Aspirin reduced the incidence of colorectal cancer during 23-year follow-up in healthy men or patients with recent TIA


Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Gastroenterology ★★★★★★★☆ Oncology ★★★★★★★★★☆

Q U E S T I O N
In healthy men or patients with recent transient ischemic attack (TIA) or minor ischemic stroke, does aspirin reduce the incidence of colorectal cancer during long-term follow-up?

M E T H O D S
Design: Long-term posttrial follow-up of 2 randomized controlled trials (British Doctors Aspirin Trial [BDAT] and UK Transient Ischaemic Attack Aspirin Trial [UK-TIA trial]).

Allocation: Unclear allocation concealment for the BDAT and [concealed†] for UK-TIA trial.

Blinding: Unblinded for BDAT; blinded [clinicians, patients, and data collectors for UK-TIA trial‡]; and blinded (outcome assessors) for both trials for long-term follow-up.†

Follow-up period: Up to 23 years.

Setting: United Kingdom for BDAT; 33 centers in the United Kingdom and Ireland for the UK-TIA trial.

Patients: BDAT: 5139 [healthy]* male doctors (mean age 62 y, 31% smokers) who did not take aspirin regularly and had no contraindications to aspirin and no history of peptic ulcer disease, stroke, or myocardial infarction. UK-TIA trial: 2449 patients > 40 years of age (mean age 60 y, 73% men, 53% smokers) who had a recent TIA or minor ischemic stroke and no history of regular aspirin use, major disabling stroke, aspirin intolerance, alcoholism, chronic renal failure, peptic ulceration, or severe nonvascular disease.

Intervention: BDAT: aspirin, 500 or 300 mg/d (n = 3429*), or no intervention (n = 1710*) for 5 to 6 years. UK-TIA trial: aspirin, 1200 mg/d (n = 815‡), 300 mg/d (n = 8064), or placebo (n = 814‡) for 1 to > 7 years.

Conclusions

In healthy men or patients with recent transient ischemic attack or minor ischemic stroke, aspirin reduced the incidence of colorectal cancer during up to 23 years of follow-up. The effect was seen only after 10 years of follow-up.

Source of funding: No external funding.

Aspirin vs no intervention or placebo for preventing colorectal cancer in healthy men or patients with recent transient ischemic attack or minor ischemic stroke

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Trial (n)</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT/NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 9 y</td>
<td>BDAT (5139)</td>
<td>0.8% vs 1.0%</td>
<td>RRR 14% (−49 to 55)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>UK-TIA (2449)</td>
<td>1.1% vs 1.0%</td>
<td>RRR 8.0% (−49 to 44)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Pooled (7588)</td>
<td>0.9% vs 1.0%</td>
<td>RRR 8.0% (−49 to 44)</td>
<td>NS</td>
</tr>
<tr>
<td>10 to 19 y</td>
<td>BDAT (5139)</td>
<td>1.5% vs 2.2%</td>
<td>RRR 36% (3 to 58)</td>
<td>128 (79 to 1532)</td>
</tr>
<tr>
<td></td>
<td>UK-TIA (2449)</td>
<td>0.9% vs 1.8%</td>
<td>RRR 49% (0 to 75)</td>
<td>114 (75 to ∞)</td>
</tr>
<tr>
<td></td>
<td>Pooled (7588)</td>
<td>1.3% vs 2.1%</td>
<td>RRR 40% (13 to 58)</td>
<td>120 (83 to 370)</td>
</tr>
<tr>
<td>0 to 23 y</td>
<td>BDAT (5139)</td>
<td>2.7% vs 3.7%</td>
<td>RRR 30% (3 to 49)</td>
<td>92 (56 to 918)</td>
</tr>
<tr>
<td></td>
<td>UK-TIA (2449)</td>
<td>2.3% vs 2.8%</td>
<td>RRR 18% (−37 to 51)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Pooled (7588)</td>
<td>2.5% vs 3.4%</td>
<td>RRR 26% (3 to 44)</td>
<td>115 (68 to 998)</td>
</tr>
</tbody>
</table>

†BDAT = British Doctors Aspirin Trial; UK-TIA = UK Transient Ischaemic Attack Aspirin Trial; NS = not significant; other abbreviations defined in Glossary. RRR, RRI, NNT, NNH, and CI calculated from hazard ratios and control event rates in article.

