Who is responsible for the care of patients treated with warfarin therapy?

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Warfarin is the predominant anti-coagulant for protection against stroke in patients with atrial fibrillation and/or mechanical valve replacement. It is also used for management of venous thromboembolism. In Australia, warfarin use is rising at a rate of 9% per annum,[1] with about 30% of patients commencing therapy being aged over 70 years.[2] Despite its efficacy, warfarin remains a major contributor to potentially preventable medication-related adverse events.[3,4] Annual rates of major bleeding range from 1% to 7%, with minor bleeding in 16% of patients with atrial fibrillation.[5,6] A major determinant of bleeding is over-anticoagulation, as reflected by a high international normalised ratio (INR).

Previous research has focused on drug, genetic and patient factors known to increase risk of either sub- or supra-therapeutic response. However, it is increasingly recognised that system of care and qualitative factors such as medication compliance, cognition, warfarin knowledge, and social support[7-10] have a major role in determining the safety of warfarin use.

Anticoagulation therapy with warfarin encompasses a variety of care models, including specialist anticoagulation clinics, pharmacist-assisted care, and point-of-care monitoring. In some Australian states, it typically involves sharing of clinical responsibility between specialists, general practitioners and a pathology service. Within this model, the GP is commonly the care coordinator, while also providing day-to-day management of episodic and chronic conditions.

We proposed to investigate potential weaknesses in management of warfarin therapy, by exploring the possible contributing factors to elevated INRs in community-dwelling patients. The data are qualitative and hypothesis-generating in nature and provide the foundation for a larger project investigating the relative contribution of patient and warfarin care system variables that contribute to over-anticoagulation.

METHODS

Participants

Previously stabilised patients, who subsequently developed an INR ≥ 6.0, were recruited sequentially by a large, private met-

ABSTRACT

Objective: To identify potential weaknesses in the system of managing warfarin therapy.

Design, participants and setting: A structured interview-based study of 40 community-dwelling patients taking warfarin and with an international normalised ratio ≥ 6.0 and 36 of their treating doctors (35 general practitioners and 1 specialist), conducted between July and November 2007. Patients all received services from and were recruited sequentially by a large, private metropolitan pathology provider in Melbourne.

Main outcome measures: Patients' demographic, clinical, cognitive and psychosocial characteristics, warfarin knowledge, medication complexity and adherence; and doctors' experience with, approach to and involvement in warfarin management, and their perception of responsibility for warfarin management and patient education.

Results: Interviews revealed multiple difficulties, including cognitive dysfunction, possible depression, and medication non-adherence, in 30 of 40 patients. Of 36 doctors interviewed, 12 were unaware of these difficulties in their patients. Five doctors considered they had sole responsibility for their patients' anticoagulation, while 15 confirmed a mutual relationship with the pathology service, and 16 deferred total responsibility to the pathology provider. Only 14/36 doctors reported conducting patient education at commencement of warfarin therapy, with the other 22 stating this was the responsibility of the initiating specialist, pathology service or dispensing pharmacist.

Conclusions: There is a need for improved role clarification in coordinating warfarin management. We propose exploring the possibility of a Warfarin Suitability Score to assist better recognition of patients in whom treatment may be problematic, along with a model of care using practice nurses with GPs to facilitate optimal patient care.

ropolitan pathology provider between July and November 2007. Stabilised patients were defined as those who had completed initial dose titration and had INRs within their target range (± 0.2 INR units) for a subsequent period of at least 3 months. Eligible patients were aged ≥ 18 years and were community-dwelling in metropolitan Melbourne. Exclusion criteria included elevated INRs occurring during hospitalisation or in nursing homes. Eligible patients and their treating doctors were contacted by the pathology provider for consent to be interviewed by the researchers.

