

Warfarin dosing and follow-up: adherence to the local guideline at a health centre in Malta

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ABSTRACT

Background

Point-of-care testing (POCT) describes any test performed outside hospital where the result influences patient management.

Objective

This study aimed to establish whether warfarin dosing and follow-up at the local point-of-care (POC) clinic at Cospicua Health Centre (CHC) was performed in adherence to the locally provided 'Clinical Standard Operations Procedures for Health Centre POC-Based ACC Guideline' which is based on previous guidelines as published by the British Committee for Standards in Haematology (BCSH) on POCT.

Method

A set of five random consecutive entries for each of 50 randomly selected patients attending the POC clinic at CHC between January and September 2019 were analysed. The data collected included indication for anticoagulation, International Normalised Ratio (INR) result on date of dosing, new warfarin dose prescribed and follow-up given in days/weeks. Eligibility criteria included records of a minimum of five consecutive uninterrupted visits and a target INR range of 2-3, 2.5-3.5 or 3-4.

Result

A total of 250 entries were studied, and found to be mostly female patients (60%). The most common indication for anticoagulation in the population was atrial fibrillation (70%). Warfarin dosing was performed according to the local guideline in 80.4% of recorded entries. However, follow-up date given was only according to the local guideline in 42.8% of cases.

Conclusion

The lack of guideline adherence to local dosing and follow-up recommendations may lead to unsafe warfarin prescribing, increased healthcare resource expenditure and unnecessary appointments at busy POC clinics. Stricter adherence to the local guideline and implementation of an improved system of documentation remains desirable. The reasons behind this needs to be studied further when dedicated software was made available to doctors to aid in warfarin dosing.

Keywords

Point-of-care testing, warfarin, International Normalised Ratio.

INTRODUCTION

Community point-of-care testing (POCT) has greatly facilitated the means by which patients requiring anticoagulation are tested in a comfortable, fast and streamlined manner. Not only does this achieve moderate-to-high time in therapeutic range (TTR) more readily (Mooney, et al., 2019) but it also results in an increased patient satisfaction (Riva, et al., 2020) and longer TTR from POCT (Okuyama, et al., 2014). Similar results were also shown in other point-of-care (POC) tests, such as haemoglobin A1c (HbA1c), lipid profile and comprehensive metabolic panels (Crocker, et al., 2013). In Malta, POCT is cheaper than the laboratory-centralized system for INR testing (Zammit, et al., 2011) and is equally accurate (Riva, et al., 2017).

The POC service was extended to Cospicua Health Centre (CHC) in July 2014, complementing the previous method of venous sampling. The machine provides an immediate result within a matter of seconds, enabling the attending doctor to issue a prescription for warfarin dose and duration for follow-up at the time of testing. Records of the result and prescription are recorded in the patient's file and on a dedicated booklet which are kept by the clinic and patient respectively. This novel means of INR testing has improved the quality of life for many of the local citizens and service users as it does not necessitate visits to the island's general hospital and there is no delay for warfarin prescriptions. It also enables further assessment of the patient at the time of testing in scenarios where the INR result is grossly outside the therapeutic range.

When prescribing warfarin and advising follow-up, the doctor may refer to the easily accessible local guideline 'Clinical Standard Operation Procedures for Health Centres POC Based ACC' [hereafter local guideline] (see Table 1) which is based on the guidelines published by the British Committee for Standards in Haematology (BCSH) on POCT (Keeling, et al., 2011). Alternatively doctors may use the DAWN AC Anticoagulation Software which guides dosing. The programme is available at CHC and doctors received training in its use by the end of 2018.

During the authors' assignment to this clinic it was noted that this local guideline was not always being adhered to and that the relevant software was not in use. Furthermore there appeared to be issues with the dedicated POC documentation section in the patient's file. In view of this, the authors decided to conduct a formal study with the primary aim of assessing the adherence of doctors prescribing warfarin dose and follow-up duration at the CHC POC clinic with the local '*Clinical Standard Operation Procedures for Health Centres POC Based ACC*' guideline. Secondary aims included identification of possible limiting factors to local guideline adherence.

