

Are patients on warfarin with high INR treated according to published guidelines?

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Citation

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Abstract

Objective: Australasian guidelines for the treatment of over-anticoagulation have been published. We aimed to determine whether emergency department [ED] patients taking warfarin who have high INR were treated according to guidelines. **Methods:** This retrospective observational study included ED patients taking warfarin with $\text{INR} \geq 4$. Data included demographics, warfarin indication, bleeding evidence and subsequent management. Outcome of interest was proportion treated according to guidelines; analysed by descriptive statistics. **Results:** 201 patients were studied; median age 74 years, 47% female. Atrial fibrillation was the main indication for warfarin [63%]. 48 patients [24%] presented with bleeding, of which 22 were classified as major bleeds. All patients with major bleeding received reversal treatment; with 64% receiving recommended triple therapy. 33% in the non-bleeding group received reversal treatment. **Conclusion:** There was reasonably good compliance with the guidelines, especially for patients with major bleeding. Vitamin K doses were suboptimal in a significant proportion of cases.

Support: This work was undertaken with departmental funds only. No external support was received.

INTRODUCTION

An elevated INR is a major determinant in the risk of bleeding in anticoagulated patients. ^{1, 2} Previous research has established a high prevalence of a supra-therapeutic INR in the Emergency Department [ED] population taking warfarin. ³

In 2004, the Warfarin Reversal Consensus Group, on behalf of the Australasian Society of Thrombosis and Haemostasis, published consensus guidelines for warfarin reversal. ¹ The aim of this study was to determine whether patients taking warfarin who have an abnormally high INR measured in the ED are being treated according to those guidelines.

METHODS

This observational study was conducted by explicit retrospective medical record review. ⁴ Participants were patients on warfarin presenting to the ED of Western or Sunshine Hospitals [community teaching hospitals with annual ED census of 33,000 and 60,000 respectively] during the period January 2006 and June 2007 who had an INR

reading of ≥ 4 . Patients were identified from a pathology database.

Data was collected onto an explicit data form. Data collectors were not blinded to the study hypothesis. Data collected included demographics, indication for warfarin, evidence of bleeding, subsequent treatment and ED disposal. Patients who experienced bleeding were categorised as major and minor. Major bleeding was defined as gastrointestinal bleeding [haematemesis and/or malaena], intracranial haemorrhage and any bleeds that led to subsequent haemodynamic compromise or need for surgery. This group was considered to correlate with the 'clinically significant' category identified in the guidelines. Minor bleeds were defined as uncomplicated bleeds which self ceased and did not have any of the above features. This group included bruising.

INR was measured by the hospital pathology service. The upper extreme could only be set at the highest reporting point of the laboratory: [$\text{INR} > 8.5$]. The guideline treatment of $\text{INR} > 9$ was interpreted as applying to $\text{INR} > 8.5$. Treatment was classified as reduction or cessation of warfarin therapy, administration of Vitamin K, Fresh Frozen

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Plasma [FFP], Prothrombinex or combinations of these.

The primary outcome of interest was the proportion of patients treated according to the Australasian guidelines for management of over-anticoagulation. Data was analysed using descriptive statistics. A study period, starting a year after the guidelines were disseminated, was chosen to allow time for the guidelines to have been implemented while giving a sample size such that reasonable conclusions could be drawn. Our aim was 150 patients. The study was approved as a quality improvement activity under the NHMRC Quality Assurance guidelines and formal ethics approval was not required.

RESULTS

201 patients were included in the analysis. The derivation of the sample is shown in Figure 1. The median age was 74 years [range 16-94], with 47% being female. The main indication for warfarin use was atrial fibrillation [64%], followed by valve replacement [21%] and pulmonary embolism/ deep venous thrombosis [19%]. Indication for warfarin was unclear in only 2 patients [1%]. Most patients [78%] had been taking warfarin for more than one year. INR distribution is shown in Figure 2.

