Self-management of oral anticoagulation with low- or conventional-intensity INR did not differ for thromboembolism prevention

Koertke H, Zittermann A, Tenderich G, et al. **Low-dose oral anticoagulation in patients with mechanical heart valve prostheses: final report from the early self-management anticoagulation trial II.** Eur Heart J. 2007;28:2479-84.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★☆☆ Hematol/Thrombo ★★★★★★☆

QUESTION

In patients with mechanical heart valves, does self-management of oral anticoagulation with a low-intensity target international normalized ratio (INR) reduce thromboembolic events?

METHODS

Design: Randomized controlled trial (RCT) (Early Self-Controlled Anticoagulation Trial [ESCAT II]).
Allocation: {Concealed}†.*
Blinding: {Unblinded}†.*
Follow-up period: 24 months.
Setting: 6 clinics in Germany.
Patients: 2673 patients ≥ 18 years of age (mean age 60 y, 72% men) with mechanical aortic, mitral, tricuspid, or double heart-valve replacements. Exclusion criteria were contraindication to vitamin K antagonists (VKAs), peptic ulcer disease with bleeding, and history of coagulopathy or hypercoagulability.
Intervention: Low-intensity target INR of 1.8 to 2.8 for patients with aortic valves and 2.5 to 3.5 for patients with mitral or double valves (n = 1327) or conventional-intensity target INR of 2.5 to 4.5 (n = 1346). All patients were trained in INR self-management, had to check INR values weekly in the first year and every 2 weeks in the second year, and had clinical assessments every 6 months.
Outcomes: Thromboembolic events (heart-valve prosthesis thrombosis or arterial thromboembolism requiring inpatient treatment or causing long-term disability) and major bleeding (requiring transfusion, surgery or endoscopy, and inpatient care or causing long-term disability), and mortality.
Patient follow-up: 80%.

MAIN RESULTS

Groups did not differ for thromboembolic events, bleeding, or mortality (Table).

CONCLUSION

Self-management of oral anticoagulation with low- or conventional-intensity international normalized ratio did not differ for thromboembolic events in patients with mechanical heart valve prostheses.

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*See Glossary.
†Information provided by author.

Self-management of oral anticoagulation with low- vs conventional-intensity international normalized ratio in patients with mechanical heart-valve prostheses‡

Outcomes at 24 mo	Low	Conventional	RRR (95% CI)	NNT
Thromboembolism	0.38%	0.52%	28% (–116 to 76)	Not significant
Bleeding	2.3%	2.5%	7.8% (–50 to 43)	Not significant
			RRI (CI)	NNH
Mortality	4.9%	4.5%	9.9% (–22 to 55)	Not significant

‡Abbreviations defined in Glossary. RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

Although Koertke and colleagues conducted a large RCT, it is considered exploratory because no null-hypothesis or sample size calculations were provided on superiority or noninferiority of the intervention group compared with the control group. Therefore, any conclusions on the efficacy and safety of low-intensity compared with conventional-intensity anticoagulation should be made with caution. Instead, the important messages of this RCT relate to self-management of oral anticoagulation. First, the study convincingly showed that the intensity of anticoagulation by INR self-management can be fine-tuned toward different prespecified INR values. Second, fine-tuned VKA therapy has a very low rate of complications for both thromboembolism and bleeding.

This study confirms 2 biological phenomena of VKA therapy in patients with mechanical heart valves. First, bleeding is more prevalent than thromboembolism, which provides a focus for patient management (1). Second, within the INR range of 2.0 to 3.0, no relation exists between the intensity of anticoagulation and bleeding (1). These points provide a strong argument for maintaining anticoagulation intensity as close to this INR range as possible. Self-management helps to ensure that patients are within this safety zone.

Application of Koertke and colleagues' results to clinical practice should be considered within the context of probable patient selection bias, and results are probably applicable only to patients who are capable of anticoagulation self-management and are willing to perform it. Such patients were selected before inclusion, and selection continued during the trial, as shown by a 20% dropout rate. These selected patients are likely to be at lower risk for complications than others. Nevertheless, this study supports the growing body of evidence that INR self-management (including training, self-adjustment of INR, and close clinical follow-up) is a desirable approach among patients who are willing and able to perform it (2).

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Reference

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2. **Heneghan C, Alonso-Coello P, Garcia-Alamino JM, et al.** Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. Lancet. 2006;367:404-11.