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The Association Between Aspirin Use and the Risk of Esophageal Cancer Incidence and Prognosis: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 March 2025 and was last updated on 6 March 2025.

INTRODUCTION

Review question / Objective Objective: To investigate the effects of aspirin on the risk of esophageal cancer development and the prognosis of esophageal cancer patients. Methods: Databases including CNKI, PubMed, Web of Science, Cochrane Library, and Embase were searched to identify relevant studies. Odds ratios (ORs) and hazard ratios (HRs) were pooled to evaluate the association between aspirin and esophageal cancer risk or prognosis, respectively. Subgroup analyses were conducted, and meta-analysis was performed using Stata 18.0 software.

Condition being studied Esophageal cancer is a relatively common malignancy with high incidence and mortality rates, and generally poor prognosis. The 5-year overall survival for patients with distant metastasis is only about 5%. According to the latest global cancer statistics report, esophageal cancer ranked 11th in incidence and 7th in mortality among global cancers in 2022, accounting for 2.6% and 4.6% respectively. Risk factors for esophageal cancer include genetics, smoking, alcohol consumption, poor dietary habits, obesity, and gastroesophageal reflux. Preventive measures involve risk reduction (smoking cessation, alcohol abstinence, weight management) and chemoprevention (cyclooxygenase inhibitors, statins, metformin, proton pump inhibitors). Common treatment modalities include surgery, radiotherapy, chemotherapy, immunotherapy, and targeted therapy.

Aspirin, originally derived from willow bark extract, was first synthesized in the late 19th century. As a white crystalline powder, it exhibits antipyretic, analgesic, anti-inflammatory, anti-rheumatic, and antiplatelet aggregation effects, and is widely used clinically for preventing atherosclerotic vascular diseases. Some studies suggest that aspirin may have potential therapeutic effects in cancer treatment, showing preventive and ameliorative effects on certain tumors. However, its impact on esophageal cancer development and prognosis improvement remains unclear and inconsistent. Some studies indicate that aspirin may reduce

esophageal cancer risk and improve patient prognosis, while others found no preventive effect and even possible survival rate reduction in esophageal cancer patients. Therefore, researchers conducted this meta-analysis to further investigate whether aspirin can reduce esophageal cancer incidence and improve patient prognosis, aiming to provide evidence for clinical treatment.

METHODS

Search strategy Using computer to search from CNKI, PubMed, Web of Science, Cochrane Library and Embase database to January 10, 2025. The search strategy is :((Aspirin) OR (Acetylsalicylic acid)) AND ((esophageal cancer) OR (carcinoma of esophagus) OR (esophagusneoplasm)).

Participant or population Esophageal cancer patients.

Intervention Exposure: Aspirin.

Comparator Aspirin user and non-user.

Study designs to be included Case-control atudy; cohort study; randomized controlled trail.

Eligibility criteria
Inclusion Criteria:
① Study types: Case-control studies, cohort studies, randomized controlled trials (RCTs);
② Study population: Exposure group (esophageal cancer patients) and control group (non-esophageal cancer patients);
③ Intervention: Aspirin use;
④ Outcome measures: Effect estimates (e.g., odds ratio [OR], relative risk [RR], hazard ratio [HR]) for the association between aspirin use and esophageal cancer incidence, overall survival, or cancer-specific mortality.
Exclusion Criteria:
① Unavailable full texts or studies providing non-target data;
② Duplicate publications from identical data sources;
③ Case reports, conference abstracts, guidelines, reviews, etc.;
④ Studies focusing on COX-2 inhibitors without specifying aspirin use;
⑤ Non-Chinese/English publications.

Information sources CNKI, PubMed, Web of Science, Cochrane Library and Embase database.

Main outcome(s) Effect estimates (e.g., odds ratio [OR], relative risk [RR], hazard ratio [HR]) for the association between aspirin use and esophageal cancer incidence, overall survival, or cancer-specific mortality.

Data management Using Endnote 21 to manage data.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS) was used to assess the quality of case-control studies and cohort studies, with a score of ≥7 indicating high-quality studies. For randomized controlled trials (RCTs), the Cochrane Risk of Bias Tool was applied, categorized as follows: Grade A: All items were rated as low risk; Grade B: At least one item was rated as unclear risk; Grade C: At least one item was rated as high risk.

Strategy of data synthesis The literature data were analyzed using Stata 18.0 software. Meta-analyses were performed for odds ratios (ORs) and hazard ratios (HRs) to obtain pooled effect sizes with 95% confidence intervals (CIs). Heterogeneity among included studies was assessed using the Q statistic and I^2 statistic. A fixed-effect model was applied when $P \geq 0.1$ and $I^2 \leq 50\%$, whereas a random-effects model was used when P 50%. Sensitivity analysis was conducted by sequentially removing individual studies (leave-one-out method) to test the robustness of the meta-analysis results. Publication bias was evaluated via funnel plots and statistical tests (e.g., Begg's or Egger's test) for factors with ≥10 included studies, and $P < 0.05$ indicated significant publication bias. Engauge Digitizer software was employed to extract HR values from Kaplan-Meier curves.

Subgroup analysis Subgroup analysis was performed according to the variables including area, type of esophageal cancer, type of study design.

Sensitivity analysis We use Stata 18.0 software, inputing command: metaninf lnhr selnhr, eform label(namevar=study) random.

Language restriction English and Chinese.

Country(ies) involved China.

Keywords aspirin; esophageal cancer; incidence; prognosis; meta-analysis.

Contributions of each author

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