



## PERITONEAL CARCINOMATOSIS SECONDARY TO OVARIAN CANCER: PROGNOSTIC IMPACT, THERAPEUTIC APPROACHES, AND CLINICAL OUTCOMES – A SYSTEMATIC REVIEW

## CARCINOMATOSE PERITONEAL SECUNDÁRIA AO CÂNCER DE OVÁRIO: IMPACTO PROGNÓSTICO, ABORDAGENS TERAPÊUTICAS E DESFECHOS CLÍNICOS – UMA REVISÃO SISTEMÁTICA

## CARCINOMATOSIS PERITONEAL SECUNDARIA AL CÁNCER DE OVARIO: IMPACTO PRONÓSTICO, ENFOQUES TERAPÉUTICOS Y RESULTADOS CLÍNICOS – UNA REVISIÓN SISTEMÁTICA

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### ABSTRACT

**Introduction:** Peritoneal carcinomatosis represents the most common pattern of dissemination in advanced ovarian cancer and remains a major determinant of prognosis, treatment complexity, and survival outcomes. Despite advances in systemic therapy and surgical techniques, peritoneal involvement continues to be associated with high morbidity and mortality. The integration of cytoreductive surgery, systemic chemotherapy, and intraperitoneal strategies has reshaped the therapeutic landscape, yet optimal patient selection and timing of interventions remain debated.

**Objective:** The main objective of this systematic review was to evaluate the prognostic impact of peritoneal carcinomatosis secondary to ovarian cancer. Secondary objectives included assessing the effectiveness of different therapeutic approaches, comparing surgical and nonsurgical strategies, analyzing clinical outcomes and survival metrics, and identifying factors associated with treatment response and disease progression.

**Methods:** A systematic search was conducted across PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Studies published within the last five years were prioritized, with extension up to ten years when necessary. Eligible studies included clinical trials and observational studies evaluating prognosis and treatment outcomes in ovarian cancer-related peritoneal carcinomatosis. Data were synthesized qualitatively with structured comparison of interventions and outcomes.

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**Results and Discussion:** A total of 20 studies met the inclusion criteria and were included in the final analysis. The evidence indicates that complete or near-complete cytoreduction remains the strongest prognostic factor for survival, while the role of hyperthermic intraperitoneal chemotherapy and novel systemic agents shows variable benefit depending on disease burden and patient selection. Emerging data support individualized, multidisciplinary strategies to optimize outcomes while minimizing treatment-related morbidity.

**Conclusion:** Peritoneal carcinomatosis secondary to ovarian cancer continues to pose significant prognostic and therapeutic challenges. Current evidence supports aggressive yet carefully selected surgical approaches combined with tailored systemic therapy. Ongoing refinement of patient selection criteria and integration of emerging treatments are essential to improve long-term outcomes.

**Keywords:** Ovarian Neoplasms. Peritoneal Neoplasms. Cytoreductive Surgery. Antineoplastic Combined Chemotherapy.

## RESUMO

**Introdução:** A carcinomatose peritoneal representa o padrão mais comum de disseminação no câncer de ovário avançado e permanece como um dos principais determinantes do prognóstico, da complexidade terapêutica e dos desfechos de sobrevida. Apesar dos avanços na terapia sistêmica e nas técnicas cirúrgicas, o acometimento peritoneal continua associado a elevada morbidade e mortalidade. A integração da cirurgia citorreductora, da quimioterapia sistêmica e de estratégias intraperitoneais remodelou o cenário terapêutico; contudo, a seleção ideal de pacientes e o momento adequado das intervenções ainda são objeto de debate.

**Objetivo:** O objetivo principal desta revisão sistemática foi avaliar o impacto prognóstico da carcinomatose peritoneal secundária ao câncer de ovário. Como objetivos secundários, buscou-se avaliar a eficácia de diferentes abordagens terapêuticas, comparar estratégias cirúrgicas e não cirúrgicas, analisar desfechos clínicos e métricas de sobrevida, além de identificar fatores associados à resposta ao tratamento e à progressão da doença.

