Priority Updates from the Research Literature from the Family Physicians Inquiries Network

PURLs®

A safer way to prevent VTE recurrence

Rather than extend oral anticoagulation therapy for patients at high risk for recurrence of venous thromboembolism, advise them to take an aspirin a day.

Altaf Kaiseruddin, MD; Sonia Oyola, MD; Goutham Rao, MD
The University of Chicago

PURLs EDITOR

Bernard Ewigman, MD, MSPH
The University of Chicago

PRACTICE CHANGER

After patients with unprovoked venous thromboembolism (VTE) complete a 6- to 18-month course of oral anticoagulation therapy, consider a switch to aspirin.[1]

STRENGTH OF RECOMMENDATION

A: Based on one well-designed, randomized controlled trial (RCT).

Becattini C, Agnelli G, Schenone A, et al. Aspirin for preventing the recurrence of venous thromboembolism. *N Engl J Med.* 2012;366:1959-1967.

ILLUSTRATIVE CASE

A 62-year-old patient comes to your office for follow-up of a primary unprovoked venous thromboembolus. He has been on an oral anticoagulant for 12 months. Should he continue anticoagulation therapy despite the increased risk for major bleeding?

Patients who survive VTE—defined as either deep venous thrombosis or pulmonary embolism—are put on anticoagulant therapy to prevent a recurrence, typically for 6 to 18 months. But about 20% of patients with unprovoked VTE have a recurrence within 2 years of anticoagulation withdrawal.[2] Extending anticoagulation prevents recurrences but increases the risk of bleeding.[3]

Is aspirin a viable alternative?

Until recently, the efficacy of aspirin for the prevention of recurrent VTE was unknown. Becattini et al investigated it in the multicenter RCT detailed in this PURL.

STUDY SUMMARY

Aspirin can prevent recurrence with minimal risk

To determine whether aspirin was a viable alternative to oral anticoagulation, the researchers compared aspirin with placebo in patients with primary unprovoked VTE who had completed a course of oral anticoagulation treatment. To be considered for the study, patients had to be >18 years and have had their first-ever objectively confirmed, symptomatic unprovoked proximal deep vein thrombosis, pulmonary embolism, or both. They also had to have completed 6 to 18 months of anticoagulant therapy, with a target international normalized ratio (INR) of 2.0 to 3.0. Exclusion criteria included a history of cancer, clinically significant thrombophilia, atrial fibrillation, and a bleeding event that occurred during the course of anticoagulation therapy.

Becattini et al identified 403 eligible patients. Two weeks after stopping anticoagulation, patients were randomly assigned to receive either aspirin 100 mg once daily (n=205) or placebo (n=198) for 2 years. (One patient in the placebo group never received treatment.) At baseline, there were no significant differences in patient characteristics. All were evaluated every 3 months in the first year and every 6 months in the second year.

CONTINUED

For patients with unprovoked VTE who had completed a course of oral anticoagulation, aspirin was effective in preventing a recurrence—with no apparent increase in the risk of major bleeding.

The primary efficacy outcome was objectively confirmed recurrent VTE. The primary safety outcome was major bleeding, defined as bleeding that occurred in a critical location (eg, intracranial bleeding), was associated with a decrease of hemoglobin of at least 2 g/dL, required a transfusion of 2 units of whole blood or red blood cells, or was fatal. Overt bleeding, which required medical intervention but did not meet the criteria for major bleeding, was a secondary safety outcome.

Twenty-eight of the 205 patients in the aspirin group experienced a recurrence, compared with 43 of the 197 patients on placebo (6.6% vs. 11.2% per year; hazard ratio [HR]=0.58; 95% confidence interval [CI], 0.36-0.93; *P*=.02). Adverse events were reported by 7 patients in the aspirin therapy group and 6 in the placebo group. One patient in each group experienced major bleeding, and 3 in each group experienced clinically relevant but nonmajor bleeding. Withdrawal rates were similar (10 in the treatment group vs 9 controls), as were the number of patients who developed new indications for aspirin or anticoagulation therapy or were lost to follow-up.

An analysis adjusted for age, sex, index event (deep vein thrombosis or pulmonary embolism), and duration of initial anticoagulation treatment confirmed that aspirin reduced the risk of recurrence (adjusted HR=0.53; 95% CI, 0.32-0.85; *P*=.009). No association was found between recurrent VTE and duration of anticoagulation therapy (6 months vs longer). Nor was there a difference in recurrence rates based on the index event.

WHAT'S NEW

Aspirin has a key role in preventing recurrence

This study found that for patients with unprovoked VTE who completed a course of oral anticoagulation, aspirin was effective in preventing a recurrence, with no apparent increase in the risk of major bleeding. Protection in Year 2 was nearly as great as in Year one.[1]

CAVEAT

Patients were followed for just 2 years

It is unclear whether continuing aspirin therapy beyond 2 years would continue to confer protection against a VTE recurrence without an increase in adverse effects.

CHALLENGE TO IMPLEMENTATION

Some patients can't tolerate chronic aspirin therapy

Although this study investigated aspirin in a dosage of 100 mg/d, this strength is not readily available in the United States.[4] There is no evidence to suggest that the 81-mg strength that is available in this country would provide a diminished antiplatelet effect. And, as is already customary, patients undergoing chronic aspirin therapy must be monitored for major bleeding, GI irritation, and renal compromise. A few patients will be ineligible for prophylaxis due to a history of intolerance to aspirin or nonsteroidal anti-inflammatory drugs. JFP

ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center for Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

References

1. Becattini C, Agnelli G, Schenone A, et al. Aspirin for preventing the recurrence of venous thromboembolism. *N Engl J Med*. 2012; 366:1959-1967.
2. Prandoni P, Lensing AW, Cogo A, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med*. 1996;125:1-7.
3. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2 suppl): e419S-494S.
4. Daily Med. Aspirin. Available at: http://dailymed.nlm.nih.gov/dailymed/search.cfm?startswith=aspirin. Accessed September 6, 2012.