Reviewer’s report

Title: Prostate cancer-specific survival among warfarin users in the Finnish Randomized Study of Screening for Prostate Cancer

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Reviewer: Randall Harris

Reviewer’s report:

Introduction: The investigation is justified by a few prior investigations showing that Warfarin intake might modify mortality among prostate cancer (PCa) patients.

Methods: The study examines effects of Warfarin and other anticoagulants on mortality in men diagnosed with incident prostate cancer in a large cohort of Finnish men. Statistical methodology (Cox regression, sensitivity analysis and lagged analysis) appears to be appropriate.

Results: The study investigated the effect of warfarin and other anticoagulants on mortality in 6,537 men diagnosed with prostate cancer (PCa) during 1995-2009 within a cohort of 80,458 Finnish men. Post-diagnostic use of low dose low intensity warfarin was associated with an increased risk of PCa death (overall HR 1.47, 95% CI 1.13-1.93). However, no risk increase or decrease was observed among short term users or among high-intensity users in a lagged analysis of the data. The tables of results are complete and provide adequate information for checking the rigor of statistical methods used.

Discussion: The study observed elevated risk of PCa death with short term use of Warfarin "which is probably explained by a higher risk of thrombotic events prompting warfarin use in patients with terminal PCa."

This in fact is a form of "protopathic bias" as described by Horwitz and Feinstein in their classic paper. The authors should acknowledge this important paper and source of bias in the epidemiologic literature.

Conclusion: The conclusion of the report appears to be justified by the results. In a population-based setting, warfarin or other types of anticoagulants are not associated with improved prostate cancer prognosis. Conversely, in short-term use risk of PCa death was increased, which is most likely due to thrombosis caused by an advanced cancer, as the risk increase was not observed in long term.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
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Yes

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I am able to assess the statistics

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