**Métodos:** Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e na International Clinical Trials Registry Platform. Estudos publicados nos últimos cinco anos foram priorizados, com extensão para até dez anos quando necessário. Foram incluídos ensaios clínicos e estudos observacionais que avaliaram prognóstico e desfechos terapêuticos na carcinomatose peritoneal relacionada ao câncer de ovário. Os dados foram sintetizados de forma qualitativa, com comparação estruturada das intervenções e dos desfechos.

**Resultados e Discussão:** Um total de 20 estudos atendeu aos critérios de inclusão e foi incorporado à análise final. As evidências indicam que a citorredução completa ou quase completa permanece como o fator prognóstico mais relevante para a sobrevida, enquanto o papel da quimioterapia intraperitoneal hipertérmica e de novos agentes sistêmicos apresenta benefícios variáveis, dependentes da carga tumoral e da seleção dos pacientes. Dados emergentes sustentam estratégias individualizadas e multidisciplinares para otimizar os resultados, minimizando a morbidade relacionada ao tratamento.

**Conclusão:** A carcinomatose peritoneal secundária ao câncer de ovário continua a representar um importante desafio prognóstico e terapêutico. As evidências atuais apoiam abordagens cirúrgicas agressivas, porém criteriosamente selecionadas, combinadas com terapia sistêmica personalizada. O aprimoramento contínuo dos critérios de seleção de

pacientes e a integração de tratamentos emergentes são fundamentais para melhorar os desfechos em longo prazo.

**Palavras-chave:** Neoplasias Ovarianas. Neoplasias Peritoneais. Cirugia Citorreductora. Quimioterapia Antineoplásica Combinada.

## RESUMEN

**Introducción:** La carcinomatosis peritoneal representa el patrón más frecuente de diseminación en el cáncer de ovario avanzado y continúa siendo un determinante clave del pronóstico, la complejidad del tratamiento y los resultados de supervivencia. A pesar de los avances en la terapia sistémica y en las técnicas quirúrgicas, el compromiso peritoneal sigue asociado a una elevada morbilidad. La integración de la cirugía citorreductora, la quimioterapia sistémica y las estrategias intraperitoneales ha redefinido el panorama terapéutico; sin embargo, la selección óptima de pacientes y el momento adecuado de las intervenciones siguen siendo objeto de debate.

**Objetivo:** El objetivo principal de esta revisión sistemática fue evaluar el impacto pronóstico de la carcinomatosis peritoneal secundaria al cáncer de ovario. Como objetivos secundarios, se incluyeron la evaluación de la eficacia de diferentes enfoques terapéuticos, la comparación entre estrategias quirúrgicas y no quirúrgicas, el análisis de los resultados clínicos y las métricas de supervivencia, así como la identificación de factores asociados con la respuesta al tratamiento y la progresión de la enfermedad.

**Métodos:** Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y en la International Clinical Trials Registry Platform. Se priorizaron los estudios publicados en los últimos cinco años, con extensión hasta diez años cuando fue necesario. Se incluyeron ensayos clínicos y estudios observacionales que evaluaron el pronóstico y los resultados terapéuticos en la carcinomatosis peritoneal asociada al cáncer de ovario. Los datos se sintetizaron de forma cualitativa, mediante una comparación estructurada de las intervenciones y los resultados.

**Resultados y Discusión:** Un total de 20 estudios cumplió con los criterios de inclusión y fue incorporado en el análisis final. La evidencia indica que la citorreducción completa o casi completa continúa siendo el factor pronóstico más sólido para la supervivencia, mientras que el papel de la quimioterapia intraperitoneal hipertérmica y de los nuevos agentes sistémicos muestra beneficios variables según la carga tumoral y la selección de los pacientes. Los datos emergentes respaldan estrategias individualizadas y multidisciplinarias para optimizar los resultados y minimizar la morbilidad relacionada con el tratamiento.

**Conclusión:** La carcinomatosis peritoneal secundaria al cáncer de ovario sigue representando un desafío significativo desde el punto de vista pronóstico y terapéutico. La evidencia actual respalda enfoques quirúrgicos agresivos, cuidadosamente seleccionados, combinados con terapia sistémica personalizada. El perfeccionamiento continuo de los criterios de selección de pacientes y la integración de tratamientos emergentes son esenciales para mejorar los resultados a largo plazo.

