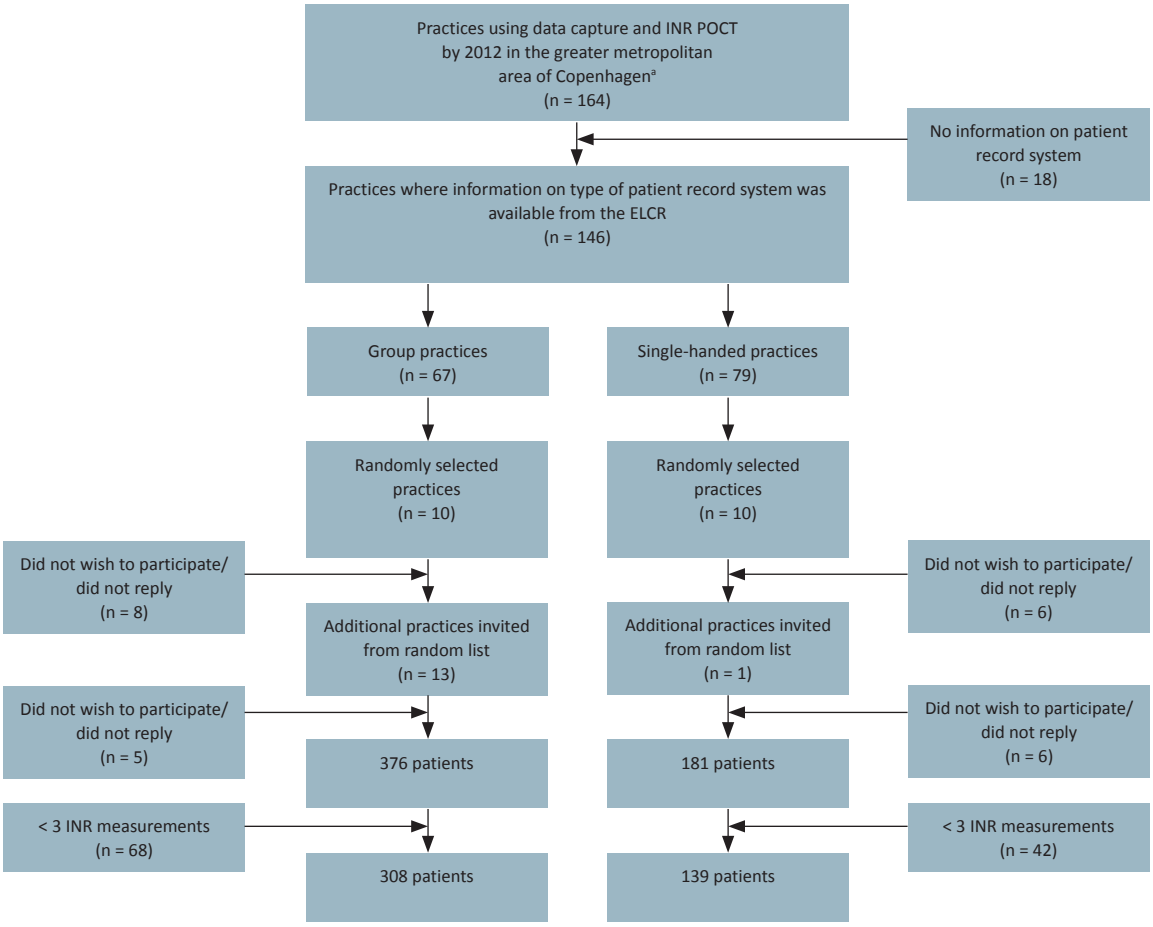
FIGURE 1

Trial flow chart.



ELCR = Elective Laboratory of the Capital Region of Denmark; INR POT = international normalised ratio point of care testing.
a) > 3 INR-measurements per month.

was chosen. A stepwise random selection procedure was used in order to reach the targeted ten practices in each group: if a practice declined to participate or did not reply, another randomly selected practice was invited. We identified patients in OACT monitored by INR POCT retrospectively by regional reimbursement for one or more INRs in the study period. Both patients in ongoing treatment and patients who initiated their warfarin treatment during the study period were included.

