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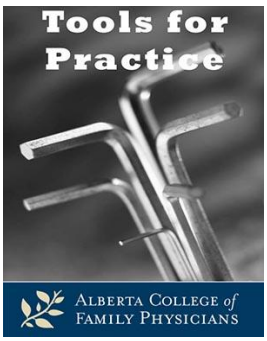

ASA after warfarin for unprovoked VTE: does the little clot-fighter make sense?

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

Bottom line: Once warfarin treatment for unprovoked VTE is complete, ASA (100mg daily) prevents recurrent VTE for one in 19 patients over 2.5 years with no increase in bleeding. ASA does not replace warfarin or novel anticoagulants for the initial treatment of VTE.

Evidence:
Two randomized controlled trials (WARFASA[1] & ASPIRE[2]) of patients with their first unprovoked VTE (deep vein thrombosis, pulmonary embolism, or both) treated with warfarin for approximately 12 months, then randomized to ASA 100mg daily or placebo,

- Pooled results[2] for 1225 total patients, mean age 57, 57% males followed for approximately 2.5 years found:
  - Statistically significant reduction in:
    - VTE recurrence: 19.1% placebo versus 13.8% ASA, Number Needed to Treat (NNT)=19
    - Major vascular events: (VTE, myocardial infarction, stroke or CV death): 22.4% placebo versus 15.9% ASA, NNT=14
  - No difference in (data pooled and analyzed by author GMA):
    - Major Bleeds: 1.2% placebo vs 1.5% ASA.
    - Mortality: 3.8% placebo vs 3.6% ASA.

Limitations:
Protocol change (WARFASA – likely to help find statistical significance), shortfall in 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.[3,4]
  - Risks continue over time: Approximately 15-20% at 3 years, 30% at 5 years.[3,4]
  - Males and those with unprovoked VTE have ~2x higher recurrence risk than females or provoked VTE.[3,4]

- While ASA reduces relative risk of recurrent VTE by 32%,[1,2] warfarin and novel anti-coagulants (e.g. Rivaroxiban) reduce the risk by about 80%, but also increase bleed risk by 60-400% (warfarin generally higher).[5-8]
- Duration of therapy with warfarin or novel anticoagulants should be based on balancing VTE recurrence and bleed risk.[9]
    - ASA is not a substitute for initial VTE treatment with warfarin or novel anticoagulants.

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