**Palabras clave:** Neoplasias Ovárica. Neoplasias Peritoneales. Cirugía Citorreductora. Quimioterapia Antineoplásica Combinada.



## 1 INTRODUCTION

Peritoneal carcinomatosis is the predominant pattern of metastatic spread in epithelial ovarian cancer and represents a defining feature of advanced-stage disease.<sup>1</sup> Its presence reflects both the biological aggressiveness of the tumor and the anatomical propensity of ovarian cancer cells to disseminate within the peritoneal cavity.<sup>1</sup> This dissemination pattern is associated with impaired survival, increased symptom burden, and substantial therapeutic complexity.<sup>1</sup> Historically, peritoneal involvement was considered a marker of incurable disease, leading to a predominantly palliative treatment approach.<sup>2</sup> However, advances in surgical techniques and systemic therapies have progressively shifted this paradigm.<sup>2</sup> Contemporary management strategies now emphasize aggressive tumor debulking combined with multimodal oncologic treatment.<sup>2</sup>

Ovarian cancer remains one of the leading causes of gynecologic cancer–related mortality worldwide, largely due to late-stage diagnosis and extensive peritoneal spread at presentation.<sup>3</sup> The absence of early specific symptoms contributes to delayed detection, allowing widespread intraperitoneal dissemination before clinical recognition.<sup>3</sup> As a result, peritoneal carcinomatosis is identified in the majority of patients at the time of initial diagnosis.<sup>3</sup> The prognostic implications of peritoneal disease burden have been extensively studied, with tumor volume and distribution emerging as key determinants of survival.<sup>4</sup> Quantitative and qualitative assessments of peritoneal involvement are increasingly used to guide therapeutic decision-making.<sup>4</sup> These parameters influence not only prognosis but also the feasibility and expected benefit of aggressive surgical intervention.<sup>4</sup>

Cytoreductive surgery has become a cornerstone in the management of ovarian cancer–related peritoneal carcinomatosis.<sup>5</sup> The extent of residual disease after surgery is consistently recognized as one of the strongest predictors of overall and progression-free survival.<sup>5</sup> Complete macroscopic cytoreduction is associated with significantly improved outcomes compared with suboptimal debulking.<sup>5</sup> Nevertheless, achieving complete cytoreduction often requires extensive multivisceral resections, which may increase perioperative morbidity.<sup>6</sup> This reality underscores the importance of careful patient selection and specialized surgical expertise.<sup>6</sup> Balancing oncologic benefit with surgical risk remains a central challenge in clinical practice.<sup>6</sup>

In parallel with surgical advances, systemic chemotherapy has undergone significant evolution over the past decade.<sup>7</sup> Platinum-based regimens combined with taxanes remain the backbone of treatment for advanced ovarian cancer with peritoneal involvement.<sup>7</sup> More recently, targeted therapies and maintenance strategies have been incorporated into standard care algorithms.<sup>7</sup> Agents such as angiogenesis inhibitors and poly(ADP-ribose)



polymerase inhibitors have demonstrated survival benefits in selected patient populations.<sup>8</sup> Their role in the context of extensive peritoneal carcinomatosis continues to be actively investigated.<sup>8</sup> Treatment response appears to be influenced by both molecular characteristics and disease distribution.<sup>8</sup>

Hyperthermic intraperitoneal chemotherapy has emerged as a controversial adjunctive strategy in the management of ovarian cancer-related peritoneal carcinomatosis.<sup>9</sup> By delivering heated chemotherapy directly into the peritoneal cavity, this approach aims to enhance local drug penetration and cytotoxicity.<sup>9</sup> Clinical trials have reported heterogeneous results regarding survival benefit and toxicity.<sup>9</sup> As a consequence, the integration of hyperthermic intraperitoneal chemotherapy into routine practice remains debated.<sup>10</sup> Differences in patient selection, surgical timing, and chemotherapy protocols contribute to inconsistent findings across studies.<sup>10</sup> Clear consensus regarding its optimal use has yet to be established.<sup>10</sup>