Data collection and analysis

Data were collected through structured interviews using both forced-response and open-ended questions. Patient interviews were conducted in their homes and focused on demographic and clinical characteristics, psychosocial risk factors, and ability to manage complex medication and understand issues relating specifically to warfarin. Patients were assessed with standardised measures including the Montreal Cognitive Assessment,[11] the five-item Geriatric Depression Scale,[12] Duke Social Support Index,[13] Barthel Index of functional independence,[14] Medication Regimen Complexity Index,[15] and Morisky Medication Adherence Scale.[16]
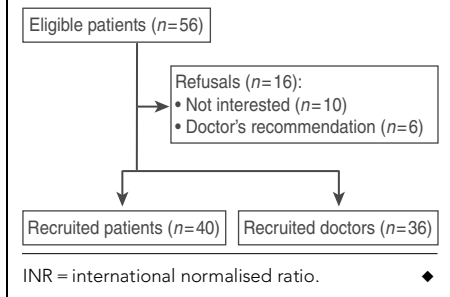
Doctors of recruited patients were interviewed independently at their practices. Doctors' appreciation of the patient's status and record of current medications was compared with details gained from the patient interview, to determine the level of concordance between the two. Information was also sought about the doctors' experience with, approach to and involvement in warfarin management.

The study protocol was approved by Monash University's Standing Committee on Ethics in Research Involving Humans and the Cabrini Human Research Ethics Committee.

RESULTS

Forty of 56 eligible patients (response rate, 71%) and 36 of their 40 treating doctors (35

1 Recruitment process of eligible patients with an INR ⩾ 6 and their treating doctors

Eligible patients (*n* = 56)

Refusals (*n* = 16):
• Not interested (*n* = 10)
• Doctor's recommendation (*n* = 6)

Recruited patients (*n* = 40)   Recruited doctors (*n* = 36)

INR = international normalised ratio.   ◆

GPs and one specialist physician; response rate, 90%) were recruited (Box 1).

Doctors' experience with and approach to warfarin management

Twenty of the 36 doctors reported caring for more than 20 patients taking warfarin. All stated that specialists routinely initiate therapy and refer patients back to the GPs for ongoing management. Although many doctors (23/36) stated that they were comfortable in prescribing warfarin, more than a third (13) reported never making a unilateral decision to prescribe warfarin, preferring referral to a specialist (Box 2). All doctors provided routine prescriptions. Pathology services were used for monitoring and dosing by 32 doctors, primarily due to their time constraints. All doctors reported receiving timely notification of results from the pathology service.

Responsibility for routine warfarin management

Five of 36 doctors considered they had sole responsibility for routine management, 15 regarded management as involving a mutual relationship with the pathology service, and 16 deferred total responsibility to that service (Box 2). In contrast, most patients (33/40) regarded the pathology service to be their first port of call for any anticoagulation concerns. In instances requiring "after hours" medical intervention due to an elevated INR, 22 GPs expected to be collaboratively involved, while 14 had an understanding that the pathology service haematologist would contact the patient directly with the recommended intervention.

Although routine warfarin prescriptions were provided by treating doctors, 35/40 patients reported never having discussed their warfarin with their treating doctor until this instance of an elevated INR.

2 Doctors' experience with and approach to warfarin management

Variable	Doctors (n = 36)*
Initiation of warfarin	
Never by the general practitioner without referral to a specialist	13
Routine management of monitoring and dosing	
Pathology service only	32
GP and pathology service	4
Communication process between pathology service and GP regarding notification of INR results or non-attendance	
Notification of routine and abnormal results	36
Abnormal results requiring intervention after hours	
GP expects to be contacted by pathology service, and then GP manages patient	22
GP expects pathology service to contact patient directly	14
GP's impression of who is responsible for patients' anticoagulation	
GP has sole responsibility	5
Pathology service has sole responsibility	16
GP and pathology service have shared responsibility	15
GP's opinion on who is responsible for delivering warfarin education	
GP is responsible at the time of treatment initiation with warfarin	14
Others (specialists, pathology services, pharmacies, etc)	22
Routine follow-up of education carried out by GP	0
How GP feels warfarin would be managed in an ideal world	
Collaboratively between specialist, GP and pathology service	8
By GP, due to global knowledge of patient	10
By pathology service	14
By an anticoagulation clinic or self-management by patient with "point of care" devices	4

INR = international normalised ratio. * 35 GPs and one specialist physician.   ◆

Patient education

Fourteen GPs reported that they were responsible for patient education at the time of treatment initiation, while 22 believed this to be the responsibility of the initiating specialist, pathology service or local pharmacist. No doctors reported regular follow-up of patient warfarin education.