Figure 1

Figure 1: Derivation of the sample

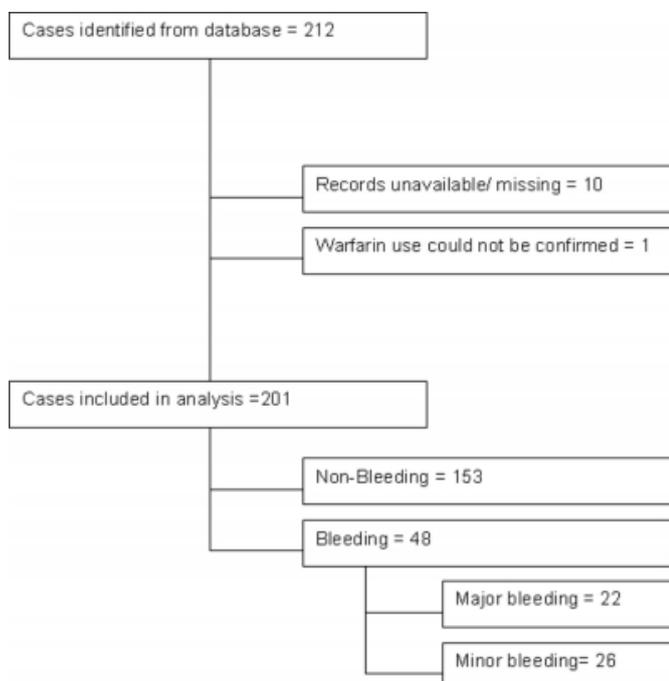
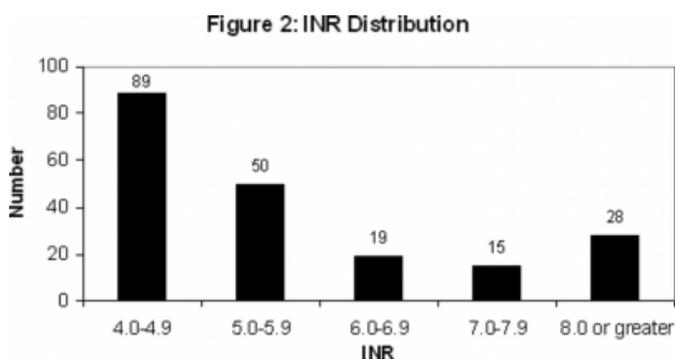


Figure 2



48 patients [24%] were experiencing bleeding [22 major, 26 minor]. Of the 153 non-bleeding patients, 19 had been referred to the ED for a high INR only and the remainder presented with non-warfarin related complaints.

Reversal treatment was given to a total of 88 patients [44%]. All patients experiencing major bleeding received reversal therapy and 14 of these [14/22; 64%] received the recommended triple reversal combination [vitamin K, Prothrombinex and FFP]. [Table 1]. In 53% of patients [10/19], vitamin K was given in less than recommended doses. Table 2 shows the treatment of the minor bleeding group. Fifteen patients [58%] received reversal treatment. Vitamin K was the mainstay of treatment however 2 patients also received FFP. The non-bleeding group received reversal treatment as detailed in Table 3. 48 patients [31%] received Vitamin K, with 17 [35%] receiving doses of 5mg and higher. In two cases, only Prothrombinex and FFP were given.

Figure 3

Table 1: Summary of treatment for the major bleeding group

Treatment	Number [%]
Triple therapy: Vitamin K, FFP and prothrombinex	14 [63.6%]
Vitamin K + FFP	3 [13.6%]
FFP + Prothrombinex	3 [13.6%]
Vitamin K + Prothrombinex	2 [9.1%]
Some combination therapy	22 [100%]

Figure 4

Table 2: Summary of treatment for the minor bleeding group

Treatment	INR <5 [11]	INR 5-8.5 [12]	INR >8.5 [3]
Vitamin K: n [%]	4 [36]	8 [67]	3 [100]
Dose >5mg: n [%treated]	2 [50]	0 [0]	2 [67]
FFP Units: n [%]	0 [0]	0 [0]	2 [67]
Prothrombinex: n [%]	0 [0]	0 [0]	0 [0]