Accurate prognostic stratification is essential for optimizing treatment strategies in patients with peritoneal carcinomatosis secondary to ovarian cancer.<sup>11</sup> Several scoring systems and imaging-based assessments have been proposed to quantify peritoneal disease burden.<sup>11</sup> These tools aim to predict resectability, surgical outcomes, and survival.<sup>11</sup> Despite their clinical utility, variability in assessment methods limits comparability across studies.<sup>12</sup> Standardization of prognostic metrics is therefore critical to improve evidence synthesis and clinical decision-making.<sup>12</sup> Robust prognostic models may facilitate personalized treatment planning and improve patient counseling.<sup>12</sup>

The complexity of managing ovarian cancer-related peritoneal carcinomatosis highlights the need for a multidisciplinary approach.<sup>13</sup> Optimal care involves close collaboration among gynecologic oncologists, surgical oncologists, medical oncologists, radiologists, and supportive care teams.<sup>13</sup> Such integration is associated with improved treatment coordination and potentially better outcomes.<sup>13</sup> Given the rapidly evolving therapeutic landscape, continuous appraisal of emerging evidence is essential.<sup>14</sup> Systematic reviews play a key role in synthesizing data, identifying knowledge gaps, and guiding evidence-based practice.<sup>14</sup> A comprehensive evaluation of recent literature is therefore warranted to inform contemporary management strategies.<sup>14</sup>

## 2 OBJECTIVES

The main objective of this systematic review was to critically evaluate the prognostic impact of peritoneal carcinomatosis secondary to ovarian cancer in the context of contemporary oncologic management. Secondary objectives were to analyze the

effectiveness of cytoreductive surgery in patients with peritoneal dissemination, to assess the role of systemic chemotherapy and targeted therapies on survival outcomes, to evaluate the clinical benefits and limitations of intraperitoneal treatment strategies including hyperthermic intraperitoneal chemotherapy, to identify prognostic factors associated with treatment response and disease progression, and to explore implications for individualized, multidisciplinary clinical decision-making in advanced ovarian cancer.

### **3 METHODOLOGY**

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, with a predefined protocol outlining objectives, eligibility criteria, and methodological steps. A comprehensive literature search was performed using PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform to identify relevant studies addressing peritoneal carcinomatosis secondary to ovarian cancer. The search strategy combined controlled vocabulary and free-text terms related to ovarian cancer, peritoneal carcinomatosis, prognosis, cytoreductive surgery, chemotherapy, and clinical outcomes.

Eligible studies included randomized controlled trials, prospective and retrospective observational studies, and comparative cohort analyses published within the last five years, with extension up to ten years when fewer than ten eligible studies were identified. Studies involving human participants were prioritized, while animal or in vitro studies were considered separately and excluded from the main synthesis. There were no language restrictions, and studies with small sample sizes were included but explicitly recognized as a limitation during interpretation. Case reports, narrative reviews, editorials, and studies lacking outcome data relevant to prognosis or treatment were excluded.

Study selection was performed independently by two reviewers who screened titles and abstracts, followed by full-text assessment of potentially eligible articles. Discrepancies were resolved through consensus or consultation with a third reviewer. Data extraction was conducted using standardized forms, capturing study characteristics, population details, interventions and comparators, outcome measures, and main conclusions. The selection process was documented using a PRISMA flow diagram to ensure transparency and reproducibility.

## 4 RESULTS

The systematic search across all selected databases identified a total of 1,248 records related to peritoneal carcinomatosis and ovarian cancer. After removal of duplicates, 812 unique records remained and were screened based on titles and abstracts. Of these, 732 records were excluded due to irrelevance to the study objectives, non-clinical design, or lack of outcome data. Eighty full-text articles were assessed for eligibility, resulting in the exclusion of 60 studies primarily due to inappropriate population, insufficient outcome reporting, or overlapping datasets. Ultimately, 20 studies met all inclusion criteria and were included in the qualitative synthesis and final analysis.

Table 1 summarizes the characteristics, interventions, outcomes, and main conclusions of all studies included in this systematic review, ordered chronologically from oldest to most recent.

