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Sarcopenia and ovarian cancer

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ABSTRACT

Defined as the loss of the muscular mass, sarcopenia is a common finding in neoplastic patients, multiple mechanisms such as nutritional deficiency, proinflammatory tumoral related status or physical inactivity being cited. However, the loss of the muscular mass in such cases is associated with significant impact in regard to the type of treatment in such cases; in consequence, as expected the disease-free survival and overall survival might be influenced. The aim of the current paper is to discuss about the most important mechanisms leading to sarcopenia in ovarian cancer patients as well as the impact on the long-term outcomes.

Keywords: sarcopenia, ovarian cancer, chemotherapy, prognosis

INTRODUCTION

Ovarian cancer, one of the most commonly encountered gynaecologic malignancy affecting women worldwide and, in the meantime, the most lethal one. In order to improve the outcomes of ovarian cancer patients, multiple therapeutic strategies had been proposed [1]. Therefore, cases in which complete debulking surgery seems not to be feasible, neoadjuvant therapies combining standard chemotherapy with monoclonal antibodies and PARP2 inhibitors have been proposed [2-4]; however, different responses to therapy had been encountered. Moreover, in certain cases the benefits of the neoadjuvant chemotherapeutic agents therefore, attention was focused on identifying new prognostic markers which might provide a better selection of patients who could benefit most from an aggressive therapeutic approach [5-7].

Sarcopenia and cancer

Defined as the lost of skeletal muscle and function, sarcopenia is widely encountered in elderly patients and might be responsible for a series of complications

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inducing increased rates of morbidity and mortality [8,9]. Meanwhile, increasing number of cancers is encountered in elderly patients, therefore association between cancer and sarcopenia represents rather a quiet frequent finding [10]. Meanwhile it has been demonstrated that sarcopenia is commonly associated with gynaecologic malignancies such as ovarian cancer and negatively impacts on the chemotherapy response of the disease; in this respect it is widely accepted the fact that sarcopenic ovarian cancer patients are expected to report a poorer disease free and respectively overall survival rate [11].

Introduced for the first time by Rosenberg in 1989 like an age-related muscle mass loss, sarcopenia is now defined as low muscle strength, low muscular quality and quantity respectively [12,13]. In order to identify patients with sarcopenia, multiple variants have been proposed, such as questionnaires, physical examination or imagistic techniques; however, it is considered that in neoplastic patients, who routinely undergo follow-up imagistic screenings such as computer tomography (CT) or magnetic resonance imaging (MRI), the most valuable tool in order to identify and study the dynamics of this parameter is represented by such imagistic studies. One of the most widely accepted tool in order to estimate the body composition is represented by a cross sectional CT scan at the level of the third lumbar vertebra, which is able to estimate the total body skeletal muscle, fat distribution and total mass of adipose tissue [14].

When it comes to the pathogenesis of sarcopenia in oncological patients, multiple mechanisms have been propose; therefore, it seems that low nutritional intake, physical inactivity and increased levels of circulating cytokines such as Interleukin 6 (IL6) and tumor necrosis factor alpha (TNFα) play a crucial role [15,16].

Therapeutic strategies in sarcopenic ovarian cancer patients

As mentioned before, sarcopenia has multiple causes in oncological patients. Therefore, in order to alleviate the symptoms produced by this disorders, the causes which induce it should be treated; therefore, in cases in which is estimated that sarcopenia is caused by a poor nutritional status, this could be improved by draining the ascites and decreasing the intra-abdominal pressure, creating a stoma, administrating anti-emetics during chemotherapy or even administration of parenteral nutrition [17]. Meanwhile, cases in which the presence of sarcopenia seems to be caused by the association of a high tumoral burden inducing in this way a significantly increased proinflammatory status, debulking surgery could play a significant role; therefore, once the tumoral mass decreases, there is hope that the inflammatory status of the patient's corrects and therefore sarcopenia will disappear [18].

An interesting study conducted on this issue was presented by Polen et al. in 2022; according to this study group, patients submitted to curative intent primary debulking surgery followed by adjuvant chemotherapy reported significant modifications in terms of sarcopenia correction [19]. Another significant paper conducted on this theme was published by Can et al. in 2022; the study included 75 patients with advanced stage ovarian cancer, 26% of them being sarcopenic. After dividing the study group in sarcopenic and non-sarcopenic cases, the authors came to demonstrate that non-surgical complications such as respiratory, cardiac or renal complications were significantly higher among sarcopenic patients while surgical complications were similar between the two groups; moreover, the length of hospital in stay as well as the mortality rate were significantly higher among sarcopenic patients. In this study the degree of sarcopenia was established by psoas muscle area measurements at the CT scans [20].

The association between sarcopenia and chemotherapeutic toxicity represents an important subject which has been widely studied so far. Therefore, initial studies conducted on this issue came to demonstrate the fact that the presence of sarcopenia represents a significant risk factor for chemotoxicity in cases receiving capecitabine; in this respect, Prado et al underlined the fact that capecitabine related toxicity is expected in 50% of sarcopenic patients versus 20% non-sarcopenic patients [21]. Moreover, it seems that sarcopenia significantly increases severe adverse reactions related to chemotherapy such as grade 3 and 4 complications, imposing in this way dose reduction or delaying certain cycles of chemotherapy; in such cases, the most commonly encountered side effect is tumor relapse, expressed through a shorter disease-free interval and overall survival interval respectively [22]. However, these findings seem also to be influenced by the tumoral. subtype; therefore, in the study conducted by Stoley et al and published in 2020 the authors included 119 sarcopenic patients and 82 non-sarcopenic patients diagnosed with epithelial ovarian cancer and demonstrated that sarcopenia did not influence in a significant manner the median overall survival rate; however, sarcopenic patients necessitated more often the change of the chemotherapeutic regimen and a higher trend to neutropenia [23].

CONCLUSIONS

Sarcopenia represents a serious health issue affecting patients with oncological disorders such as ovarian cancer. The mechanisms which are responsible for this association are multiple; depending on the causes which seem to influence most this association, different therapeutic strategies have been proposed such as

nutritional counselling, ascites evacuation, placing stomas and, if possible, debulking surgery. In cases in which chemotherapy is needed, it should not be omitted the fact that dose adjustment might be needed in order to avoid the apparition of severe side effects.

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