Information regarding practice demographics and number of list patients was collected from the Capital Region of Denmark. Information regarding the number and type of employees, weekly working hours, sampling procedure, registration of results and use of decision support was registered at practice visits. Two of the authors (TL and THP) visited each practice independently of each other on different dates to collect two data sets. These sets were later compared for discrepancies, which were then checked against the patient records of the practice.

For each patient, the following data were extracted: INRs, dates of sampling, laboratory code (International Union of Pure Applied Chemistry (IUPAC) or other) for each INR measurement, indication for treatment according to the International Classification of Primary Care (ICPC). If the INR measurement was not registered in the electronic laboratory record, the alternative method of registration was noted, e.g. in the text field or in an analogue laboratory file.

Information on type of electronic health record system and POCT device was obtained from the ELCR. The analytical performance of POCT instruments in the study group and in a control group (246 POCT instruments) was assessed from data collected at the ELCR from the year 2012. A split-sampling procedure was used where a routine capillary blood test (INR_{POCT}) is compared to the result from a vein blood sample from the same individual analysed at ELCR (INR_{ELCR}). The ratio of INR_{POCT}/INR_{ELCR} is an indicator of analytical performance with 1.0 corresponding to the highest degree of performance.

Outcome measures

The TTR for individual patients (i-TTR) was calculated according to the method proposed by Rosendaal et al [9], which uses linear interpolation to assign an INR value to each day between two successively observed INRs. If the sampling interval exceeded 60 days, values were not interpolated. Patients with less than three consecutive INRs were excluded in order to achieve a meaningful estimation of the TTR. Likewise, patients who initiated warfarin treatment had the first two weeks of INRs excluded from the analysis. For patients with heart valve disease, an INR target interval of 2.0-3.5 was chosen. In addition, the mean TTR for each practice (c-TTR) was calculated and used in the statistical analysis.

Statistics

Categorical variables are described by frequency and percentage, continuous variables by their mean and standard deviation (SD). We used multivariable, multilevel linear regression to examine the association of each of the practice organisation characteristics and patient treatment management characteristics with TTR. Each characteristic was analysed separately, but its effect was adjusted for the patient's age and sex. A practice random effect was used to adjust for the correlation of patients within each practice. We used SAS version 9.3 for data management and for statistical analyses. A p-value below 0.05 was considered significant.

Ethics

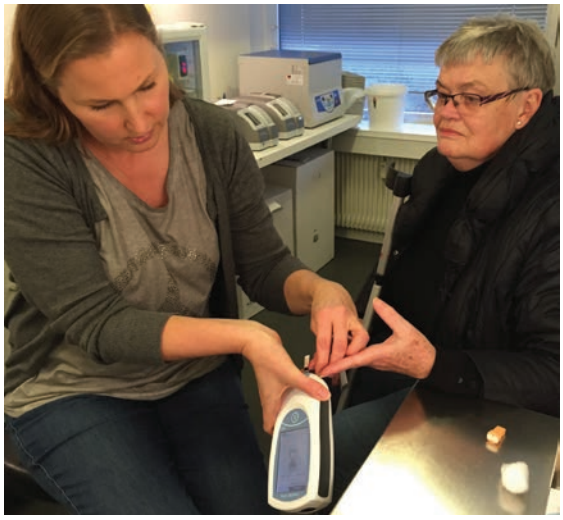
The study fulfils the Declaration of Helsinki II and was approved by the Danish Data Protection Agency and by the Committee for Multicentre Studies of the Danish College of General Practitioners.

Trial registration: not relevant.

RESULTS

The characteristics of the 20 participating practices (Figure 1) are shown in **Table 1**. In all practices but one, nurses were responsible for blood sampling, analysis of blood samples and registration of INRs in the patient record system. No practices had defined exact INR limits for involvement of the GP in treatment decisions regarding dosage and thresholds for repeat blood sampling after an out-of-range INR measurement. In 18 practices (90%), dosage adjustments were made using an analogue decision support.

A total of 557 patients were identified, 447 of whom (80.3%) had three or more INRs performed in the study period (**Table 2**). Seven patients started warfarin treatment in the study period and had the first two weeks of treatment excluded from analysis. Of 447 patients, 39 had no ICPC code (8.7%) and 30 patients (6.7%) had none of their INRs laboratory coded.