**Table 1**

| Reference                  | Population / Intervention / Comparison   | Outcomes  | Main conclusions  |
|----------------------------|--|---|---|
| Zambrano-Vera et al., 2021 | Women aged 65 years or older with epithelial ovarian cancer and peritoneal carcinomatosis. Overall survival, progression-free survival, perioperative morbidity, and mortality were assessed.  | Overall survival, hyperthermic intraperitoneal chemotherapy was feasible in selected elderly patients and preclude aggressive locoregional therapy when appropriate.  | The study concluded that cyoreductive surgery plus  |
| Chambers et al., 2021      | Women with advanced or recurrent epithelial ovarian cancer and peritoneal carcinomatosis. Sites of recurrence, extra-cytoreductive surgery plus peritoneal failure rates, hyperthermic intraperitoneal chemotherapy and survival outcomes were assessed. | first cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy, supporting vigilant systemic surveillance and the importance of systemic disease control. | The study concluded that a substantial proportion of first recurrences occurred outside the peritoneal cavity after |
| Glenon et al., 2021        | Patients undergoing interval Renal cytoreductive surgery with perioperative cisplatin-based hyperthermic complications, short-term intraperitoneal chemotherapy toxicity, and associated with improved oncologic tolerability of cisplatin-based         | The study concluded that sodium thiosulphate was and associated with improved oncologic tolerability of cisplatin-based   |   |

| Reference               | Population / Intervention / Comparison   | Outcomes  | Main conclusions   |
|-------------------------|--|---|--|
| Gil-Moreno et al., 2021 | were managed with or without outcomes sodium thiosulphate for toxicity assessed. mitigation.   | were hyperthermic intraperitoneal chemotherapy without compromising immediate perioperative outcomes in the interval setting. | The trial concluded that the and peritoneal dissemination Device-related adverse device strategy was feasible received an implantable events, feasibility and demonstrated acceptable metastatic tumor cell trap endpoints, and safety in early testing, device as an adjunct strategy to biological performance supporting further evaluation focalize intraperitoneal spread measures and were monitored for safety assessed. and performance. |
| Jónsdóttir et al., 2021 | Patients with ovarian cancer and peritoneal carcinomatosis were assessed using the peritoneal cancer index before cytoreductive surgery and analyzed for predictors of incomplete cytoreduction.   | Rates of complete cytoreduction and predictive performance of peritoneal cancer index thresholds were assessed.               | The study concluded that the peritoneal cancer index was a strong predictor of incomplete cytoreduction and could support preoperative stratification and surgical planning.   |
| Asp et al., 2022        | Patients with advanced ovarian cancer undergoing primary progression-free debulking surgery were survival were assessed evaluated for prognostic value according to peritoneal of peritoneal cancer index and cancer index and tumor extent in the context of residual disease residual disease. | Overall survival and disease status.  | The study concluded that higher tumor extent measured by peritoneal cancer index adversely influenced survival outcomes, reinforcing disease burden as a prognostic determinant even in surgically treated cohorts.  |
| Egger et al., 2022      | Patients with high-grade ovarian cancer and peritoneal carcinomatosis were scored by peritoneal cancer index and evaluated for associations with complete cytoreduction, complications, and survival.  | Completeness of cytoreduction, severe perioperative complications, and survival outcomes were assessed.                       | The study concluded that peritoneal cancer index predicted complete cytoreduction and correlated with outcomes, and that preventing severe complications was particularly important in patients with high tumor load.  |
| Raouf et al., 2022      | Patients with ovarian and other gynecologic malignancies with implementation   | Feasibility, technical implementation   | The study concluded that pressurized intraperitoneal   |

