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FROM THE FAMILY PRACTICE INQUIRIES NETWORK

What is the interval for monitoring warfarin therapy once therapeutic levels are achieved?

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EVIDENCE-BASED ANSWER

The international normalized ratio (INR) should be measured monthly once therapeutic levels are achieved and are stable for at least 8 weeks, although treatment should be individualized and an increased frequency may be required by some patients (**Table**) (strength of recommendation [SOR]: **C**, consensus statements). For highly compliant patients with stable levels and a clear understanding of factors that influence anticoagulation (changes in health, diet, medications), routine monitoring may be extended to 6 weeks (SOR: **B**, single randomized controlled trial [RCT]) or longer (SOR: **C**, case series). Patient-managed warfarin therapy, using biweekly self-measurements, results in more time in therapeutic range than routine physicianmanaged care (SOR: **A**, RCTs).

Approach to monitoring of INR for long-term anticoagulation

Clinical scenario	Suggested approach
Initiation of warfarin	Monitor daily until stable, then gradually increase interval to weekly, biweekly, monthly if stable
INR reaches therapeutic level	Recheck 2 weeks x 2, then every 4 weeks if stable
INR therapeutic for 8 to 10 weeks consecutively	May increase interval to 6 weeks with high compliance and good patient education; increase frequency with illness, medication change, history of highly variable INR levels
INR outside target	Recheck in 1 to 2 weeks; if persists, adjust dose and

range within 1.0 points	recheck in 1–2 weeks
INR > from target range but less than 5	Adjust dose, recheck in 1 week
INR between 5 and 8.9	Hold warfarin 1 to 2 days, recheck 24 to 48 hours, adjust dose, consider oral vitamin K, but may lead to warfarin resistance
INR >9	Hold warfarin, closely monitor. Bleeding risk increases with higher INR levels. Management may include admission, administration of oral or IV vitamin K, transfusion with fresh frozen plasma if INR very high or high risk of bleeding

EVIDENCE SUMMARY

Under- or over-treatment with warfarin can result in life-threatening complications. Limited research exists to guide the selection of an interval for monitoring anticoagulation in stabilized patients. One RCT compared INR monitoring in an anticoagulation clinic at 6 weeks and 4 weeks among 124 patients with a prosthetic heart valve on stable oral anticoagulant treatment and found no difference in thromboembolic or hemorrhagic events.[1] A study in the United Kingdom used a 14-week interval for selected patients, but it used no comparison group.[2] Kent et al developed a computer-based model to compute the optimum interval for monitoring anticoagulation that considers the variability of the patient's previous levels and costs associated with testing and potential complications. This model achieved a maximum interval of 11 weeks for very stable patients.[3]

More frequent testing results in higher time in therapeutic range, particularly when patients selfmonitor. A German study of 200 patients with prosthetic heart valves found that they tested within a therapeutic range 48% of the time when monitored by their physician "as usual" (average interval 24 days), and 64% of the time when the interval was increased to 2 weeks.[4] When the same patients then went to self-monitoring every 8, 4, and 2 days, they achieved therapeutic levels 76%, 89%, and 90% of the time, respectively. Bleeding and thromboembolic complications were not reported, but have been demonstrated elsewhere to be lower among patients who self-test frequently (eg, twice weekly) when compared with usual care (average interval 19 days) (4.49% and 0.9% vs 10.9% and 3.6%; number needed to treat [NNT]=15.6 for bleeding, NNT=37 for thromboembolism).[5]

RECOMMENDATIONS FROM OTHERS

The American College of Chest Physicians (ACCP) recommends individualizing management as the optimal frequency of INR monitoring varies according to patient compliance, dosing decisions, duration of therapy and

changes in health, diet, or medications.[6] The ACCP, the American Heart Association,[7] Micromedex DrugPoints System,[8] Goodman and Gilman's *Pharmacological Basis of Therapeutics.*,[9] and Cecil's *Textbook of Medicine.*[10] all recommend monthly monitoring once stable. The Institute for Clinical Systems Improvement's *Anticoagulation Therapy Supplement Management.*[11] and *Managing Oral Anticoagulation Therapy Clinical and Operation al Guidelines.*[12] also recommend monthly monitoring for stable patients, but suggest that the interval can be increased to 6 weeks for selected stable patients.

CLINICAL COMMENTARY

Clear and consistent communication between physician and patient is essential

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Once a month warfarin monitoring remains a sensible interval after the therapeutic level is achieved. Maintaining a standard routine simplifies the many instructions that physicians give and patients receive. This clear, consistent plan can improve coordination of care by medical staff and compliance by patients. Additionally, monitoring has secondary benefits; it reinforces the risks associated with warfarin, and it provides further opportunities to educate the patient.

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