Epithelial Ovarian Cancer: The Importance of Early Diagnosis and Individualized Treatment with Combination Chemotherapy and Targeted Therapy

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LITERATURE REVIEW

RESUMO

O câncer de ovário epitelial é uma neoplasia maligna que representa a maioria dos casos de câncer ovariano. Caracteriza-se pela agressividade, diagnóstico muitas vezes tardio e desafios terapêuticos. O diagnóstico precoce é crucial para melhorar as taxas de sobrevivência e qualidade de vida das pacientes. O tratamento individualizado, combinando quimioterapia e terapia-alvo, tem sido uma abordagem promissora para otimizar resultados terapêuticos e minimizar efeitos adversos. Objetivo: analisar e sintetizar as evidências disponíveis sobre a importância do diagnóstico precoce e do tratamento individualizado com quimioterapia combinada e terapia-alvo no câncer de ovário epitelial. Metodologia: Utilizando o checklist PRISMA, esta revisão foi conduzida com base em artigos publicados nos últimos 10 anos. As Bases de dados utilizadas foram: PubMed, Scielo, Web of Science. Os descritores: "câncer de ovário epitelial", "diagnóstico precoce", "tratamento individualizado", "quimioterapia combinada", "terapia-alvo". Os Critérios de inclusão: estudos originais em humanos, publicados em inglês ou português, abordando o diagnóstico precoce e/ou tratamento individualizado do câncer de ovário epitelial. Os Critérios de exclusão: estudos em animais, revisões sistemáticas, estudos com amostras não representativas. Resultados: Os resultados desta revisão destacam a importância do diagnóstico precoce por meio de técnicas de imagem e marcadores tumorais. Além disso, evidenciam a eficácia da quimioterapia combinada, especialmente regimes contendo platina e taxanos, juntamente com terapia-alvo, como inibidores de PARP, na melhoria das taxas de resposta e sobrevida em pacientes com câncer de ovário epitelial. Conclusão: O diagnóstico precoce e o tratamento individualizado com quimioterapia combinada e terapia-alvo desempenham um papel fundamental na gestão do câncer de ovário epitelial. Esta abordagem multifacetada pode melhorar significativamente os resultados clínicos e a qualidade de vida das pacientes, destacando a importância de estratégias terapêuticas personalizadas neste contexto clínico desafiador.

Palavras-chave: "câncer de ovário epitelial", "diagnóstico precoce", "tratamento

individualizado", "quimioterapia combinada", "terapia-alvo".

ABSTRACT

Epithelial ovarian cancer is a malignant neoplasm that represents the majority of ovarian cancer cases. It is characterized by aggressiveness, often late diagnosis and therapeutic challenges. Early diagnosis is crucial to improving patients' survival rates and quality of life. Individualized treatment, combining chemotherapy and targeted therapy, has been a promising approach to optimize therapeutic results and minimize adverse effects. Objective: to analyze and synthesize the available evidence on the importance of early diagnosis and individualized treatment with combined chemotherapy and targeted therapy in epithelial ovarian cancer. Methodology: Using the PRISMA checklist, this review was conducted based on articles published in the last 10 years. The databases used were: PubMed, Scielo, Web of Science. The descriptors: "epithelial ovarian cancer", "early diagnosis", "individualized treatment", "combined chemotherapy", "targeted therapy". Inclusion criteria: original studies in humans, published in English or Portuguese, addressing the early diagnosis and/or individualized treatment of epithelial ovarian cancer. Exclusion criteria: animal studies, systematic reviews, studies with non-representative samples. Results: The results of this review highlight the importance of early diagnosis through imaging techniques and tumor markers. Furthermore, they highlight the effectiveness of combination chemotherapy, especially regimens containing platinum and taxanes, together with targeted therapy, such as PARP inhibitors, in improving response rates and survival in patients with epithelial ovarian cancer. Conclusion: Early diagnosis and individualized treatment with combination chemotherapy and targeted therapy play a key role in the management of epithelial ovarian cancer. This multifaceted approach can significantly improve patients' clinical outcomes and quality of life, highlighting the importance of personalized therapeutic strategies in this challenging clinical context.

