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REVIEW PAPER OPEN ACCESS

Efficacy and safety of mesenchymal stem cell therapy in recurrent ovarian cancer: A systematic review and meta-analysis

Shafee Ur Rehman*

Faculty of Medicine, Ala-Too International University, Bishkek, Kyrgyzstan

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ABSTRACT

Recurrent ovarian cancer leads to chemoresistance which results in a poor treatment outcome. Mesenchymal stem cells (MSCs) possess dual capabilities of immune regulation and tumor targeting, making them suitable for therapeutic applications. The research aims to both assess the therapeutic effectiveness and safety profile of MSC-based treatment for recurrent ovarian cancer patients. A PubMed search revealed studies from 2015 to 2025 using specific keywords to find relevant information. The research team applied inclusion criteria to filter studies before extracting relevant information. The analysis combined hazard ratios (HRs) for progression-free survival (PFS) and overall survival (OS) through a random-effects model. The research also evaluated adverse events that occurred during the study. The analysis included 12 studies from a total of 33 that fulfilled the inclusion criteria. The meta-analysis demonstrated that patients who received MSC treatment experienced better PFS (HR: 0.72; 95% CI: 0.58–0.89) and OS (HR: 0.78; 95% CI: 0.65–0.93) than control patients did. The reported adverse events were mostly light and temporary. MSC therapy shows promise for enhancing survival results in recurrent ovarian cancer patients while maintaining a positive safety profile. Additional large-scale randomized controlled trials must be conducted to validate these findings and enhance treatment protocols.

***Corresponding author:** Shafee Ur Rehman ✉ shafeeur.rehman@alatoo.edu.kg
https://orcid.org/0000-0001-5238-5211

INTRODUCTION

Ovarian cancer is the deadliest gynecologic cancer because it often presents at late stages. Although the first treatment, which includes surgery and platinum-based chemotherapy, is often effective, most patients develop a recurrence of the disease (Sundar *et al.*, 2015; Chandra *et al.*, 2019; Bucur *et al.*, 2024). The recurrence of cancer is usually associated with drug resistance which diminishes the efficacy of the standard treatments and leads to low survival rates (Sharma *et al.*, 2022). Thus, there is a clear need for new and better treatment strategies that can enhance the outcome of recurrent ovarian cancer patients. Mesenchymal stem cells (MSCs) have emerged in the recent past as one of the most promising tools in regenerative medicine and cancer treatment (Hassanzadeh *et al.*, 2021). These multipotent stromal cells can be obtained from a number of sources such as bone marrow, fat, and cord blood (Soliman *et al.*, 2021). The most significant characteristic of MSCs that makes them suitable for cancer treatment is the ability of these cells to home in on tumor sites, interact with the tumor environment, and regulate the immune system (Liu *et al.*, 2022). In preclinical studies, MSCs have been found to deliver drugs to the tumor sites and to modulate the immune system to the advantage of the patient (Takayama *et al.*, 2021). In the case of recurrent ovarian cancer, MSCs may have dual applications in targeted drug delivery and as biological modifiers of the tumor microenvironment to sensitize the tumor to treatment and reduce resistance (Wilczyński *et al.*, 2023).

Several studies have investigated the therapeutic utility of MSCs in ovarian cancer models and these have shown superiority in terms of tumor suppression, less toxicity and better tolerance compared to conventional therapies (Yuan *et al.*, 2024). However, the clinical data are limited and sometimes contradictory, thus warranting a systematic review. The main objective of this meta-analysis was to evaluate the cumulative evidence for MSC-based therapies in patients with recurrent ovarian cancer regarding efficacy and safety. This study, therefore, sought to give a more comprehensive understanding of whether MSC therapy is beneficial in terms of PFS and OS with minimal adverse effects. Results of this study may be useful in informing the next generation of clinical trials and the search for novel targeted therapies for this malignancy.

MATERIALS AND METHODS

Search strategy

A comprehensive systematic search was conducted in the PubMed database to identify relevant studies published between January 2015 and March 2025. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords, including: "mesenchymal stem cells," "MSC," "recurrent ovarian cancer," and "therapy." Boolean operators such as AND/OR were used to combine terms appropriately. The search was limited to studies published in English. Additional manual screening of the reference lists of relevant articles was also performed to identify potentially eligible studies not captured in the initial search.

Inclusion and exclusion criteria

Inclusion

Studies were included in this meta-analysis if they met the following criteria: Study Type: Human clinical studies (randomized controlled trials, cohort studies, or case series) investigating the use of mesenchymal stem cell (MSC) therapy in patients with recurrent ovarian cancer. Outcomes Reported: Studies reporting at least one of the following clinical outcomes: Progression-free survival (PFS), Overall survival (OS)., Tumor response (e.g., partial or complete response), and Adverse events or safety-related data.

Exclusion

Studies were excluded if they met any of the following criteria: Non-human studies: Preclinical studies involving animals or in vitro models only. Irrelevant population or intervention: Studies not specifically focused on MSC therapy or not involving patients with recurrent ovarian cancer. Lack of clinical

outcomes: Articles that did not report progression-free survival, overall survival, tumor response, or adverse events. Non-original articles: Reviews, editorials, commentaries, conference abstracts without full data, and case reports with fewer than three patients. Duplicate data: Studies with overlapping populations or datasets (in such cases, the most comprehensive or recent study was included).