International normalised ratio measurements using point of care testing is a very common procedure in general practice. The procedure as well as dosage adjustments of warfarin treatment is generally performed by practice nurses.

In total, 3,570 INR values were obtained from the GPs' electronic patient records. The mean number of INRs per patient was 6.9 (SD: = 3.5). Overall, the mean INR was 2.5 (SD = 0.8), and the mean interval in days between INRs was 22 days (SD = 15).

TABLE 1

Patient characteristics (n = 447)..

Gender, n (%)	
Men	259 (58)
Women	188 (42)
Age, yrs, mean (standard deviation)	73 (10.8)
Indication[a] (%)	
Atrial fibrillation	351 (71.6)
Deep vein thrombosis	52 (10.6)
Pulmonary embolus	19 (3.8)
Heart valve disease	25 (5.1)
Other heart condition	4 (0.8)
No ICPC code	39 (8.0)
Patients with an ICPC code, n (%)	
Yes	408 (91.3)
No	39 (8.7)
Patients with mean duration between INRs, n (%)	
< 10 days	25 (5.6)
10-20 days	165 (36.9)
21-30 days	187 (41.8)
31-40 days	66 (14.8)
> 40 days	4 (0.9)
Patients with INR laboratory code, n (%)	
> 80% of samples	377 (84.3)
< 20% of samples	70 (15.7)
None	30 (6.7)

ICPC = International Classification of Primary Care; INR = international normalised ratio.
a) Based on the first ICPC-code in electronic patient record at any time. Patients can have > 1 diagnosis.

TABLE 2

Multivariable, multilevel linear regression model for the association of each of the practice organisation characteristics and patient treatment management characteristics with time in therapeutic range.

	n (%)	TTR[a] (95% CI), pp	p-value
Practice characteristics (n = 20)			
Practice type		4.2 (–0.7-9.0)	0.09
Single-handed	10 (50)		
Group	10 (50)		
Nurse weekly working hours per GP		–1.1 (–5.8-3.7)	0.65
> 25 h per week	11 (55)		
≤ 25 h per week	9 (45)		
Practices with		1.6 (–3.0-6.0)	0.49
> 1,600 patients	11 (55)		
≤ 1,600 patients	9 (45)		
Practices with		3.5 (–1.0-8.0)	0.13
> 20 patients in OACT treatment	14 (70)		
≤ 20 patients in OACT treatment	6 (30)		
Co-operation with other practices		0.9 (–6.3-4.4)	0.73
Yes	14 (70)		
No	6 (30)		
Use of decision support		6.4 (–1.9-15.0)	0.13
Yes	18 (90)		
No	2 (10)		
Use of paper back-up file[b]		4.4 (–11.0-18.0)	0.16
Yes	6 (30)		
No	14 (70)		
Months registered for data-capture		1.5 (–3.2-6.1)	0.53
> 24 months	14 (70)		
≤ 24 months	6 (30)		
Quality controls, n/yr (2012)		–1.9 (–6.5-2.7)	0.40
> 11	11 (55)		
≤ 11	9 (45)		
Use of CoaguChek with other practices		0.9 (–6.3-4.4)	0.73
Yes	14 (70)		
No	6 (30)		
Share nurse with other practice		5.1 (2.2-12.0)	0.16
Yes	2 (10)		
No	18 (90)		
Patient characteristics (n = 447)			
Patients with mean duration between INRs			
< 10 days	25 (5.6)	–21 (–31–-11)	0.0002
10-20 days	165 (36.9)	–11 (–16–-6)	0.0001
20-30 days	187 (41.8)	0	
30-40 days	66 (14.8)	13 (6.9-20.0)	0.0003
> 40 days	4 (0.9)	17 (–5.6-40.0)	0.1314
Patients with an ICPC code		–12 (–20.0-–3.7)	0.0062
Yes	408 (91.3)		
No	39 (8.7)		
Patients with an INR laboratory code		3.4 (–3.0-9.8)	0.28
> 80% of samples	377 (84.3)		
< 20% of samples	70 (15.7)		

CI = confidence interval; EPR = electronic patient record; GP = general practitioner; ICPC = International Classification of Primary Care; INR = international normalised ratio; OACT = oral anticoagulation treatment; PP = percentage points; TTR = time in therapeutic range.

a) Difference in TTR attributable to the corresponding practice characteristic adjusted for gender and age.

b) In addition to entry in the EPR, the INRs were also entered in a paper file.