| Reference            | Population / Intervention / Comparison  | Outcomes   | Main conclusions   |
|----------------------|---|--|--|
| Lee et al., 2022     | Patients with advanced-stage ovarian cancer treated with Progression-free neoadjuvant chemotherapy survival, underwent interval debulking surgery, with hyperthermic postoperative intraperitoneal chemotherapy morbidity versus interval debulking assessed. surgery alone.  | overall and were   | continued investigation of intraperitoneal aerosol approaches for patients not suitable for aggressive cytoreduction. The study concluded that adding hyperthermic intraperitoneal chemotherapy to interval debulking surgery was associated with favorable oncologic signals in selected patients without a clear excess of short-term complications. |
| Lyu et al., 2022     | Patients with ovarian cancer undergoing interval debulking surgery after neoadjuvant chemotherapy were compared perioperative survival endpoints and chemotherapy were compared perioperative safety between those receiving outcomes hyperthermic intraperitoneal assessed. chemotherapy and those not receiving it. | safety were  | The study concluded that interval debulking surgery plus hyperthermic intraperitoneal chemotherapy did not demonstrate an obvious advantage over surgery alone in the studied cohort, highlighting the importance of patient selection and protocol standardization.   |
| Fagan et al., 2023   | Patients undergoing cytoreductive surgery for ovarian cancer with peritoneal carcinomatosis were evaluated using peritoneal cancer index to predict complete cytoreduction. Complete cytoreduction rates and predictive accuracy of peritoneal cancer index cutoffs were assessed.                                    |  | The study concluded that a lower peritoneal cancer index threshold was strongly associated with achieving complete cytoreduction, supporting routine integration of burden scoring into operative decision-making.   |
| Aronson et al., 2023 | Patients with primary stage III epithelial ovarian cancer treated with neoadjuvant chemotherapy underwent   | Overall survival and progression-free survival were assessed | The study concluded that hyperthermic intraperitoneal chemotherapy at interval cytoreductive surgery   |

| Reference                   | Population / Intervention / Comparison   | Outcomes  | Main conclusions  |
|-----------------------------|--|---|---|
| Lee et al., 2023            | interval cytoreductive surgery in updated long-term analyses with hyperthermic intraperitoneal chemotherapy versus interval surgery without hyperthermic intraperitoneal chemotherapy in a randomized phase 3 framework with long-term follow-up.  |   | conferred durable long-term survival benefit, supporting its consideration in appropriately selected stage III patients.  |
| Somashekhar et al., 2023    | Patients with advanced epithelial ovarian cancer and peritoneal carcinomatosis underwent cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy in upfront versus interval settings using a prospective registry with retrospective analysis.  | Overall survival, progression-free survival, perioperative outcomes assessed. | The study concluded that cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy was feasible in and both upfront and interval settings and that outcomes were depended on careful selection, completeness of cytoreduction, and treatment sequencing. |
| Ghirardi et al., 2024       | Patients undergoing interval debulking surgery for advanced ovarian cancer received morbidity, hyperthermic intraperitoneal completeness of chemotherapy including cytoreduction, expanded indications such as oncologic outcomes FIGO stage IV disease and were treatment after extended prospectively. neoadjuvant chemotherapy. | and assessed  | The study concluded that expanding hyperthermic intraperitoneal chemotherapy to broader interval debulking scenarios was feasible with acceptable perioperative outcomes, although oncologic benefit required cautious interpretation and further validation.       |
| Durán-Martínez et al., 2024 | Patients with primary advanced epithelial ovarian cancer   | Length of hospital stay, time to systemic laparoscopic interval               | The study concluded that a  |

| Reference           | Population / Intervention / Comparison  | Outcomes   | Main conclusions   |
|---------------------|---|--|--|
| Classe et al., 2024 | receiving interval cytoreductive therapy plus surgery plus hyperthermic postoperative intraperitoneal chemotherapy morbidity, were compared between oncologic outcomes feasible in highly selected laparoscopic and open surgical approaches.   | resumption, cytoreductive surgery plus hyperthermic intraperitoneal and chemotherapy approach was patients and was associated with faster recovery while maintaining comparable short-term oncologic results.                        | The trial concluded that adding hyperthermic intraperitoneal chemotherapy Overall survival and to complete cytoreductive safety surgery at first platinum-based perioperative outcomes were sensitive recurrence improved overall survival in specialist-center settings, supporting its consideration for selected relapse cases. |
| Sp et al., 2024     | Patients with advanced ovarian cancer undergoing optimal cytoreductive surgery within a large hyperthermic intraperitoneal chemotherapy registry were evaluated for the impact of delayed initiation of adjuvant chemotherapy.  | Overall survival and progression outcomes in relation to time-to-chemotherapy were assessed.   | The study concluded that delays in starting adjuvant chemotherapy after optimal cytoreductive surgery were associated with worse oncologic outcomes, underscoring the clinical importance of recovery optimization and timely systemic treatment.  |
| Sanson et al., 2024 | Patients with epithelial ovarian cancer were evaluated for correlations between peritoneal recurrence-free cancer index, overall survival, survival and recurrence-free survival, in relation to peritoneal burden and treatment including comparisons between cancer index and sequence influenced risk initial surgery and neoadjuvant treatment sequence. chemotherapy pathways. | and was associated with worse survival and that the cancer index, overall survival, survival were assessed interaction between disease and treatment trajectories, supporting individualized triage based on burden and operability. | The study concluded that higher peritoneal cancer index survival and that the cancer index, overall survival, survival were assessed interaction between disease and treatment trajectories, supporting individualized triage based on burden and operability.   |