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INTRODUCTION

Epithelial ovarian cancer is a malignant neoplasm that represents a significant portion of ovarian cancer cases and remains one of the leading causes of death related to gynecological cancer worldwide. It is characterized by its insidious nature and is often asymptomatic in the early stages, which makes early diagnosis difficult. The lack of effective screening methods contributes to diagnosis being often late, when the disease is already in advanced stages, resulting in less favorable prognoses. However, early detection plays a crucial role in improving survival rates and treatment effectiveness.

Early diagnosis of epithelial ovarian cancer is an important clinical challenge, given the absence of specific symptoms in the early stages of the disease. Traditionally, diagnosis has been based on physical exams, symptom assessment, and tumor markers such as CA-125. However, these methods are often not sensitive enough to detect cancer at early stages, leading to the need for more advanced approaches such as imaging tests (transvaginal ultrasound, computed tomography) and genetic testing. Incorporating these techniques into the diagnostic protocol may allow early identification of suspicious ovarian lesions and facilitate timely therapeutic intervention, thereby improving patients' treatment and survival prospects.

In addition to early diagnosis, individualized treatment has emerged as a fundamental strategy in the management of epithelial ovarian cancer. Each patient presents unique characteristics, both in terms of genetic profile and response to treatment, making the personalization of therapeutic approaches essential. The era of precision medicine has brought with it a variety of targeted therapeutic options, allowing clinicians to tailor treatments based on the tumor's molecular characteristics and the patient's individual characteristics. This includes not only the choice of chemotherapeutic agents but also the use of targeted therapies such as PARP inhibitors, which have shown particular efficacy in specific subgroups of patients. By adopting an individualized treatment approach, oncologists can optimize therapeutic outcomes by maximizing efficacy and minimizing side effects, thus providing a more holistic approach to the care of patients with epithelial ovarian cancer.

Epithelial ovarian cancer is a neoplasm that continues to challenge the medical

community due to its high lethality and often late diagnosis. Early identification plays a crucial role in improving survival rates and the effectiveness of therapeutic interventions. Screening methods and biomarkers are constantly being improved to enable more accurate and reliable early detection, highlighting the importance of efficient and accessible diagnostic strategies.

Furthermore, individualized treatment has emerged as an essential approach in the management of epithelial ovarian cancer. Recognizing the molecular and biological nuances intrinsic to each patient and tumor, this strategy aims to optimize therapeutic outcomes while minimizing adverse effects. The advent of precision medicine makes it possible to select more targeted and personalized therapies, taking into account factors such as tumor histology, genetic profile and response to treatment.

In the therapeutic context, combined chemotherapy regimens have been widely used in the treatment of epithelial ovarian cancer. The combination of cytotoxic agents, such as platinum and taxanes, aims to reach multiple targets within the malignant cell replication process, increasing therapeutic efficacy and reducing the likelihood of tumor resistance. The integration of these agents into well-designed therapeutic regimens has been shown to significantly improve response and survival rates in patients with this neoplasm.

At the same time, the evolution of targeted therapy has brought a new perspective in the treatment of epithelial ovarian cancer. PARP inhibitors, for example, have emerged as an effective therapeutic option, especially in patients with specific genetic mutations, such as BRCA1/2. These therapies target specific molecular targets involved in tumor progression, providing a more favorable toxicity profile compared to conventional chemotherapy.

In addition to the direct benefits in tumor suppression, it is essential to consider the impact on patients' quality of life. Therapeutic strategies that aim to minimize treatment-associated side effects as well as provide comprehensive psychosocial support play a crucial role in optimizing well-being and adapting to the demands of epithelial ovarian cancer treatment.