Sources of funding: No external funding.

Aspirin reduced the incidence of colorectal cancer during 23-year follow-up in healthy men or patients with recent transient ischemic attack (TIA) or minor ischemic stroke, does aspirin reduce the incidence of colorectal cancer during long-term follow-up?

METHODS

Design: Long-term posttrial follow-up of 2 randomized controlled trials (British Doctors Aspirin Trial [BDAT] and UK Transient Ischaemic Attack Aspirin Trial [UK-TIA trial]).

Allocation: Unclear allocation concealment for the BDAT and [concealed†] for UK-TIA trial.

Blinding: Unblinded for BDAT; blinded [clinicians, patients, and data collectors for UK-TIA trial‡]; and blinded (outcome assessors) for both trials for long-term follow-up.†

Follow-up period: Up to 23 years.

Setting: United Kingdom for BDAT; 33 centers in the United Kingdom and Ireland for the UK-TIA trial.

Patients: BDAT: 5139 [healthy]* male doctors (mean age 62 y, 31% smokers) who did not take aspirin regularly and had no contraindications to aspirin and no history of peptic ulcer disease, stroke, or myocardial infarction. UK-TIA trial: 2449 patients > 40 years of age (mean age 60 y, 73% men, 53% smokers) who had a recent TIA or minor ischemic stroke and no history of regular aspirin use, major disabling stroke, aspirin intolerance, alcoholism, chronic renal failure, peptic ulceration, or severe nonvascular disease.

Intervention: BDAT: aspirin, 500 or 300 mg/d (n = 3429*), or no intervention (n = 1710*) for 5 to 6 years. UK-TIA trial: aspirin, 1200 mg/d (n = 815‡), 300 mg/d (n = 8064), or placebo (n = 814‡) for 1 to > 7 years.

Conclusions

In healthy men or patients with recent transient ischemic attack or minor ischemic stroke, aspirin reduced the incidence of colorectal cancer during up to 23 years of follow-up. The effect was seen only after 10 years of follow-up.

Source of funding: No external funding.

Commentary

Colorectal cancer is the second most commonly diagnosed cancer in developed countries (1). In high-risk patients, aspirin, nonsteroidal anti-inflammatory drugs, and cyclooxygenase-2 inhibitors reduced the incidence of colonic polyps in randomized controlled trials (2).

The study by Flossmann and Rothwell showed that aspirin, compared with placebo or no treatment, reduced colorectal cancer incidence. The protective effect was not apparent until after 10 years. These results contrasted with those of the Physicians’ Health Study (3) and the Women’s Health Study (4), which failed to show a protective effect. However, the aspirin doses were substantially higher in the trial by Flossmann and Rothwell.

Neither the BDAT trial nor the UK-TIA trial was designed to study the incidence of colorectal cancer, and so there was no systematic effort to detect this type of cancer. Aspirin treatment could have introduced a diagnostic access bias by causing gastrointestinal bleeding that would lead to colonoscopy and polypectomy. Estimates for effect size are also imprecise because considerable crossover occurred between the treatment groups.

Should we recommend long-term aspirin for average-risk individuals based on the study by Flossmann and Rothwell? According to the U.S. Preventive Services Task Force (5), the answer is no. Aspirin, especially at high doses, is associated with considerable gastric toxicity and an increased risk for hemorrhagic stroke. Even with the favorable results estimated by Flossmann and Rothwell, 120 participants would need to be treated for at least 5 years to prevent 1 case of colorectal cancer.

Vincent W.S. Wong, MD
Francis K.L. Chan, MD
Chinese University of Hong Kong
Hong Kong SAR, China

References