Table 1: Algorithms for warfarin dosage changes according to local guideline

Goal INR Range	Current INR	Adjustments	Recommended Follow-Up
2 - 3	< 1.5	Seek provider input to assess need for low molecular weight heparin (LMWH)	Twice weekly until INR in goal range
	1.5 – 1.7	Increase next dose by 50%, weekly dose to increase by a total of 10%	Weekly until INR in goal range
	1.8	Increase next dose by 50%, then resume normal dosing pattern	10-14 days
	1.9 – 3.2	No change	4-6 weeks
	3.3 – 3.5	Decrease next dose by 50%, then resume normal dosing pattern	10-14 days
	3.6 – 4.0	Decrease next dose by 50%, weekly dose to decrease by a total of 10%	Weekly until INR in goal range
	4.1 – 5.0	Decrease dose by 50% today and tomorrow, weekly dose to decrease by a total of 15%	Within 5 days
2.5 – 3.5	<2.0	Seek provider input to assess need for LMWH	Twice weekly until INR in goal range
	2.0 – 2.2	Increase next dose by 50%, weekly dose to increase by a total of 10%	Weekly until INR in goal range
	2.3	Increase next dose by 50%, then resume normal dosing pattern	10-14 days
	2.4 – 3.7	No change	4-6 weeks
	3.8 – 4.0	Decrease next dose by 50%, then resume normal dosing pattern	10-14 days
	4.1 – 5.0	Decrease next dose by 50%, weekly dose to decrease by a total of 10%	Weekly until INR in goal range
3 - 4	<2.0	Seek provider input to assess need for LMWH	Twice weekly until INR in goal range
	2 – 2.4	Increase next dose by 50%, weekly dose to increase by a total of 10%. Seek provider input to assess need for LMWH	Weekly until INR in goal range
	2.5 – 2.8	Increase next dose by 50%, then resume normal dosing pattern	10-14 days
	2.9 – 4.2	No change	4-5 weeks
	4.3 – 4.5	Decrease next dose by 50%, then resume normal dosing pattern	10-14 days
	4.6 – 5.0	Decrease next dose by 50%, weekly dose to decrease by a total of 10%	Weekly until INR in goal range

(NB: INR - International Normalised Ratio)

METHOD

Study Design

A preliminary literature review was carried out prior to determine the data to be collected for a descriptive, cross-sectional, retrospective study. Approval was sought and obtained from the Data Protection Officer of the Primary Health Care Department. The research study was found to present no potential issues in the domain of research ethics and data protection.

Subsequently, a spreadsheet was created whereby data collected included entry number, hospital number, age, sex, indication for warfarin, target range, date of dosing (DOD), current dose (i.e. dose prior to testing) in mg, INR result on DOD, new dose (i.e. dose prescribed on DOD) in mg, follow-up given in days/weeks and resultant INR. A drop-down menu was included for both dose and follow-up to indicate whether this was done according to the local guideline (Yes/No).

Patient Population and Data Collection

Patients were randomly selected from the population with an appointment at the POC-clinic

at CHC within a 9-month period between January and September 2019. Data was retrospectively collected primarily from the patients' clinical files and from the patients' anticoagulation booklets. Eligibility criteria included a clear record of a minimum of five consecutive uninterrupted visits and having a target INR range of 2-3, 2.5-3.5 or 3-4 (these ranges are covered by the local guideline). Interrupted entries, that is failure to attend a follow-up appointment or interim changes to the original dosing and follow-up plan, were excluded from the study. From the eligible patients, 50 random patients were selected and for these a random set of five consecutive entries of POC testing were identified (n = 250). At no point in the study did the authors encounter evidence for use of DAWN software.

RESULTS

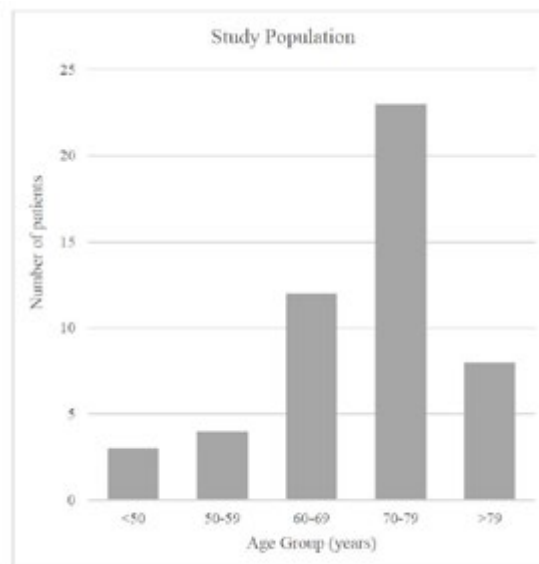
Demographics

Fifty patients were included in the study, of which 30 (60.0%) were female and 20 (40.0%) were male. Table 2 demonstrates the subject population's age statistics and Figure 1 shows the age group distribution.