Of the 40 patients, 23 recalled receiving warfarin education, predominantly in the form of verbal information upon initiation of therapy (17/23). Patients' knowledge was rudimentary — 37 patients had no understanding that warfarin could interact with other medications.

Concordance between doctors' medical records and patient characteristics

Demographic, clinical, cognitive and psychosocial characteristics of patients are shown in Box 3 and Box 4. These revealed that 30 of the 40 patients had multidimensional difficulties, including cognitive dysfunction, possible depression, and medication non-adherence. There was discordance between the doctors' and researchers' assessment of patients, with

12/36 doctors unaware of the measurable deficits in their patient's cognition, mood and/or social connectedness. In addition, 25 doctors' medication history records for their patients were inconsistent with the patients' reported medication use, including absence of current prescription and complementary medications or retention of obsolete therapies in the record.

DISCUSSION

Three-quarters of this group of patients demonstrated measurable psychosocial factors presumed to contribute to risk of medication management-related adverse events, such as cognitive dysfunction, depression, social isolation and self-reported medication non-adherence. Although this study could not determine whether the association with elevated INR was causal, it is noteworthy that most of these patients had one or more psychosocial deficits, and this was not recognised by a third of managing GPs.

Specialists recommending warfarin may have limited knowledge of a patient's psychosocial circumstances. After referring the patient

3 Demographic and clinical characteristics of 40 patients with an elevated INR (⩾ 6)

Variable	No.*
Age in years, mean (range)	75.5 (45.0–92.5)
Female	22
English as a first language	36
Completed secondary school	14
Working status	
Full-time worker	3
Retired	37
Living alone	13
Comorbid chronic conditions†	
Degenerative joint disease	16
Cardiovascular disease	25
Ophthalmic problems	14
Respiratory disease	5
Diabetes	3
Primary indication for anticoagulation	
Atrial fibrillation	19
Valve replacement	11
Pulmonary embolus	5
Deep vein thrombosis	5
Warfarin duration in years, mean (range)	6.5 (0.2–21)
< 2 years	6
2 to < 5 years	11
5 to < 10 years	14
⩾ 10 years	9
INR, mean (range)	7.3 (6.0–9.7)

INR = international normalised ratio. * Figures represent number of patients unless otherwise indicated. † 34 patients had > 1 condition. ◆

4 Cognitive and psychosocial profile of 40 patients with an elevated INR (⩾ 6)

Variable	No.	Mean score (range)
Montreal Cognitive Assessment[11]		
Mild cognitive impairment (score < 26)	26	21 (0–30)
Geriatric Depression Scale – 5 item[12]		
Possible depression (score ⩾ 2)	16	1.3 (0–5)
Duke Social Support Index[13]		
Self-reported social isolation (score ⩽ 80)	9	85 (49–100)
Barthel Index[14]		
Functional dependence requiring assistance with activities of daily living (score ⩽ 75)	6	90 (65–100)

INR = international normalised ratio. ◆

back to the GP for initiation of treatment and ongoing care, management may then be devolved to a pathology provider without transfer of this crucial information. This division of responsibility may be acceptable for many patients, but it allows room for error in high-risk patients who may not have the capacity for managing medication with small safety margins such as warfarin. Our findings suggest a need for clarification of the relative responsibilities in the coordination of warfarin management. All involved parties should ensure they are aware of a patient's psychosocial circumstances, to appropriately inform the risk–benefit ratio of therapy for the individual. Appropriate patient assessment and collaborative discussion between the GP and specialist before the commencement of therapy could empower both in the clinical decision and enhance coordination of care. In the absence of such discussion, the GP may feel medicolegally obliged to fulfil a treatment plan initiated by a specialist, despite having reservations about the risk.

There is also a need for a more systematic approach to facilitate comprehensive assessment of individual risk, such as establishing a warfarin risk score. Validated bleeding-risk assessments, including $CHADS_2$[17] and $HEMORR_2HAGES$,[18] consider numerous clinical characteristics but neglect psychosocial factors. We are currently developing a Warfarin Suitability Score that takes into account variables including contraindications, age, comorbid illnesses, intellectual function, depression, social supports, complexity of medication regimens, and medication management capability. This score may improve recognition of patients for whom treatment is more likely to be problematic and who may require assistance with warfarin management.