| Reference           | Population / Intervention / Comparison  | Outcomes   | Main conclusions   |
|---------------------|---|--|--|
| Jochum et al., 2025 | Patients with advanced ovarian cancer were compared between primary cytoreductive surgery and interval cytoreductive surgery strategies in relation to long-term survival outcomes. | Long-term progression-free and overall survival were assessed across advanced-stage subgroups. | The study concluded that primary cytoreductive surgery was associated with clinically meaningful long-term survival across cytoreductive surgery in selected patients, supporting careful triage toward upfront surgery when complete cytoreduction is achievable. |

## 5 RESULTS AND DISCUSSION

The included studies consistently demonstrated that the extent of peritoneal disease remains a central determinant of prognosis in ovarian cancer, with higher tumor burden correlating with poorer survival outcomes.<sup>15</sup> Quantification tools such as the Peritoneal Cancer Index were repeatedly shown to predict both the feasibility of complete cytoreduction and long-term survival.<sup>15</sup> These findings reinforce the concept that disease distribution, rather than stage alone, should guide therapeutic planning.<sup>15</sup>

Several observational and prospective analyses confirmed that complete macroscopic cytoreduction represents the strongest independent prognostic factor in patients with peritoneal carcinomatosis secondary to ovarian cancer.<sup>16</sup> Patients achieving no residual disease consistently demonstrated superior overall and progression-free survival compared with those with any residual tumor.<sup>16</sup> These benefits persisted across age groups and treatment settings, underscoring the oncologic value of aggressive surgical management when feasible.<sup>16</sup>

The role of primary versus interval cytoreductive surgery was explored in multiple studies, revealing nuanced survival differences dependent on patient selection and disease burden.<sup>17</sup> Evidence suggested that primary cytoreductive surgery may offer superior long-term survival in patients deemed resectable at presentation.<sup>17</sup> Conversely, interval surgery following neoadjuvant chemotherapy appeared advantageous in reducing perioperative morbidity among patients with initially unresectable disease.<sup>17</sup>

Hyperthermic intraperitoneal chemotherapy was one of the most extensively investigated adjunctive strategies across the included studies.<sup>18</sup> Randomized and long-term follow-up data indicated that its addition at the time of interval cytoreductive surgery could confer durable survival benefits in selected patients with stage III disease.<sup>18</sup> However,



heterogeneity in protocols and patient characteristics contributed to variable outcomes across cohorts.<sup>18</sup>

Safety and tolerability of hyperthermic intraperitoneal chemotherapy were addressed in several studies focusing on perioperative morbidity and toxicity.<sup>19</sup> While some reports noted increased surgical complexity, overall complication rates were acceptable in high-volume centers.<sup>19</sup> Strategies such as nephroprotection protocols were shown to mitigate chemotherapy-related toxicity without compromising oncologic efficacy.<sup>19</sup>

Beyond hyperthermic intraperitoneal chemotherapy, alternative intraperitoneal approaches such as pressurized intraperitoneal aerosol chemotherapy were explored in early-phase clinical studies.<sup>20</sup> These investigations primarily demonstrated feasibility and safety in heavily pretreated patients not eligible for aggressive cytoreduction.<sup>20</sup> Although oncologic efficacy data remain limited, such approaches may expand palliative options in refractory disease.<sup>20</sup>

The prognostic significance of patient-related factors, including age and comorbidity burden, was addressed in multiple cohorts.<sup>21</sup> Advanced age alone was not associated with inferior survival when optimal cytoreduction was achieved.<sup>21</sup> These findings challenge chronological age as a limiting factor and emphasize functional status and disease biology in treatment decision-making.<sup>21</sup>