The aim of this systematic literature review is to investigate the efficacy and safety of combination chemotherapy and targeted therapy in the treatment of epithelial

***Epithelial Ovarian Cancer: The Importance of Early Diagnosis and Individualized
Treatment with Combination Chemotherapy and Targeted Therapy***
Ana Clara Rodrigues Franco, *et. al.*

ovarian cancer, exploring the current literature to identify the most promising therapeutic regimens. Furthermore, we intend to evaluate the impact of these approaches on the response to treatment, overall survival and quality of life of patients. By analyzing and synthesizing the available evidence, this review seeks to provide valuable insights to guide clinical practice and advance the management of this challenging neoplasm.

METHODOLOGY

The methodology adopted in this systematic review followed the guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. The PubMed, Scielo and Web of Science databases were consulted to identify relevant studies published in the last 10 years. The descriptors used were "epithelial ovarian cancer", "combined chemotherapy", "targeted therapy", "treatment efficacy" and "patient survival".

For the inclusion criteria, original studies in humans, published in English or Portuguese, that investigated the effectiveness of combined chemotherapy and/or targeted therapy in the treatment of epithelial ovarian cancer were considered. Furthermore, studies that evaluated response to treatment, overall survival and/or quality of life of patients as main outcomes were included. Studies that reported clinical, histological or molecular results were considered relevant for the analysis.

On the other hand, exclusion criteria were applied to remove animal studies, systematic reviews, meta-analyses, and studies with non-representative samples. Studies that did not provide clear information about the therapeutic regimens used or that presented inadequate methodological designs were also excluded. Additionally, studies that focused exclusively on epidemiological or prognostic aspects without directly addressing treatment were excluded from the analysis.

The selection of studies was carried out independently by two reviewers, with disagreements resolved by consensus or by consultation with a third reviewer. Data extraction was conducted according to a pre-established form, including information on study characteristics, studied population, therapeutic interventions, evaluated outcomes and main results. This systematic approach allowed for a comprehensive

analysis of the available literature on the topic, providing a solid basis for synthesizing the results and conclusions of this review.

RESULTS

15 articles were selected. Early diagnosis of epithelial ovarian cancer is one of the fundamental pillars in the effective management of this neoplasm. Because it is often asymptomatic in the early stages, ovarian cancer is often diagnosed in advanced stages, which significantly reduces the chances of successful treatment and reduces patient survival. Therefore, screening and early identification strategies are essential to improve clinical outcomes. Imaging tests, such as transvaginal ultrasound and computed tomography, have been used to detect ovarian abnormalities, but their effectiveness in early detection of ovarian cancer is still limited. Furthermore, biomarkers such as CA-125 have been studied as screening tools, however, due to the lack of specificity, their isolated use is not sufficient for early diagnosis. Therefore, a multifaceted approach is needed that integrates several early detection methods to increase the sensitivity and specificity of the diagnosis, enabling early therapeutic interventions and improving patients' treatment and survival prospects.

Individualized treatment of epithelial ovarian cancer represents a therapeutic approach increasingly adopted in clinical practice. Understanding the molecular and biological heterogeneity of this neoplasm, this strategy aims to adapt therapeutic interventions to the specific characteristics of each patient and their tumor. This includes considerations such as tumor histology, general health status, genetic profile and response to previous treatments. Individualization of treatment can influence therapeutic choices, such as the selection of chemotherapy agents and targeted therapies, as well as the sequence and duration of therapeutic regimens. Furthermore, treatment personalization also extends to the management of adverse effects, aiming to minimize the negative impact on patients' quality of life. Therefore, individualized treatment not only increases therapeutic efficacy, but also provides a more compassionate and patient-centered approach, taking into account individual needs and preferences.

Combination chemotherapy plays a central role in the treatment of epithelial

ovarian cancer and is frequently used in both the adjuvant and metastatic settings. This therapeutic approach consists of the simultaneous administration of multiple chemotherapy agents with different mechanisms of action, aiming to maximize the antitumor response and reduce the development of resistance. The most commonly employed combination chemotherapy regimens include the combination of platinum (such as carboplatin or cisplatin) and taxanes (such as paclitaxel or docetaxel), which have demonstrated efficacy in reducing tumor size and increasing survival in patients with epithelial ovarian cancer. Furthermore, the use of multiple chemotherapy agents allows administration in smaller doses, thus minimizing adverse effects associated with drug toxicity. Therefore, combined chemotherapy continues to be a crucial and widely used therapeutic option in the management of this neoplasm, providing significant benefits in response to treatment and patient survival.

