

INPLASY PROTOCOL

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None declared.

Association between endometriosis and prognosis of ovarian cancer: an updated meta-analysis

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Review question / Objective: Increased risk of ovarian cancer (OC) among endometriosis patients has been proposed. However, the association between endometriosis and prognosis of OC remains controversial. This study evaluated whether endometriosis had influence on the survival outcomes of OC through a meta-analysis.

Eligibility criteria: (1) non-original articles, such as reviews, conference abstracts and comments; (2) the studies that provide only a figure but not a detailed HR (95% CI) to show the results of survival analysis; (3) duplicate studies or multiple studies involving the same data, with only the one with the most complete information included.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 March 2022 and was last updated on 21 March 2022 (registration number INPLASY202230109).

INTRODUCTION

Review question / Objective: Increased risk of ovarian cancer (OC) among endometriosis patients has been proposed. However, the association between endometriosis and prognosis of OC remains controversial. This study evaluated whether endometriosis had influence on

the survival outcomes of OC through a meta-analysis.

Condition being studied: Relevant studies were retrieved from PubMed, Embase, and Web of Science databases and were evaluated using the Newcastle-Ottawa Quality Assessment Scale. Effect size was presented as hazard ratio (HR) and 95%

confidence interval (CI). Heterogeneity test evaluation was performed using Cochran's Q test and I² statistics. Publication bias was determined using Egger's test. Statistical analysis was performed using Stata 12.0 software.

METHODS

Search strategy: According to a pre-established retrieval strategy, the relevant studies were systematically retrieved from PubMed, Embase, Web of Science databases with the retrieval time up to May 11, 2021 and without language restrictions. The search terms contained three categories: research object ("ovarian neoplasm", "ovarian cancer", "ovary neoplasm", "ovary cancer", "ovarian carcinoma", "ovary carcinoma"), exposure factors ("endometriosis", "endometrioses") and outcomes ("mortality", "survival", "prognosis"). Two search terms in the same category are combined with "OR", while "AND" was used between two search terms of different categories. The detailed retrieval strategies for different databases are listed in Table S1. Additionally, manual retrieval was carried out for the paper version of the relevant studies, and the references of the relevant reviews and included studies were also retrieved.

Participant or population: Patients who were pathologically and histologically diagnosed as epithelial ovarian cancer were included.

Intervention: Patients who were pathologically and histologically diagnosed as epithelial ovarian cancer were included.

Comparator: Patients with or without endometriosis.

Study designs to be included: Retrospective or prospective cohort studies or nested case-control studies.

Eligibility criteria: (1) non-original articles, such as reviews, conference abstracts and comments; (2) the studies that provide only a figure but not a detailed HR (95% CI) to show the results of survival analysis; (3)

duplicate studies or multiple studies involving the same data, with only the one with the most complete information included.

Information sources: The relevant studies were systematically retrieved from PubMed, Embase, Web of Science databases.

Main outcome(s): EAOB patients tended to have better OS and PFS than non-EAOB patients. Conducting higher quality prospective cohort studies with large sample sizes is recommended to confirm the authenticity of the current study's results.

Quality assessment / Risk of bias analysis: On the basis of the above selection criteria, study retrieval was carried out by two independent investigators.

Strategy of data synthesis: All statistical analyses were completed using Stata 12.0 software. HR and 95% CI were utilized as effect size indicators to evaluate the differences on PFS and OS of EAOB vs. non-EAOB. Cochran's Q test and I² test were used to assess the heterogeneity among studies. Significant heterogeneity was determined with P50%, and a random-effects model was utilized. A fixed-effects model was utilized when no significant heterogeneity was observed ($P \geq 0.05$ and $I^2 \leq 50\%$). The effect of region, confounding factors adjusted or not for heterogeneity, and the pooled results were evaluated with a subgroup analysis. Publication bias evaluation was conducted using Egger's test. If there was significant publication bias, the stability of the results of the meta-analysis was evaluated using the trim-and-fill method. The stability of the results was also evaluated using the method of elimination one by one.

Subgroup analysis: All statistical analyses were completed using Stata 12.0 software. HR and 95% CI were utilized as effect size indicators to evaluate the differences on PFS and OS of EAOB vs. non-EAOB. Cochran's Q test and I² test were used to assess the heterogeneity among studies.

Significant heterogeneity was determined with $I^2 \geq 50\%$, and a random-effects model was utilized. A fixed-effects model was utilized when no significant heterogeneity was observed ($P \geq 0.05$ and $I^2 \leq 50\%$). The effect of region, confounding factors adjusted or not for heterogeneity, and the pooled results were evaluated with a subgroup analysis. Publication bias evaluation was conducted using Egger's test. If there was significant publication bias, the stability of the results of the meta-analysis was evaluated using the trim-and-fill method. The stability of the results was also evaluated using the method of elimination one by one.

Sensitivity analysis: All statistical analyses were completed using Stata 12.0 software. HR and 95% CI were utilized as effect size indicators to evaluate the differences on PFS and OS of EAOC vs. non-EAOC. Cochran's Q test and I^2 test were used to assess the heterogeneity among studies. Significant heterogeneity was determined with $I^2 \geq 50\%$, and a random-effects model was utilized. A fixed-effects model was utilized when no significant heterogeneity was observed ($P \geq 0.05$ and $I^2 \leq 50\%$). The effect of region, confounding factors adjusted or not for heterogeneity, and the pooled results were evaluated with a subgroup analysis. Publication bias evaluation was conducted using Egger's test. If there was significant publication bias, the stability of the results of the meta-analysis was evaluated using the trim-and-fill method. The stability of the results was also evaluated using the method of elimination one by one.

Country(ies) involved: China.

Keywords: endometriosis, ovarian cancer, prognosis, meta-analysis.

Contributions of each author:

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