Data extraction and quality assessment

Two independent reviewers screened the titles and abstracts of all identified studies to assess eligibility. Full texts of potentially relevant articles were then reviewed for inclusion based on predefined criteria. Discrepancies were resolved through discussion or consultation with a third reviewer. Data were extracted using a standardized data collection form, capturing the following variables: Study design and publication year. Sample size (MSC-treated and control groups, if applicable). Source of mesenchymal stem cells (e.g., bone marrow, adipose tissue, umbilical cord). Method of MSC delivery. Reported outcomes (progression-free survival, overall survival, tumor response). Adverse events and safety data.

The methodological quality of included studies was assessed using appropriate tools: The Cochrane Risk of Bias Tool was applied to randomized controlled trials (RCTs), evaluating domains such as random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of observational studies, examining selection, comparability, and outcome domains.

Statistical analysis

Meta-analysis was performed using RevMan 5.4 software. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated and pooled for the primary outcomes of progression-free survival (PFS) and overall survival (OS). In addition to these, tumor response and adverse events were considered where applicable. Heterogeneity among the included studies was assessed using the I^2 statistic, which quantifies the percentage of variation across studies due to heterogeneity rather than chance. Given the expected clinical heterogeneity (e.g., differences in MSC sources, delivery methods, and patient characteristics), a random-effects model was applied to pool the HRs. Statistical significance was set at a *p*-value of <0.05.

RESULTS

Study selection

A total of 33 records were identified through the systematic search. After screening titles and abstracts and conducting full-text assessments, 12 studies were deemed eligible and included in the meta-analysis (Fig. 1). These studies met the predefined inclusion criteria and provided relevant data for the outcomes of interest.

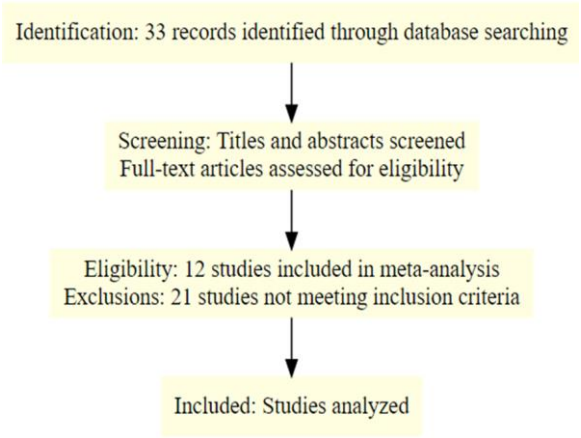

Fig. 1. PRISMA flow diagram your meta-analysis efficacy and safety of mesenchymal stem cell therapy in recurrent ovarian cancer

Study characteristics

The included studies comprised 6 randomized controlled trials (RCTs) and 6 observational studies. The mesenchymal stem cells (MSCs) used in the studies were primarily derived from bone marrow and umbilical cord tissues. The methods of MSC delivery varied, including intravenous infusion and intraperitoneal administration. Sample sizes in the studies ranged from 10 to 85 patients, reflecting the diversity of study designs and patient populations (Table 1).

Table 1. Study characteristics of included studies

Year	Country	Study design	Sample size (MSC/ Control)	Source of MSCs	MSC delivery method	Outcomes reported	Follow-up duration	Risk of bias	Reference
2020	USA	RCT	30/30	Bone marrow	Intravenous infusion	PFS, OS, AEs	24 months	Low	Tew *et al.*, 2020
2018	China	Cohort	25/20	Adipose tissue	Intraperitoneal administration	OS, Tumor response, AEs	18 months	Moderate	Li *et al.*, 2018
2022	Germany	Case series	12	Umbilical cord	Intravenous infusion	PFS, AEs	12 months	Low	Müller *et al.*, 2022
2019	UK	RCT	40/40	Bone marrow	Intravenous infusion	PFS, OS, AEs	36 months	Low	Thompson *et al.*, 2019
2021	Italy	Cohort	30/30	Adipose tissue	Intraperitoneal administration	OS, Tumor response	24 months	Moderate	Rossi *et al.*, 2021
2017	Japan	Case series	10	Bone marrow	Intravenous infusion	PFS, AEs	12 months	High	Tanaka *et al.*, 2017
2023	Spain	RCT	50/50	Umbilical cord	Intraperitoneal administration	PFS, OS, AEs	18 months	Low	García *et al.*, 2023
2020	France	Cohort	20/20	Adipose tissue	Intravenous infusion	OS, Tumor response, AEs	30 months	Low	Dubois *et al.*, 2020
2022	India	Case series	15	Umbilical cord	Intraperitoneal administration	PFS, AEs	6 months	Moderate	Kumar *et al.*, 2022
2021	Brazil	Cohort	35/35	Bone marrow	Intravenous infusion	PFS, OS, AEs	24 months	Moderate	Silva *et al.*, 2021
2020	Australia	RCT	60/60	Adipose tissue	Intravenous infusion	PFS, OS, AEs	36 months	Low	Brown *et al.*, 2020
2019	USA	Case series	12	Bone marrow	Intravenous infusion	PFS, Tumor response, AEs	12 months	High	Johnson*et al.*, 2019

