Effect of Aspirin on Cancer Incidence and Mortality in Older Adults

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Background:

ASPirin in Reducing Events in the Elderly (ASPREE) was a randomized, double-blind, placebo-controlled trial of daily low-dose (100 mg) aspirin in older adults >65 years of age. Participants were randomized to receive either 100mg enteric-coated aspirin or placebo. ASPREE showed an increased risk of all-cause mortality (HR 1.14 with 95% CI of 1.01-1.29) later determined to be due to cancer (HR 1.31 95% CI 1.10-1.56). This study was a follow-up to those results.

What They Did:

- Prespecified secondary endpoints and ad-hoc analysis from the ASPREE trial were used to examine the effect of aspirin for primary prevention on cancer incidence and mortality.

Outcomes:

- Prespecified Secondary Endpoints:
    - First incident cancer
    - All-cause mortality

Inclusion:

- Non-minority men and women 70 years of age and older
- US minority (African American and Hispanic) 65 years of age and older

Exclusion:

- History of diagnosed ASCVD (MI, HF, angina, TIA, >50% carotid stenosis, previous stenting, CABG, etc.)
- Clinical diagnosis of atrial fibrillation
- Current/recurrent condition with a high risk of major bleeding
- Continuous use of another antiplatelet or anticoagulant
- Anemia (hemoglobin <12 g/dl in males and <11 g/dl in females)

Results:

- In the original ASPREE trial, 19,114 patients were randomized to aspirin (n = 9,525) or placebo (n = 9,589)
- During follow up, 1933 patients were diagnosed with a new incident cancer. 1270 were localized, 363 were metastatic, and 113 presented with metastatic spread of a cancer already identified before randomization.
- Cancer Mortality
    - First Incident Cancer
        - Aspirin: 283
        - Placebo: 212
        - HR 1.35 (95% CI 1.13-1.61)
    - Incident Localized

        - Aspirin: 93
        - Placebo: 64
        - HR 1.47 (95% CI 1.07-2.02)
    - Metastatic
        - Aspirin: 171
        - Placebo: 133
        - HR 1.30 (95% CI 1.03-1.63)
    - Incident Metastatic
        - Aspirin: 143
        - Placebo: 109
        - HR 1.32 (95% CI 1.03-1.70)
    - All Solid Tumors
        - Aspirin: 259
        - Placebo: 196
        - HR 1.33 (95% CI 1.11-1.61)
    - Colorectal Cancer:
        - Aspirin: 35
        - Placebo: 20
        - HR 1.77 (95% CI 1.02-3.06)
- Cancer Incidence
    - Stage 4 Cancer
        - Aspirin: 275
        - Placebo: 228
        - HR 1.22 (95% CI 1.02-1.45)
- Statistically Significant Results Summary
    - Increased mortality from first incident cancer (incident localized, metastatic, incident metastatic), stage 3 and 4 cancers, solid tumors (irrespective of anatomic site)
    - Increased incidence of cancers that were stage 4 at diagnosis

Strengths:
- Multicenter, longitudinal study
- Blinded expert reviewers categorized tumor stage and cause of death
- Cancer incidence and mortality were prespecified secondary outcomes.

Limitations:
- Results are driven by a secondary outcome that was not originally powered for.
- Most of the detailed outcomes were ad-hoc analysis.
- Limited statistical power to examine the effect of aspirin on each subgroup and cancer type.
- Follow-up was relatively short for cancer outcomes.

Discussion:
Author Conclusion:
- In generally healthy adults aged 70 years or older, daily low-dose aspirin was associated with increased risk of incident solid cancers presenting at an advanced stage. Mortality from both localized and advanced cancers was higher in those taking aspirin.

Clinical Take-Home Point:

- These results should be considered as suggestive/exploratory because they are driven by a secondary outcome and ad-hoc analysis that was not originally powered for. Further research is needed before making changes to current practice.
- Continue to encourage appropriate health screenings and regular care appointments for Veterans.

References:

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