Targeted therapy has emerged as a promising therapeutic strategy in the treatment of epithelial ovarian cancer, offering a more targeted and specific approach compared to conventional chemotherapy. PARP inhibitors (poly(ADP-ribose) polymerase inhibitors), for example, have been widely studied and are now included in treatment guidelines for patients with BRCA1/2 mutations. These agents block the ability of cancer cells to repair DNA damage, leading to selective cell death in tumors deficient in DNA repair, such as those with BRCA mutations. In addition to PARP inhibitors, other targeted therapies, such as angiogenesis inhibitors (e.g., bevacizumab), have demonstrated efficacy in combination with standard chemotherapy, providing additional benefits in treatment response and patient survival. Therefore, targeted therapy represents a new frontier in the treatment of epithelial ovarian cancer, offering more precise and effective therapeutic options, especially for patients with tumors that present specific molecular characteristics.

Treatment of epithelial ovarian cancer, including combination chemotherapy and targeted therapy, has demonstrated a significant impact on patient survival. Clinical studies have consistently demonstrated improvements in overall survival rates in patients undergoing combination treatments compared to those receiving conventional therapy alone. These benefits are especially pronounced in patients with early-stage or advanced-stage tumors, where response to treatment can directly influence prognosis. Furthermore, the inclusion of targeted therapies, such as PARP inhibitors, has been

*Epithelial Ovarian Cancer: The Importance of Early Diagnosis and Individualized
Treatment with Combination Chemotherapy and Targeted Therapy*
Ana Clara Rodrigues Franco, *et. al.*

associated with prolonged survival in patients with specific genetic mutations, such as BRCA1/2. This highlights the importance of personalized therapeutic strategies and the identification of predictive biomarkers to guide clinical decision making and improve clinical outcomes in patients with epithelial ovarian cancer. Ultimately, the effectiveness of these therapeutic approaches in improving survival highlights the significant advances made in the management of this neoplasm and reinforces the continued importance of research and development of new therapeutic strategies to address the clinical challenges associated with epithelial ovarian cancer.

Improving the quality of life of patients with epithelial ovarian cancer is a crucial aspect in the overall management of the disease. In addition to the direct benefits in tumor suppression and survival, therapeutic strategies should aim to minimize the adverse effects of treatment and promote the physical, emotional and social well-being of patients. This includes adequate management of cancer- and treatment-related symptoms, such as nausea, fatigue, and pain, as well as comprehensive psychosocial support to manage the stress and anxiety associated with cancer diagnosis and treatment. Interventions such as psychological support, nutritional therapy, supervised physical exercise, and social work services can play a significant role in improving patients' quality of life. Therefore, a multidisciplinary and integrated approach is essential to ensure that patients with epithelial ovarian cancer receive not only effective treatment, but also comprehensive care that takes into account their individual needs and promotes a better quality of life throughout the course of the disease.

Treatment resistance continues to be a significant challenge in the management of epithelial ovarian cancer, limiting the effectiveness of available therapies and contributing to disease recurrence. Resistance can develop to both conventional chemotherapy and targeted therapies, thus reducing the therapeutic options available to patients. Multiple resistance mechanisms have been identified, including genetic changes, such as mutations in genes related to DNA repair, and modifications in the tumor microenvironment that promote the survival and proliferation of cancer cells. Strategies to overcome resistance include the development of new therapeutic agents, such as second-generation PARP inhibitors, that aim to overcome specific resistance mechanisms. Furthermore, combination therapeutic approaches that target multiple molecular targets have shown promise in preventing and overcoming treatment

***Epithelial Ovarian Cancer: The Importance of Early Diagnosis and Individualized
Treatment with Combination Chemotherapy and Targeted Therapy***
Ana Clara Rodrigues Franco, *et. al.*

resistance. Therefore, understanding the mechanisms underlying resistance and developing targeted therapeutic strategies are areas of active and critical research to improve clinical outcomes and survival for patients with epithelial ovarian cancer.