Table 2: Tabulation of age statistics for subject population

Descriptive statistic	Age (years)
Range	47 - 84
Mean	70.18
Median	72
Mode	72

Figure 1: Column graph showing distribution of age groups in subject population



Indication for anticoagulation

The majority of subjects (70.59%) were on warfarin for atrial fibrillation (AF) whilst the least common conditions requiring anticoagulation were aortic valve replacement (AVR – 3.92%) and mitral stenosis (MS – 3.92%). Other conditions encountered in the subject population included deep vein thrombosis (DVT – 9.8%), mitral valve replacement (MVR – 5.88%) and pulmonary

embolism (PE – 5.88%). One patient was being anticoagulated simultaneously for MS and AF (see Table 3).

A therapeutic INR range of 2-3 was indicated in 46 patients (92%), whilst the desired range for the remaining 4 patients (8%) was 2.5-3.5 (one AVR and three MVR). None of the patients in the study had a desired INR range of 3-4.

Table 3: Indication for anticoagulation for the subject population

Indication for Anticoagulation	Number of Patients with condition
Atrial fibrillation (AF)	35
Mitral valve replacement (MVR)	3
Aortic valve replacement (AVR)	2
Deep vein thrombosis (DVT)	5
Pulmonary embolism (PE)	3
Mitral stenosis (MS)	1
MS + AF	1

Adherence to local guideline

When dosing warfarin at POCT, almost one fifth of prescribing doctors (19.6%) diverged from the respective local guideline according to the patient's desired INR range, with a tendency towards under dosing. For the remaining majority, i.e. 201 of 250 entries (80.4%), the dose of warfarin given was according to the local guideline's recommendations (see Figure 2). When the Rosendaal method of calculating therapeutic time in range (TTR) was used to assess the result (Rosendaal, et al., 1993), patients who were given warfarin according to local guidelines had a higher TTR (74.9%) when compared with those for which the local guideline were not observed (41.1%).

Only 42.8% of all entries had a follow-up appointment scheduled according to the local guideline. Out of the remaining 57.2%, the great majority opted for an earlier appointment

(see Figure 3). Indeed 92% of the latter had an earlier appointment; if these were given a correct appointment these patients would have been spared a total of 150 days, one of whom was brought earlier by 28 days. In contrast, the remaining patients were given a later appointment for a total of 30 days, with one given an appointment 14 days later than was indicated. The TTR in patients given warfarin according to local guideline and those in which the local guideline was not observed was comparable at 68.2% and 68.1% respectively.

Figure 2: Pie chart showing the proportion of doctors who adhered to the proposed changes in warfarin dosing as per the algorithms for warfarin dosage changes according to local guideline (see Table 1)

