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Immune Cell Prognostic Significance in Endometrial Cancer: A Comprehensive Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - N/A.

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 2 September 2024 and was last updated on 2 September 2024.

INTRODUCTION

Review question / Objective This meta-analysis aimed to investigate the prognostic value of various immune cell types in endometrial cancer, with the goal of identifying novel prognostic biomarkers and therapeutic targets.

Rationale Endometrial cancer (EC) is a prevalent malignancy affecting women. It originates from the endometrium, the lining of the uterus, and its development is commonly associated with the hormonal fluctuations and metabolic disturbances that accompany aging and obesity . Globally, the incidence of endometrial cancer has been rising, increasingly becoming a considerable public health issue . This cancer is characterized by a multifaceted etiology, diverse clinical presentations, and varying outcomes. The traditional clinical and histological parameters used to forecast patient prognosis frequently fail to fully explain the heterogeneity observed in disease progression and survival rates . Consequently, there is an urgent need to pinpoint additional prognostic factors that can enhance the precision of predicting patient outcomes.

Condition being studied Endometrial cancer is a malignant tumor that arises from the endometrium, the lining of the uterus. It is the most common type of cancer affecting the female reproductive system. The condition typically occurs after menopause, with symptoms such as abnormal uterine bleeding, pain during urination or sexual intercourse, and changes in bowel habits. Endometrial cancer be classified into two main types: type I and type II, based on the characteristics of the cancer cells and their behavior.This comprehensive meta-analysis focuses on investigating the prognostic significance of immune cells in endometrial cancer. Immune cells, including lymphocytes, macrophages, and dendritic cells, play a crucial role in the body's defense against cancer. Abnormalities in the distribution and function of

immune cells within the tumor microenvironment have been observed in various cancers, including endometrial cancer.The analysis aims to identify the association between the presence and activation of specific immune cell subsets and the clinical outcome of patients with endometrial cancer. By examining the expression levels of immune cell-related markers and their correlation with patient survival, this study seeks to provide insights into the potential mechanisms underlying the immune response in endometrial cancer and to identify novel therapeutic targets.

METHODS

Search strategy We retrieved pertinent articles from PubMed, Medline, and Embase from the date of establishment of the database to May 31, 2024. The articles were searched by the approach of free words and subject words, with the key words of endometrial cancer, endometrial carcinoma, endometrial neoplasm, tumor infiltrating lymphocytes, tumor derived activated cells, prognosis, prognostic, survival, and outcome.

Participant or population Patients with endometrial cancer (stages I to IV) confirmed by postoperative pathology.

Intervention NA.

Comparator NA.

Study designs to be included Comparator *If applicable, define which comparative intervention will be applied to the target population.

Eligibility criteria The inclusion criteria were as follows: 1) Patients with endometrial cancer (stages I to IV) confirmed by postoperative pathology. 2) Patients who had not received any chemotherapy or radiotherapy prior to surgery. 3) Patients without other concurrent malignancies. 4) Studies reporting on the prognostic value of total tumor-infiltrating lymphocytes (TILs) or specific TIL subgroups (including CD3+ T cells, CD4+ T cells, CD8+ T cells, FoxP3+ lymphocytes, and others) in endometrial cancer. 5) Studies with complete records and detailed explanations of the hazard ratios (HR) and 95% confidence intervals (CI) of the outcome data. Exclusion criteria included: 1) Non-clinical primary studies: such as literature reviews, conference abstracts, case reports, animal experimental studies, editorials, etc. 2) In cases where two or more studies by the same author were published, only the most recent data was included. 3) If the same study provided both univariate and multivariate Cox regression analysis data, preference was given to the multivariate Cox regression analysis data for higher precision. The relevant literature that met the criteria was retrieved and reviewed for exclusion and selection by two researchers, who examined the titles, abstracts, full texts, and duplicates. Only literature that conformed to the inclusion criteria was selected. In cases of discrepancies, the results were resolved through discussion.

Information sources Data were extracted by two reviewers. The extracted information included details about the author, nationality of study subjects, age, study sample size, clinical stage, TILs subgroups, TILs data, tumor grading, cut of value, median follow-up time, patient cohort, and outcome measures.

Main outcome(s) Overall Survival (OS) is the period from the date of tumor surgery to the date of death; Progression-Free Survival (PFS) refers to the time from the start of treatment until disease progression or patient death occurs; Disease-Free Survival (DFS) is defined as the time from surgery until disease recurrence or death; Disease-Specific Survival (DSS) is defined as the survival time obtained after excluding deaths due to the tumor disease itself and deaths related to tumor treatment. If disagreements arise during the data extraction process, they are resolved through discussions with the third author until consensus is reached by the two authors.

Quality assessment / Risk of bias analysis Two reviewers conducted independent assessments of the quality of the selected studies using predefined tools, and disagreements were resolved through consensus. Observational studies, including case-control and cohort studies, were evaluated using an adapted version of the Newcastle–Ottawa Scale (NOS).

Strategy of data synthesis Use a random-effects model to account for the heterogeneity between studies, which is common in meta-analysis due to differences in study design and patient populations.

Subgroup analysis Discuss the implications of the subgroup analyses for the understanding of the prognostic role of immune cells in endometrial cancer.Consider whether certain subgroups may benefit more from targeted therapies that modulate the tumor immune microenvironment.

Sensitivity analysis Conduct sensitivity analyses to assess the impact of excluding studies on the overall results.

Country(ies) involved China.

Keywords Immune cell infiltration, Prognostic biomarkers, Tumor microenvironment, Personalized treatment, Endometrial cancer.

Contributions of each author
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