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Evidence Updated: New evidence
Bottom Line: Minor change
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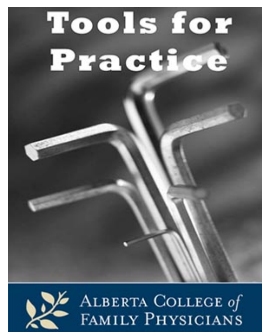

ASA After Warfarin for Unprovoked VTE: Does the Little Clot-Fighter Make Sense?

Clinical Question: When stopping oral anticoagulants (like warfarin) after treatment for venous thromboembolism (VTE), should ASA be offered?

Bottom Line: Once patients have completed warfarin treatment for unprovoked VTE, low-dose ASA prevents recurrent VTE for one in 19 patients over two years with no increase in bleeding. ASA does not reduce VTE recurrence as effectively as oral anticoagulants, and does not replace them for the initial treatment of VTE.

Evidence: Two Randomized Controlled Trials (WARFASA[1] and ASPIRE[2]) of patients with 1st unprovoked VTE (deep vein thrombosis, pulmonary embolism, or both), most initially treated with warfarin for six-12 months, then randomized to ASA 100 mg daily or placebo for ~two years.

- Pooled results[3] for 1224 patients, mean age 57, 57% male:
  - Statistically significant reduction in:
    - VTE recurrence: ASA 13.1%, placebo 18.4%, Number Needed to Treat (NNT)=19.
    - Major vascular events (VTE, myocardial infarction, stroke or cardiovascular death): ASA 14.8%, placebo 21.2%, NNT=16.
  - No difference in:
    - Major bleeds: ASA 1.5%, placebo 1.2%.
    - Mortality: ASA 3.2%, placebo 3.8%.
- Limitations: Protocol changes (WARFASA – likely to help find statistical difference), both trials stopped early due to poor recruitment (e.g. ASPIRE 'aspired' to recruit 3000 patients).

Context:

- Overall risk of recurrent VTE after warfarin treatment is ~7-11% in the first year.[4,5]
  - Risk remains elevated: ~15-20% at three years, 30% at five years.

    - Males and those with unprovoked VTE have ~two times higher recurrence risk than females or provoked VTE.
- While ASA reduces relative risk of recurrent VTE by 32%,[1-3] warfarin and direct oral anticoagulants (DOACs), such as rivaroxaban, reduce the risk by $\geq$80%.
    - Anticoagulants (especially warfarin) increase major bleed risk by up to 2.5-fold.[6,7]
- Duration of therapy with warfarin or DOAC should be based on balancing VTE recurrence and bleed risk.[8]
    - ASA is not a substitute for initial VTE treatment with warfarin or DOAC.

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