Figure 5

Table 3: Summary of treatments given to patients without bleeding symptoms

Treatment	INR <5 [65]	INR 5-8.5 [74]	INR >8.5 [14]
FFP Units: n [%]	2 [3]	2 [3]	1 [7]
Vitamin K: n [%]	3 [5]	33 [45]	12 [86]
Dose > 5 mg: n [% treated]	1 [33]	11 [33]	5 [42]
Prothrombinex: n [%]	2 [3]	2 [3]	1 [7]
Packed cells: n [%]	0 [0]	2 [3]	0 [0]
Warfarin Ceased: n [%]	44 [68]	61 [82]	14 [100]
All Treatments [FFP, Vit K, Prothrombinex]: n [%]	1 [2]	0 [0]	0 [0]

DISCUSSION

This is the first Australian study to investigate compliance with the Warfarin Reversal Consensus Guidelines¹ in ED patients. We found reasonably good compliance with the guidelines for patients with major bleeding with respect to agents administered, but doses were below those recommended in a significant proportion of cases, especially for vitamin K. Treatment of non-bleeding patients with INR <5 (65 patients) was well adhered to. Most patients in that group did not receive any active treatment (95%), with warfarin doses omitted or reduced as is recommended by the guidelines. Treatment for the non-bleeding group escalated in line with INR, which is also consistent with the guidelines. This study did not allow us to evaluate the risk of bleeding perceived by the treating physician, which is a factor contributing to decision making in the guidelines. Variation in perceived risk may explain the small number of patients in the non-bleeding group who received treatments in addition to Vitamin K.

Similar studies have been conducted in the USA investigating compliance with the American College of Chest Physicians guidelines for reversal of warfarin⁵. In a scenario-based survey, Wilson et al⁶ found poor compliance with the guidelines, with inappropriate dosages and routes of administration being common. Fan et al, in a retrospective

study focusing on vitamin K administration to reverse the effects of warfarin, also found poor compliance with the guidelines.⁷ Salamat in the UK reported that the introduction of guidelines did not improve use of prothrombin complex extract or vitamin K.⁸ As we did not have pre-guideline data, we are unable to comment on whether the guideline improved practice in the study ED.

The administration of Vitamin K doses varied quite considerably in our study, with doses ranging from 0.5mg to 10mg. Errors were both over-treatment of non-bleeding patients and under-treatment of patients with major bleeding. The problem may be one of understanding the role of Vitamin K in each scenario; complete reversal in those with major bleeding and partial reversal in those without bleeding. Additionally, Prothrombinex was also prescribed less frequently than recommended for reasons that are not apparent.

The uptake of guidelines in clinical settings has been reported to have widely varying success: from very poor to good. Key success factors appear to be the quality and format of the guidelines, clinical leadership, the perceived relevance of the guidelines and dissemination/ implementation strategies.⁹ That compliance with the warfarin reversal guidelines is reasonably good in this study [albeit in a single health service] suggest that the guidelines may be achieving reasonable uptake.

This study has some limitations that should be considered when interpreting the results. Data was collected by medical record review methodology, which is subject to well-known problems with documentation/ missing data. To minimise the problems associated with this method we used explicit data collection and clear, pre-defined definitions of terms. The project was undertaken at two ED within a single health service that share staff and policies. Results may not be generalisable to other settings. Patients were identified for inclusion based on a high INR measured in the ED. There may have been patients taking warfarin who did not have an INR measured in the ED who may have been suitable for this study. Although they are unlikely to have been in the major bleeding group, this may have introduced a selection bias. Additionally, although not the focus of this study, approximately 50% of patients on warfarin who suffer major bleeding have INR <4 and also require reversal therapy. Data was not collected on this group. This methodology did not allow us to collect data on physician's estimate of bleeding risk in those patients without bleeding, thus we are

unable to provide detailed analysis of compliance with the guidelines for the non-bleeding 'at risk' group.

CONCLUSION

There was reasonably good compliance with the guidelines, especially for patients with major bleeding, with respect to agents administered, however doses were not optimal in a significant proportion of cases, particularly for Vitamin K.

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