Use of ASA after warfarin for unprovoked VTE

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Clinical question
When stopping oral anticoagulants (like warfarin) after treatment of venous thromboembolism (VTE), should acetylsalicylic acid (ASA) be offered?

Bottom line
Once warfarin treatment for unprovoked VTE is complete, low-dose ASA prevents recurrent VTE for 1 in 19 patients over 2.5 years with no increase in major bleeding. Acetylsalicylic acid does not replace warfarin or novel anticoagulants for the initial treatment of VTE.

Evidence
Two randomized controlled trials (WARFASA1 and ASPIRE2) looked at patients with their first unprovoked VTE (deep vein thrombosis, pulmonary embolism, or both) treated with warfarin for approximately 12 months, then randomized to receive ASA (100 mg daily) or placebo.

- Pooled results2 (N = 1225, mean age 57, 57% men, followed for approximately 2.5 years) found the following:
  - A statistically significant (P < 0.05) reduction in:
    - recurrence of VTE: 19.1% for placebo versus 13.8% for ASA, number needed to treat of 19; and
    - major vascular events (VTE, myocardial infarction, stroke, or death from cardiovascular causes): 22.4% for placebo versus 15.9% for ASA, number needed to treat of 14.

- No difference in (data pooled and analyzed by author G.M.A.) major bleeds (1.2% for placebo vs 1.5% for ASA) or mortality (3.8% for placebo vs 3.6% for ASA).

- Limitations: Protocol change (in WARFASA, likely to help find statistical significance); shortfall in recruitment (eg, ASPIRE “aspired” to recruit 3000 patients).

Context
- Overall risk of recurrent VTE after warfarin treatment is approximately 7% to 11% in the first year.3,4
- Risks continue over time: approximately 15% to 20% at 3 years and 30% at 5 years.3,4
- Men and those with unprovoked VTE have about 2 times higher recurrence risk than women or those with provoked VTE.3,4
- While ASA reduces the relative risk of recurrent VTE by 32%,1,2 warfarin and novel anticoagulants (eg, rivaroxaban) reduce the risk by about 80%.5,8
- In patients with unprovoked VTE, anticoagulation will reduce recurrent VTE to about 4% (from about 30%).9
- Anticoagulation will increase major bleeds9 by 2% to 5% in those at low to moderate risk of bleeding and by about 20% in those at high risk.

- High risk of bleeding is 2 or more bleeding risk factors (eg, age older than 65, cancer, anemia, thrombocytopenia, liver or renal failure, anti-platelet therapy, etc).
- Fatality rates for recurrent VTE are about 3.6% (vs 11.3% for major bleeds).9

Implementation
The duration of anticoagulation (warfarin or novel anticoagulants) should balance VTE recurrence and bleed risk.9 The 2012 American College of Chest Physicians guidelines9 advise 3 months of therapy for patients with provoked VTE (eg, during surgery), except in active cancer when anticoagulation should be extended if possible; and 3 months of therapy and consideration of extended therapy for patients with unprovoked VTE. If bleeding risk is low to moderate, extend therapy; if risk is high, consider stopping at 3 months. How long to extended therapy is unclear from the guidelines, but therapy could be indefinite if benefit outweighs risk, leaving plenty of room for clinical judgment. Acetylsalicylic acid is not a substitute for initial VTE treatment with warfarin or novel anticoagulants, but it should be considered when anticoagulation is discontinued.

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References