INPLASY PROTOCOL

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None declared.

Concurrent chemoradiotherapy followed by adjuvant chemotherapy versus concurrent chemoradiotherapy alone in locally advanced cervical cancer: a systematic review and meta-analysis

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Review question / Objective: **To assess the efficacy and safety of adjuvant chemotherapy (ACT) following concurrent chemoradiation (CCRT) in patients with locally advanced cervical cancer (LACC) through a meta-analysis.**
Condition being studied: **As the most common gynecologic malignant neoplasm in women worldwide, cervical cancer has been recognized as a prevalent health problem, and it remains a challenge to treat cervical cancer. In 2018, there were over 36,000 new cases, with 311,365 related deaths. In many developing countries, patients were usually already at a locally advanced stage at the time of diagnosis of cervical cancer, indicating a poor outcome.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 September 2022 and was last updated on 19 September 2022 (registration number INPLASY202290089).

INTRODUCTION

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METHODS

Participant or population: Diagnosed LACC of the FIGO (International Federation of Gynecology and Obstetrics) stage IB–IVA with at least one measurable lesion and Karnofsky performance score of 70.

Intervention: Adjuvant chemotherapy (ACT) following concurrent chemoradiation.

Comparator: concurrent chemo-radiotherapy alone.

Study designs to be included: Randomized controlled trials or observational studies.

Eligibility criteria: Studies were considered eligible for meta-analysis if they met the following criteria:(1) diagnosed LACC of the FIGO (International Federation of Gynecology and Obstetrics) stage IB–IVA with at least one measurable lesion and Karnofsky performance score of 70(16); (2) RCTs (randomized controlled trials) or observational studies; (3) all patients aged 18 years or older, who had not been previously treated with immunotherapy; (4) all studies protocols were approved by the institutional ethics committee, and were performed in accordance with the Declaration of Helsinki; (5) at least 30 patients were included; (6) the outcomes of interest were survival rate and complete response rate; (7) risk estimates and associated 95%CI (or data to calculate them) were provided. The major exclusion criteria were as follows: (1) patients combined with other malignant tumors (2) the publication was in the format of an abstract, comment, or review; (3) there were no sufficient data.

Information sources: MEDLINE, PubMed, Web of Science, EMBASE and the Cochrane Central Register of Controlled Trials from the beginning to May 20, 2022.

Main outcome(s): The primary endpoints were 3-year rates of overall survival (OS) and progression-free survival (PFS).

Quality assessment / Risk of bias analysis: The quality assessment of the RCTs was evaluated using the Cochrane Handbook of 6.2.

Strategy of data synthesis: Hazard ratio (HR) and the 95% confidence interval (CI) were used to assess the survival rate of locally advanced stage cervical cancer patients who had ACT after CCRT. Due to the lack of HR information, the estimation of data from Kaplan-Meier curves were used. Risk ratio (RR) was used as the summary statistic for statistical analyses of dichotomous variables. Homogeneity of effect size across studies was tested by Q statistics at the $P<0.10$ level of significance. The I2 statistic, which is a quantitative measure of inconsistency across studies, was also calculated. We further conducted a sensitivity analysis to explore possible explanations for heterogeneity and to examine the influence of various exclusion criteria on the overall risk estimate. Finally, potential publication bias was assessed by Begg's funnel plots and Egger's regression test. All analyses were done using Stata 12.0. P value<0.05 was considered significant. All data analysis followed the PRISMA statement.

Subgroup analysis: Next, we conducted a subgroup analysis. Grade 3-4 gastrointestinal system toxicities were more frequent during the treatment of the CCRT plus ACT group (RR=1.33, 95%CI=1.01~1.75). However, there were no noticeable differences between the two groups in grade 3-4 hematological adverse events (RR=1.92, 95%CI=0.94~3.90) and genitourinary system toxicities (RR=1.58, 95%CI=0.80~3.10).

Sensitivity analysis: We further conducted a sensitivity analysis to explore possible explanations for heterogeneity and to

examine the influence of various exclusion criteria on the overall risk estimate.

Country(ies) involved: China, Department of Oncology, The Affiliated Hospital of Xuzhou Medical University, Jiangsu.

Keywords: concurrent; chemoradiotherapy; adjuvant chemotherapy; cervical cancer; meta-analysis.

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