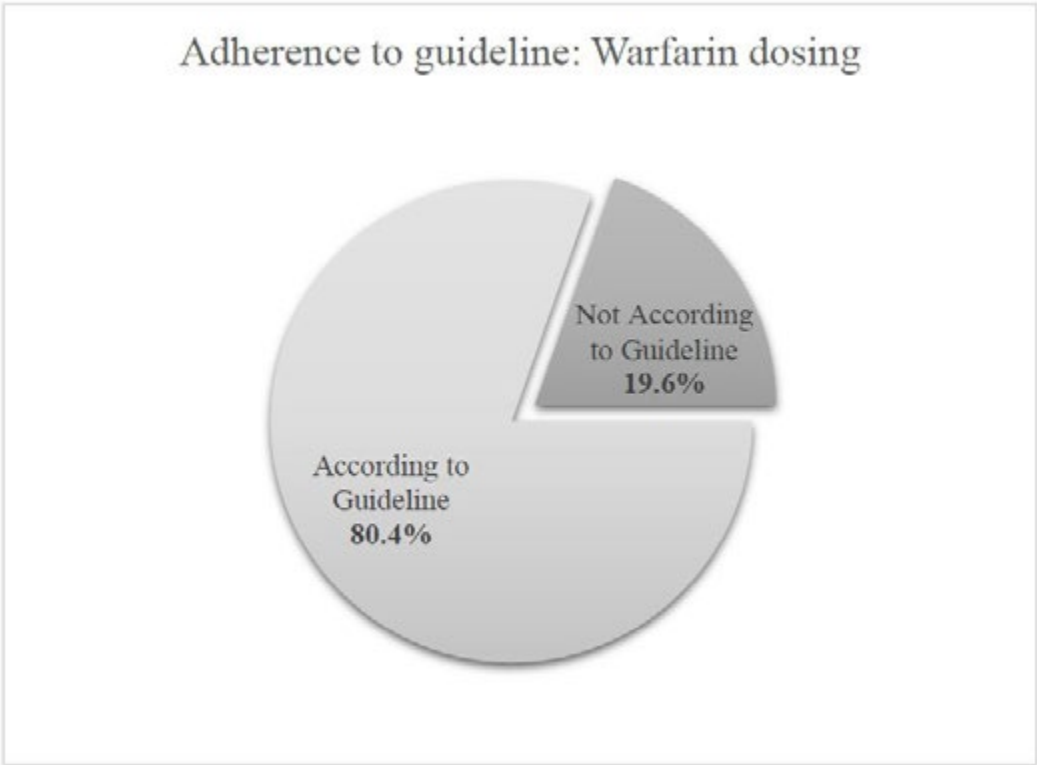
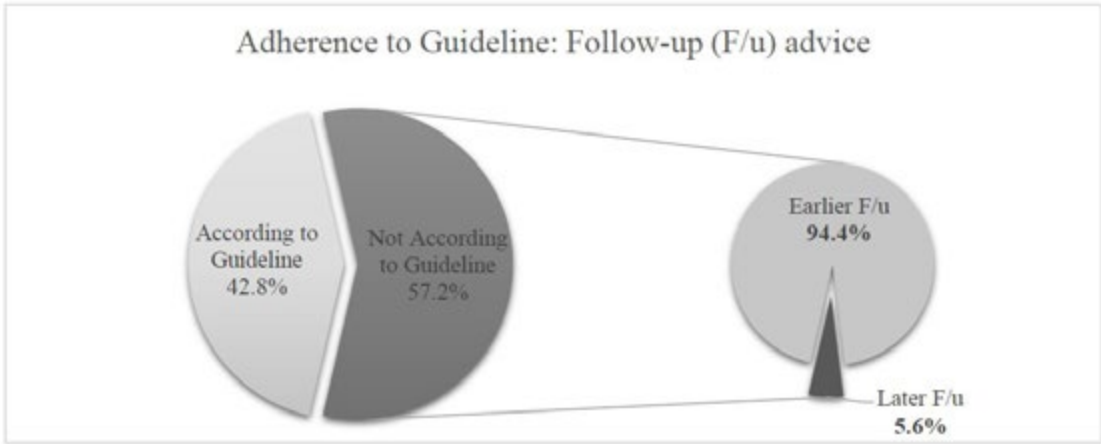


Figure 3: The pie chart on the left shows the proportion of doctors who adhered to the proposed changes in providing follow-up as per the algorithms for warfarin dosage changes according to local guideline (see Table 1). The pie chart on the right shows the proportions of earlier / later follow-ups given by the doctors who did not adhere to the follow-up advice proposed by the local guideline



DISCUSSION

The study highlighted the fact that doctors' adherence to the local standardized method guiding warfarin dosing (80.4%) and especially follow-up (42.8%) is lacking. A tendency towards under-dosing and advising earlier follow-up appointments emerged. The general tendency to offer earlier follow-up advice was however clear, with only 5.6% of the proportion of doctors not adhering to the local guideline offering follow-up appointments later than advised. This seemingly 'safer' approach did not result in better outcomes. Indeed, under-dosing decreased TTR and earlier follow-ups did not result in any benefit, with its unnecessary inconvenience for the patient, increased workload on POC clinic staff and improper allocation of healthcare resources. This is in line with the findings of Franke, et al. (2008) who had shown that adherence of doctors to a standardized protocol guiding warfarin dosing increases the percentage of patients being found within the desired INR range on follow-up testing.