Several studies highlighted the impact of surgical complexity and multivisceral resections on outcomes.<sup>22</sup> Although extensive procedures were associated with increased perioperative morbidity, they enabled higher rates of complete cytoreduction.<sup>22</sup> Survival benefits appeared to outweigh surgical risks when procedures were performed in specialized centers with multidisciplinary support.<sup>22</sup>

Systemic therapy outcomes were also influenced by peritoneal disease characteristics and treatment sequencing.<sup>23</sup> Platinum sensitivity remained a key determinant of prognosis, particularly in recurrent settings.<sup>23</sup> Maintenance strategies and targeted therapies demonstrated progression-free survival benefits in molecularly selected populations, complementing surgical management.<sup>23</sup>

Timing of adjuvant chemotherapy following cytoreductive surgery emerged as a clinically relevant factor in several analyses.<sup>24</sup> Delays in initiating systemic therapy were associated with worse survival outcomes, even after optimal cytoreduction.<sup>24</sup> These data underscore the importance of postoperative recovery optimization and coordinated care pathways.<sup>24</sup>

The volume of peritoneal disease influenced not only surgical outcomes but also recurrence patterns.<sup>25</sup> Studies reported that higher disease burden was associated with



earlier recurrence and reduced recurrence-free survival.<sup>25</sup> These findings support intensified surveillance and individualized follow-up strategies for high-risk patients.<sup>25</sup>

Comparisons with existing guidelines revealed general concordance regarding the central role of complete cytoreduction and systemic therapy.<sup>26</sup> However, discrepancies remain concerning routine use of hyperthermic intraperitoneal chemotherapy, reflecting ongoing debate within the field.<sup>26</sup> Current evidence supports selective rather than universal application of intraperitoneal strategies.<sup>26</sup>

Assessment of heterogeneity across studies revealed variability in patient selection, surgical expertise, and treatment protocols.<sup>27</sup> This heterogeneity limits direct comparison of outcomes and contributes to differences in reported effectiveness.<sup>27</sup> Standardization of reporting and treatment pathways is necessary to improve evidence synthesis.<sup>27</sup>

Certainty of evidence, as evaluated using the GRADE framework, ranged from moderate to low for most outcomes.<sup>28</sup> While randomized data support selected interventions, many conclusions are derived from observational studies with inherent risk of bias.<sup>28</sup> These limitations highlight the need for further high-quality trials.<sup>28</sup>

Overall, the synthesized evidence supports a tailored, multidisciplinary approach to managing peritoneal carcinomatosis secondary to ovarian cancer.<sup>29</sup> Optimal outcomes depend on accurate disease assessment, surgical expertise, and integration of systemic therapies.<sup>29</sup> Continued refinement of patient selection criteria is essential to maximize benefit while minimizing harm.<sup>29</sup>

## 6 CONCLUSION

The findings of this systematic review demonstrate that peritoneal carcinomatosis remains a dominant prognostic factor in ovarian cancer, with disease burden and completeness of cytoreduction exerting the greatest influence on survival. Advances in surgical techniques and adjunctive therapies have improved outcomes in selected patients. The evidence consistently supports aggressive management when complete macroscopic resection is achievable.

From a clinical perspective, these results reinforce the importance of individualized treatment planning based on disease distribution, patient fitness, and institutional expertise. Cytoreductive surgery combined with appropriately selected systemic and intraperitoneal therapies offers the best chance for prolonged survival. Multidisciplinary evaluation is essential to optimize therapeutic sequencing and perioperative care.

The existing literature is limited by heterogeneity in study design, patient populations, and treatment protocols. Many studies are observational, and randomized evidence remains

scarce for several interventions. Variability in reporting standards further complicates comparison and synthesis of outcomes.

Future research should prioritize well-designed randomized trials to clarify the role of hyperthermic intraperitoneal chemotherapy and emerging intraperitoneal strategies. Development of standardized prognostic models and validated selection criteria will be critical. Integration of molecular and imaging biomarkers may further refine personalized treatment approaches.

In conclusion, management of peritoneal carcinomatosis secondary to ovarian cancer requires evidence-based, multidisciplinary, and individualized strategies. Continued collaboration across surgical, medical, and research disciplines is essential to translate evolving evidence into meaningful improvements in patient outcomes.

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