When high-risk patients are identified, the appropriate model of shared care should be considered. Responsibility may best be confined to a single provider who can explore suitable measures, including simplifying medication regimens and enlisting family help and the assistance of pharmacists or other agencies. A practical approach to service provision would be for the GP to take on this role. Interviews highlighted doctors' time constraints as a factor that made the efficiency and reliability of the pathology service an attractive option. Time limitations are recognised as a barrier to the holistic care of elderly complex patients.[19,20] One solution may be to delegate responsibility for education and follow-up of high-risk patients to a practice nurse, rather than referral to an external pathology provider. Patient education currently provided by the participating pathology service includes written information regarding warfarin at the time of initiation and an understanding of the service provided. Appropriate scheduled remuneration of nurses and/or pathology services may improve existing, and facilitate future, quality care systems.

Division of responsibility for providing education must be clear. Although it is plausible that education was provided, almost half the patients in our study perceived they had never received any warfarin education — the majority reported no regular discussion with their doctor, and most showed measurable ignorance about anticoagulation. The possibility of recall bias in the patients as a result of cognitive deficits cannot be excluded. The contribution of insufficient education and knowledge to poor anticoagulation control has been demonstrated,[21-23] and patient report of absence of medication information has been identified as an independent predictor of future adverse events.[24]

Although the service policy of the participating pathology provider is comparable to those of other providers in Melbourne, no formalised contract of care is obtained outside the initial referral. Issues with non-compliance, instability and warfarin reversal are considered the responsibility of the referring doctor and are dealt with by the pathologist in consultation with both the patient and referrer. An appreciation of individual roles and responsibilities may be unclear in the absence of previous consultation or need for patient intervention. Similarly, agreement to patient care plans (infrequently requested of the pathology service) rarely fleshes out issues of responsibility for more complicated patients or those needing non-routine care. Clearer definitions, both at patient enrolment into anticoagulation services and by general practice care plans, could be of value.

Our study is limited by absence of a control arm to assess psychosocial deficits in patients with stable anticoagulation levels. Patients commencing warfarin for atrial fibrillation are generally elderly[2] and may be uniformly affected by cognitive and social variables. The relative contribution of these variables will be assessed in a subsequent case–control study by our group. Further, we can make no comparisons or assumptions about patients managed within public pathology services or independently by their primary care doctors, or whether the factors examined contribute to instability of anticoagulation in hospital inpatients or patients in residential care. The system of care discussed and our recommendations for change may not be generalisable to areas where private pathology providers do not assume a similar role (eg, in other Australian states where the service provides INR testing but not dosage) or where there are stated policies for warfarin management. A better study design would have been to randomly select patients from randomly selected GPs. However, although doctors in this sample were identified by their association with patients experiencing an episode of significant over-anticoagulation, they also managed patients whose anticoagulation levels were stable. This suggests their recorded experiences are likely to be representative of other practitioners.

Despite these limitations, to our knowledge this study is the first to investigate community-based warfarin care from both the treating doctor's and the patient's perspective, interviewing doctors at their practices and patients in their homes, with most other studies gathering information from databases or medical records.

The emergence of newer anticoagulant alternatives may result in reduced reliance on warfarin, however there are currently insufficient data supporting their use, cementing warfarin as the mainstay of anticoagulation therapy for now. Future directions may need to include pharmacokinetic assessment alongside systematic use of a risk assessment tool such as a validated Warfarin Suitability Score. There is also a need for role clarification when pathology services become more involved, perhaps by default, in warfarin dosing issues in patients they have presumably never met face to face in consultation. Additionally, collaborative assistance from practice nurses for time-poor GPs should be considered in the care of high-risk and elderly patients. This role would incorporate not only psychosocial dynamics, but continual education, monitoring of medication use including over-the-counter and herbal medications, review of regular INR testing, and liaison with the treating GP before provision of repeat prescriptions.

