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Systematic Review

Prognostic value of Foxp3+ regulatory T cells in endometrial cancer: a meta-analysis

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Summary

Endometrial cancer is the second most common gynecologic cancer globally, and the prognosis of advanced or recurrent endometrial cancer is very poor. Currently, the prognostic value of Forkhead box protein P3 (FoxP3)+ regulatory T cells (Tregs) in endometrial cancer is unclear. This meta-analysis aimed to evaluate prognostic significance of Foxp3+ Tregs in endometrial cancer. The authors searched the literature from databases including PubMed, Cocohrane, and Web of Science, and selected four eligible studies for further analysis. Meta-analysis of the survival data from 869 endometrial cancer patients showed that there were no significant differences in overall survival, disease-free survival, relapse-free survival or disease-specific survival between patients with high levels of Foxp3+ Tregs infiltration, and those with low levels of Foxp3+ Tregs. In summary, this meta-analysis provided systemic evidence that Foxp3+ Tregs infiltration is not significantly associated with the prognosis of patients with endometrial cancer.

Key words: Foxp3; Tregs; Endometrial cancer; Prognosis; Meta-analysis.

Introduction

Endometrial cancer is the second most common gynecologic cancer globally [1, 2]. Currently, chemotherapy is the main therapy method for advanced or recurrent endometrial cancer, but the prognosis of advanced or recurrent endometrial cancer is very poor [3, 4]. Recent evidence has shown that tumor microenvironment is crucially involved in the initiation and progression of many types of tumors [5-7]. Regulatory T cells (Tregs) emerge as important player in tumor microenvironment due to their ability to suppress T cell immunity. The immunosuppression function of Tregs is dependent on Forkhead box protein P3 (FoxP3), a transcription factor considered as the marker for Tregs [8].

Due to immunosuppression function of Tregs, Foxp3+ Tregs infiltration in tumor could predict poor prognosis of cancer patients. Nevertheless, recent studies indicated that Foxp3+Tregs increased rather than decreased the survival of patients with certain cancer types [9-11]. Currently, the prognostic value of Foxp3+ Tregs in endometrial cancer remains undecided. Therefore, the authors performed a meta-analysis on eligible studies to determine the prognostic value of Foxp3+ Tregs in endometrial cancer.

Materials and Methods

Database of PubMed, Cocohrane, and Web of Science (up to September 2018) were screened with the strategy as below: (Foxp3 OR regulatory T cells), (endometrial cancer), (Survival OR prognosis OR outcome OR mortality). The inclusion criteria were (1) all patients were confirmed as endometrial cancer, (2) FOXP3 Tregs were detected by immunohistochemical analysis; (3) survival data were available and Hazard ratio (HR), and 95% confidence interval (CI) were calculated; (4) The literature was in English. The data were independently extracted by two investigators, including publication year, the first author, the source and sample size of the subjects, follow-up duration, and patient survival. All studies were scored according to Newcastle-Ottawa Scale (NOS) criteria: (1) subject selection: 0-4, (2) comparability of subject: 0-2, and (3) clinical outcome: 0-3. Study was considered as good quality if the score was ≥ 7 [12]. All data were analyzed with STATA 12.0 program. $P < 0.05$ was deemed to be significant.

Results

The literature search was performed as shown in the flow diagram (Figure 1). A total of 17 studies published in English were selected via initial literature search. After reviewing the titles and abstracts, only six studies were selected. After careful reading the full text, only four studies were included as eligible studies because of the availability of the data on the prognosis of the patients [13-16].

The characteristics of four eligible studies are shown in Table 1 [13-16]. The authors extracted data on overall survival (OS), relapse-free survival (RFS), and disease-specific survival (DSS) from one study, respectively, and extracted data on disease-free survival (DFS) from two studies. The studied subjects were all from Europe: two studies in Netherlands, one study in Germany, and one

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