Various factors might be considered for earlier appointments, including the individual patient's

ability to maintain a moderate-to-high TTR, current or recent use of medications such as antibiotics and/or other drugs which interfere with the mechanism of cytochrome P450 (CYP450) enzymes, seasonality, diet and alcohol intake. Some of these factors may be indirectly related to each other, such as the seasonality with diet and alcohol intake. To address this limitation, entries considered in the study spanned from January until September of 2019.

These confounding factors, however, should prompt the attending doctor to refer the patient for central laboratory testing (i.e. to the central ACC) at Mater Dei Hospital (MDH) especially in the presence of 3 consecutive INRs outside the therapeutic range of 1.9-3.2 as stated in the 'Non-eligibility criteria for patient transfer from the current system to the HCPOC ACC' in the local guideline (see Table 4). When analyzing the data, it transpired that 4 of the 50 patients (8%) with INRs outside the range of 1.9-3.2 were followed-up at CHC POC clinic instead of being seen at the MDH ACC.

Table 4: Non-eligibility criteria for patient transfer from the current system to the health centre point-of-care anti-coagulant clinic (HCPOC ACC) according to the clinical standard operation procedures for HCPOC-based ACC

1	Unstable International Normalised Ratios (INRs) as defined by 3 consecutive INRs outside the therapeutic range of 1.9 – 3.2
2	Patients with a target INR >3.0
3	Patients with antiphospholipid syndrome
4	Patients with liver disease
5	Patients with severe renal failure
6	Patients on other anticoagulants including those on dual antiplatelet agents
7	Patients suffering from active cancer (receiving treatment with chemotherapy or radiotherapy)

Patients who regularly attend POC clinic at their respective health centre (HC) should not simultaneously attend the MDH ACC as the two modalities of measurement are not entirely interchangeable. Studies show that there is a positive bias of around 0.24-0.35 INR units for POCT when compared to conventional central laboratory instrumentation for INR monitoring, which becomes more significant with increasing values of INR (Dorfman, et al., 2005), thus highlighting the need to refer the patient to MDH ACC in case of unstable INRs.

The POC clinic's current documentation system can be improved. In most cases, successive entries were jotted down in random, untitled sections of the patient's file, making continuity of care difficult. A dedicated form should be used for POC clinic entries, preferably using that provided by the DAWN software, thus enabling the prescribing doctor to rapidly find the previous entry and dose accordingly and help avoiding confusion and prescribing errors. Such a form would include:

- (i) *Patient details*: name, hospital number, age, indication for warfarin, target INR range
- (ii) *Date of POC clinic appointment*
- (iii) *Last warfarin dose prescribed and follow-up advice in days/weeks*
- (iv) *Today's INR result*
- (v) *New warfarin dose and follow-up advice in days/weeks*
- (vi) *Tick-the-box option to indicate whether local guideline was adhered to*
- (vii) *Remarks section*: to include any concurrent CYP450 enzyme-inducers/inhibitors along with a justification for not following the local guideline in the respective cases
- (viii) *Name, signature and registration number of prescribing doctor*

The small sample size and performance of the study in only one out of eight public health centres in Malta are limitations to this study. This did not allow analysis of the effect of training and level of expertise on quality of care.

Nonetheless the random selection of 50 patients who regularly attend the POC clinic at CHC for

warfarin dosing remains a good representation of the regional population (when considering that 15 to 20 appointments are given daily with a maximum follow-up of no more than at 6 week intervals). The results highlight challenges in the regional adherence of the local guideline as well as identified factors influencing outcomes. Conspicuous is the lack of use of the DAWN software which would have addressed many issues highlighted above, namely correct dosing and setting of an appropriate follow-up appointment. The reasons behind the lack of use of this software remain unknown, requiring separate study and eventual implementation.

CONCLUSIONS

This study at CHC has shown that warfarin dosing in the majority of cases is in line with the provided local guideline, but improvements are necessary in the advice for follow-up. This may be achieved if local protocols are more strictly adhered to so as to ensure better TTRs, decreased patient inconvenience and increased efficacy of healthcare resources. Non-eligibility criteria for POCT should be kept in mind and patients should be referred to central laboratory instrumentation monitoring at MDH when appropriate. The implementation and use of DAWN software should facilitate the chronological recording of the patients' warfarin dosing history, with a subsequent decrease in the chance of errors in prescribing.

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