Figure 2 shows the distribution of c-TTR and the number of patients on warfarin treatment in each practice. The mean c-TTR for all practices was 67.3% (SD = 6.7%). The mean c-TTR for group practices and for single-handed practices was 70.0% (SD = 3.6%) and 64.6% (SD: 8.0), respectively. This difference was not significant (4.2 percentage points (pp), 95% CI: –0.8-9.2).

Patients with short time intervals between INRs had a significantly lower c-TTR than patients with longer intervals, e.g. 10-20 days (–0.11 pp, 95% CI: –0.16-–0.06). Similarly, patients with no ICPC diagnostic code had a significantly lower c-TTR than patients with an ICPC code (–11.8 pp; 95% CI: –19.9-–3.7). We found no significant correlation between other practice characteristics and c-TTR (Table 2).

The mean i-TTR for all 447 patients in the population was 69.3% (SD = 23.9%), and 248 patients (55.5%) had an i-TTR above 70%.

The mean of the ratio INR_{POCT}/ INR_{ELCR} was 1.050 (SD = 0.106) in the study group and 1.040 (SD = 0.123) in the control group, indicating an analytical quality in the study group equivalent to that of the control group.

DISCUSSION

In 20 general practices with a total of 447 patients treated with warfarin and managed by INR POCT, we found a mean c-TTR of 67.3%. There was a tendency for group practices to perform better than single-handed practices, but the difference was not significant. Generally, patient management was performed by practice nurses, and dosage adjustments were made using an analogue decision support chart. External quality assessment of the POCT instruments used by the GPs in the study group relative to the control group showed a high quality of analytical performance.

Few studies have addressed the quality of OACT in primary care in Denmark despite the fact that the majority of patients are managed in this setting. Holm et al reported a TTR of 69.9% among patients in OACT with warfarin in 142 general practices [6]. After completion of a shared care quality improvement programme, which included 393 patients in 64 practices, TTR increased to 76.3% [7]. In a study from the county of Funen (2005), a TTR of 79% was achieved after introduction of a computerised decision-support system in 22 practices treating 293 patients [8].

In these studies, INRs were analysed at centralised laboratories, the target INR interval was set between 2 and 3.5, and participating practices had few patients, which underlines the need for studies that are more in line with current treatment practice.

Internationally, studies of the quality of OACT in general practice have consistently shown poor results [10], and few studies have specifically addressed the use

of INR POCT in general practice [11, 12]. Furthermore, anticoagulation clinics have been shown to perform significantly better than general practices [13]. In Denmark, Skov et al reported a mean c-TTR of 73.8% at an anticoagulant clinic, indicating a slightly superior quality in these clinics [14]. Whether this result holds true for Danish anticoagulant clinics in general is not known due to the absence of systematic quality data.

In our study, we found a mean i-TTR of 69.3% which suggests that Danish GPs using INR POCT provide OACT of good quality [2]. Of all patients, 44.5% had i-TTRs below 70% and ought to be considered for treatment with a NOAC instead of warfarin. This management decision is often complex and involves taking into account contraindications, financial constraints, patient preferences and cost-benefit analyses [3]. NOACs have been shown to be non-inferior to warfarin in the prevention of thromboembolic complications in non-valvular atrial fibrillation and superior in reducing the occurrence of intracranial bleeding. These results are based on studies where the warfarin-treated groups achieved mean c-TTRs of 55-64%, i.e. thresholds that are lower than the mean c-TTR for all practices in our study [15]. We would therefore expect a less pronounced overall effect of switching from warfarin to a NOAC in our study population.

Our study indicates that some practices have more difficulties achieving high-quality OACT than others, but comparison of the performance of individual practices should be done with caution since our TTR calculations do not include a risk-adjustment measure that takes into account differences in the case-mix due to gender, age, co-morbidity, substance abuse, poly-pharmacy, hospitalisations and socio-economic conditions [16].