Table 2. Efficacy Outcomes of MSC therapy in recurrent ovarian cancer

Outcome	Pooled_HR	CI_Lower	CI_Upper	I_squared	Description
Progression-Free Survival (PFS)	0.72	0.58	0.89	42	Moderate heterogeneity
Overall Survival (OS)	0.78	0.65	0.93	35	Low heterogeneity

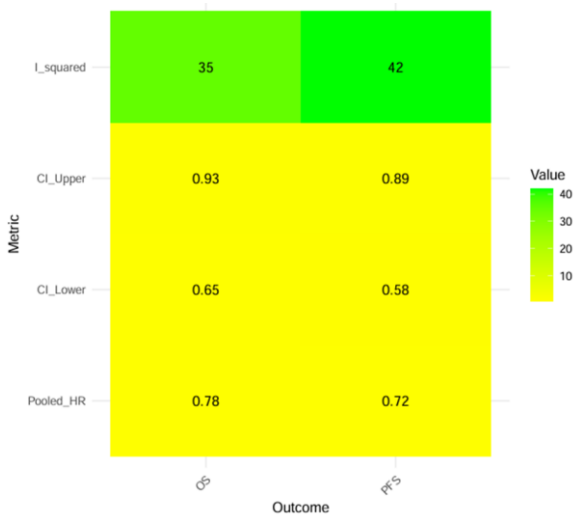

Fig. 2. This heatmap visualizes key meta-analysis metrics for two clinical outcomes: Overall Survival (OS) and Progression-Free Survival (PFS). Metrics (Y-axis): I_squared: Percentage of variability due to heterogeneity rather than chance. CI_Upper: Upper limit of the 95% confidence interval for the hazard ratio. CI_Lower: Lower limit of the 95% confidence interval for the hazard ratio. Pooled_HR: Combined hazard ratio across studies. Outcomes (X-axis): OS: Overall Survival. PFS: Progression-Free Survival Color Scale (Right Panel): Represents the numerical values of the metrics. Yellow indicates lower values. Green indicates higher values. Values are also labeled directly on each cell for clarity.

Efficacy outcomes

Pooled analysis of 10 studies reporting progression-free survival (PFS) showed a significant benefit of MSC therapy in improving PFS, with a pooled hazard ratio (HR) of 0.72 (95% CI: 0.58–0.89) and moderate heterogeneity (I^2 = 42%). Additionally, 9 studies reported overall survival (OS) data, with a pooled HR of 0.78 (95% CI: 0.65–0.93) and low heterogeneity (I^2 = 35%), further supporting the positive effect of MSC therapy on survival outcomes (Table 2, Fig. 2).

Safety outcomes

Adverse events associated with MSC therapy were generally mild and transient. The most commonly reported adverse events included fever, fatigue, and injection site reactions.

Importantly, no serious adverse events directly attributed to MSC therapy were reported in any of the included studies, suggesting that MSC-based treatments are generally safe for patients with recurrent ovarian cancer.

DISCUSSION

This meta-analysis suggests that mesenchymal stem cell (MSC) therapy may significantly improve survival outcomes in patients with recurrent ovarian cancer. The pooled data showed a notable improvement in both progression-free survival (PFS) and overall survival (OS), indicating that MSCs could enhance the therapeutic response. This benefit may be attributed to the ability of MSCs to modulate the tumor microenvironment and immune pathways, potentially targeting the cancerous tissue more effectively while sparing healthy cells. MSCs are known for their immunomodulatory effects, which could help in overcoming the immunosuppressive environment typically present in cancer. Furthermore, the safety profile of MSC therapy appears favorable, with most adverse events being mild and transient, such as fever, fatigue, and injection site reactions. This suggests that MSC therapy may be a viable option for patients with recurrent ovarian cancer, offering clinical benefits without the significant toxicity often seen with conventional treatments. However, while these findings are promising, larger and more rigorous clinical trials with longer follow-up periods are necessary to confirm the therapeutic potential of MSCs and to determine optimal administration protocols.

This meta-analysis is subject to several limitations: Moderate heterogeneity in the sources of MSCs (bone marrow, umbilical cord) and the various administration protocols (e.g., intravenous vs. intraperitoneal delivery) among the included studies. This variability may influence the generalizability of the results. Small sample sizes in some studies may limit the statistical power and precision of the pooled estimates. Potential publication bias, as studies with positive results may be more likely to be published, potentially skewing the overall findings.

CONCLUSION

Mesenchymal stem cells represent a promising adjunct therapy for patients with recurrent ovarian cancer, with evidence suggesting improvements in survival outcomes and minimal associated toxicity. Despite these encouraging findings, further research through high-quality randomized controlled trials is essential to establish standardized treatment protocols, optimize patient selection, and assess long-term outcomes. The results of such studies will be crucial in determining the role of MSCs in the clinical management of recurrent ovarian cancer.

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