COMPETING INTERESTS

Ellen Maxwell has been Director of Haematology at Melbourne Pathology, the private pathology provider recruiting patients to this study, since 2003, with primary responsibility for the anticoagulation service.

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REFERENCES

1 Baker RI, Coughlin PB, Gallus AS, et al. Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis. *Med J Aust* 2004; 181: 492-497.
2 Palareti G, Hirsh J, Legnani C, et al. Oral anticoagulation treatment in the elderly: a nested, prospective, case–control study. *Arch Intern Med* 2000; 160: 470-478.
3 Runciman WB, Roughead EE, Semple SJ, Adams RJ. Adverse drug events and medication errors in Australia. *Int J Qual Health Care* 2003; 15 Suppl 1: i49-i59.
4 Makeham MA, Saltman DC, Kidd MR. Lessons from the TAPS study. Warfarin: a major cause of threats to patient safety. *Aust Fam Physician* 2008; 37: 817-818.
5 Schulman S. Care of patients receiving long-term anticoagulant therapy. *N Engl J Med* 2003; 349: 675-683.
6 Connolly SJ, Laupacis A, Gent M, et al. Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *J Am Coll Cardiol* 1991; 18: 349-355.
7 Kimmel SE, Chen Z, Price M, et al. The influence of patient adherence on anticoagulation control with warfarin: results from the International Normalized Ratio Adherence and Genetics (IN-RANGE) Study. *Arch Intern Med* 2007; 167: 229-235.
8 Hutchison LC, Jones SK, West DS, Wei JY. Assessment of medication management by community-living elderly persons with two standardized assessment tools: a cross-sectional study. *Am J Geriatr Pharmacother* 2006; 4: 144-153.
9 Fang MC, Machtinger EL, Wang F, Schillinger D. Health literacy and anticoagulation-related outcomes among patients taking warfarin. *J Gen Intern Med* 2006; 21: 841-846.
10 Schauer DP, Moomaw CJ, Wess M, et al. Psychosocial risk factors for adverse outcomes in patients with nonvalvular atrial fibrillation receiving warfarin. *J Gen Intern Med* 2005; 20: 1114-1119.
11 Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005; 53: 695-699.
12 Nguyen HV, Inderjeeth CA, Tang E, et al. Screening for depression in hospitalised and community-dwelling elderly: the use of the 4-item, 5-item and 15-item geriatric depression scales. *Australas J Ageing* 2006; 25: 204-208.
13 Goodger B, Byles J, Higganbotham N, Mishra G. Assessment of a short scale to measure social support among older people. *Aust N Z J Public Health* 1999; 23: 260-265.
14 Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud* 1988; 10: 61-63.
15 George J, Phun YT, Bailey MJ, et al. Development and validation of the Medication Regimen Complexity Index. *Ann Pharmacother* 2004; 38: 1369-1376.
16 Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986; 24: 67-74.
17 Medi C, Hankey GJ, Freedman SB. Atrial fibrillation. *Med J Aust* 2007; 186: 197-202.
18 Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *Am Heart J* 2006; 151: 713-719.
19 Yuen KJ, Behrndt MM, Jacklyn C, Mitchell GK. Palliative care at home: general practitioners working with palliative care teams. *Med J Aust* 2003; 179 (6 Suppl): S38-S40.
20 Bruce DG, Paley GA, Underwood PJ, et al. Communication problems between dementia carers and general practitioners: effect on access to community support services. *Med J Aust* 2002; 177: 186-188.
21 Kagansky N, Knobler H, Rimon E, et al. Safety of anticoagulation therapy in well-informed older patients. *Arch Intern Med* 2004; 164: 2044-2050.
22 Palareti G, Legnani C, Guazzaloca G, et al. Risk factors for highly unstable response to oral anticoagulation: a case–control study. *Br J Haematol* 2005; 129: 72-78.
23 Tang EO, Lai CS, Lee KK, et al. Relationship between patients' warfarin knowledge and anticoagulation control. *Ann Pharmacother* 2003; 37: 34-39.
24 Metlay JP, Hennessy S, Localio AR, et al. Patient reported receipt of medication instructions for warfarin is associated with reduced risk of serious bleeding events. *J Gen Intern Med* 2008; 23: 1589-1594.