The identification of predictive biomarkers plays a crucial role in the management of epithelial ovarian cancer, providing valuable information about treatment response and patient prognosis. Several biomarkers have been investigated as potential indicators of sensitivity or resistance to different therapeutic modalities, including chemotherapy and targeted therapy. For example, mutations in genes such as BRCA1/2 have been associated with a greater response to PARP inhibitors, while increased expression of DNA repair proteins may be related to resistance to these agents. Furthermore, biomarkers such as HE4 and miRNAs have been studied as screening and prognostic tools, offering additional insights into disease progression and treatment response. Therefore, the identification and validation of accurate and reliable predictive biomarkers are essential to guide the selection of individualized treatments and improve clinical outcomes in patients with epithelial ovarian cancer.

Continuing research and advances in understanding the biology of epithelial ovarian cancer are driving the development of new therapeutic strategies and prognostic biomarkers. New studies and clinical trials are investigating innovative approaches such as immunotherapy and gene therapy, as well as new therapeutic agents targeting specific molecular pathways involved in tumor progression. Furthermore, the development of next-generation genomic sequencing techniques is allowing a more comprehensive analysis of the genetic profile of tumors, thus identifying new mutations and molecular changes that may be potential therapeutic targets. These promising advances have the potential to revolutionize the treatment of epithelial ovarian cancer, offering more effective and individualized therapeutic options that can significantly improve clinical outcomes and quality of life for patients.

The complexity of epithelial ovarian cancer demands a multidisciplinary approach in its management. Oncologists, surgeons, radiologists, mental health professionals, and other specialists must collaborate seamlessly to provide comprehensive, individualized care to patients. This approach allows for a holistic assessment of the patient's condition, considering not only the physical aspects of the

disease, but also the psychosocial and emotional aspects. For example, psychological support can help patients deal with the stress and anxiety associated with cancer diagnosis and treatment, while nutritional therapy can ensure adequate nutrition throughout the course of treatment.

Furthermore, the multidisciplinary approach also facilitates the discussion of complex cases and collaborative decision-making about the most appropriate therapeutic plan for each patient. This exchange of knowledge and experiences between different specialties allows for a more comprehensive view of the patient's clinical condition, leading to better treatment results and quality of life. Therefore, implementing multidisciplinary approaches is essential to ensure that patients with epithelial ovarian cancer receive comprehensive, individualized care that addresses all of their physical, emotional, and psychosocial needs.

CONCLUSION

In the context of epithelial ovarian cancer, early detection and individualized treatment with combined chemotherapy and targeted therapy have emerged as fundamental approaches to improving patients' clinical outcomes. Studies have shown that early diagnosis plays a crucial role in improving survival rates, highlighting the importance of efficient and accessible screening strategies. Furthermore, personalization of treatment, considering the individual characteristics of each patient and tumor, proved to be essential to optimize therapeutic results and minimize adverse effects.

Combination chemotherapy, using agents such as platinum and taxanes, has demonstrated efficacy in reducing tumor size and increasing patient survival. On the other hand, targeted therapy, including PARP inhibitors, has offered a more targeted and specific approach, especially for patients with specific genetic mutations such as BRCA1/2. Both therapeutic strategies showed promise in improving patient survival and quality of life.

Furthermore, the need for multidisciplinary approaches in the management of epithelial ovarian cancer has been widely recognized, allowing for a holistic assessment of patients' needs and collaboration between different specialties to provide

comprehensive, individualized care.

In summary, advances in early detection, personalized treatment and multidisciplinary approaches have significantly contributed to improving clinical outcomes and quality of life for patients with epithelial ovarian cancer. These findings highlight the continued importance of research and development of new therapeutic strategies to address the clinical challenges associated with this neoplasm.

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