An electronic decision-support tool has been developed which utilises electronic data capture of INRs to assist GPs in monitoring TTR and making appropriate dosage adjustments [17]. Since all practices in our study used an analogue decision support chart or no support at all, this measure could lead to an increase in quality [18].

In addition to this, our study suggests that diagnostic coding of patients leads to better quality. Since diagnostic coding is a prerequisite for gaining access to the electronic decision support tool, one might hypothesise that a more widespread systematic coding practice will contribute to better quality.

Contrary to this, laboratory coding of INRs did not influence quality. Assigning laboratory codes to laboratory values in the electronic patient record (EPR) renders data more easily accessible to staff and provides a basis for appropriate management decisions. If the INRs are entered into the EPR without a laboratory code, they will not be included in an estimation of the TTR and this will, in turn, impede correct management.

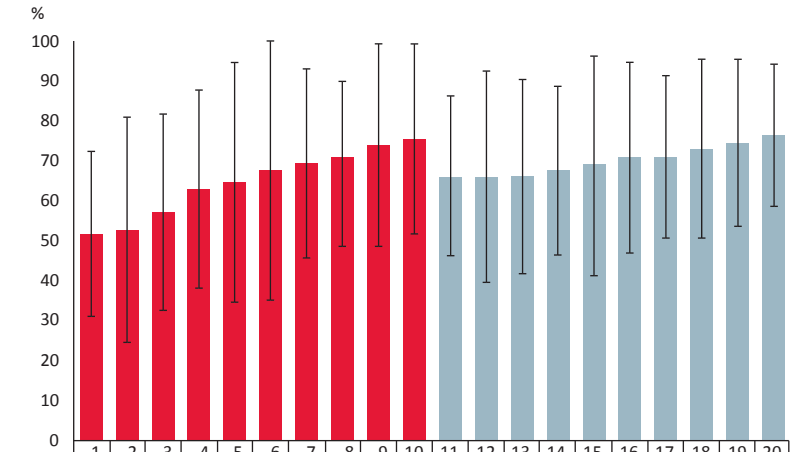
Apart from sampling interval and diagnostic coding, we found no significant correlation between the organisational characteristics of the practices and the TTR. This could be due to insufficient power of our study, but the results are in accordance with a study by Rose et al who found that organisational characteristics such as number of patients per provider, use of EPR and visit format had limited influence on performance [19]. Instead, quality improvement measures should focus on adequate staffing, adherence to evidence-based guidelines, higher staff qualifications and internal efforts to measure performance [20].

The strengths of the study are the high validity of the data collected in the individual practices and the random selection of the practices. Collecting data in person in the clinics allowed the authors to ascertain in detail how the GPs and their staff managed all aspects of the treatment.

The weaknesses of the study are the small number of practices and patients included in the study and the fact that the study was confined to the Capital Region of Denmark, which has a markedly lower number of group practices than other regions in Denmark. Furthermore, one cannot rule out selection bias since participating practices with an interest in INR POCT will be more inclined to participate in the study, which limits the generalisability of the results.

FIGURE 2

TTR in 20 practices. Mean c-TTR (standard deviation) for all practices was 67.3% (6.7%). The mean c-TTR was 64.6% (8.0%) in single-handed practices (■), and 70.0% (3.6%) for group practices (■). Mean i-TTR for all patients was 69.3% (23.9%).



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
TTR, %	52	53	57	63	65	67	69	71	74	75	66	66	66	67	69	71	71	73	74	76
Patients, n	9	15	10	16	12	6	8	23	10	30	6	26	55	31	15	24	22	35	45	49

Practice no.

c-TTR = mean TTR for each practice; i-TTR = TTR for individual patients; TTR = time in therapeutic range.

CONCLUSION

Our study shows that management of patients in OACT

with warfarin in practices using INR POCT is mainly performed by nurses and that most practices achieve good therapeutic control.

CORRESPONDENCE: *Thomas Løkkegaard,* The Research Unit for General Practice in Copenhagen, P.O. Box 2099, 1014 Copenhagen, Denmark.
E-MAIL: thl@dadlnet.dk
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