

Neutrophil to lymphocyte ratio in ovarian cancer – a new prognostic marker?

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ABSTRACT

Neutrophil to lymphocyte ratio represents a novel prognostic marker which is usually associated with the presence of proinflammatory conditions such as obesity, metabolic syndrome or certain benign and even malignant diseases. Moreover, in cases in which a malignant condition is present, the value of the neutrophil to lymphocyte ratio also seems to be positively correlated with the biological aggressivity of the tumor. The aim of the current paper is to discuss about the most relevant studies which discuss about the role of this parameter as a new biological marker in ovarian cancer patients.

Keywords: ovarian cancer, tumor biology, aggressiveness, neutrophil to lymphocyte ratio

INTRODUCTION

The dynamics of neutrophil to lymphocyte ratio has been widely studied in the last decades after the observation that during inflammatory conditions significant variations might occur. Therefore, in 2000, Jilma et al. came to demonstrate that after intravenous administration of endotoxins in a group of human volunteers a sudden drop of the neutrophil number was encountered one hour later, followed by a steep increase of

this number, a maximum value being noted at 4-6 hours after injection; moreover, at this moment a significant decrease of the lymphocyte ratio was also reported [1]. Studies conducted later on this issue underlined the fact that the most severe modification of this parameter is to be encountered after major abdominal surgeries, bacteremia or sepsis, multiple trauma and severe acute pancreatitis, being in fact the expression of the severity of the inflammatory response to stress [2]. Moreover, this parameter seems to be very relevant

when studied in dynamics in order to evaluate the evolution of a patients with systemic inflammatory response [3].

Neutrophil to lymphocyte ratio in oncological patients

Once the positive correlation ship between the value of neutrophil to lymphocyte ratio and proinflammatory status has been widely demonstrated, attention was focused on identifying other important conditions in which a similar correlation could be established. Therefore, large studies aimed to investigate the relationship between this parameter and the presence and respectively of different tumoral types; moreover, special interest was accorded on investigating the influence of this parameter on the overall prognosis; one of the first studies conducted on this issue was published by Walsh et al and was published in 2005; the study included 230 patients diagnosed with colorectal tumors and demonstrated that a preoperative value higher than 5 of the neutrophil to lymphocyte ratio was associated with significantly poorer rates of survival [4]. Once the correlation ship between inflammation and cancer has been widely demonstrated, the neutrophil to lymphocyte ratio has been widely implemented as a diagnosis and prognostic factor for estimating the evolution of different neoplastic subtypes; moreover, information regarding the biological aggressiveness and overall prognosis might be offered by analyzing this parameter [5-7].

Neutrophil to lymphocyte ratio in ovarian cancer

When it comes to ovarian cancer, the interest of discovering new prognostic markers significantly grew in the last decade due to the fact that in certain patients CA125, which has been widely accepted as the most relevant tumoral marker, did not express any modification. Moreover, in certain cases increased values of CA 125 might be observed in the absence of any malignant transformation of the ovary [8-10]. In the study conducted by Cho et al and published in 2009 the authors came to demonstrate the fact that the serum values of neutrophil to lymphocyte ratio might be elevated in ovarian cancer patients even if normal ranges of CA 125 are present; moreover the same study demonstrated that increased values of this parameter have also a predictive value in regard of the disease free survival and respectively overall survival rates, offering therefore important information about the need of associating newer lines of adjuvant therapies [11]. Moreover, other authors came to demonstrate that the number of lymphocytes reports a significant drop down whenever

ovarian cancer develops; in the paper published by Milne et al patients diagnosed with ovarian cancer had significantly lower rates of circulating lymphocytes when compared to those encountered two years previously at exactly the same patients. Moreover, once the disease was diagnosed, a significantly lower number of lymphocytes was encountered in patients which were at risk to present a more aggressive tumoral biology, more advanced stages of the disease or suboptimal debulking procedures [12]. In a more recent study conducted by Williams et al and published in 2014 in Gynecologic Oncology journal, the authors also demonstrated that a higher value of this ratio is significantly associated with decreased survival rates. The study included 519 cases with ovarian cancer diagnosis and demonstrated that higher levels of CA125 and neutrophil to lymphocyte ratio were associated with poorer survival rates while higher levels of lymphocytes represented significant predictors for improved survival; more interestingly, the values of circulating lymphocytes as well as the value of neutrophil to lymphocyte ratio persisted as significant predictors for survival even after adjustment for CA 125 levels [13].

As expected, neutrophil to lymphocyte ratio predicts not only the possibility of achieving complete debulking surgery but also the chemotherapy response; therefore, in the study conducted by Badora-Rybicka et al. and published in 2016 the authors included 315 patients diagnosed with metastatic disease originating from epithelial ovarian cancer and submitted to chemotherapy; the authors demonstrated the fact that higher pretreatment levels of neutrophil to lymphocyte ratio as well as poorer overall status, higher stages of the disease and higher levels of CA125 were significantly associated with poorer outcomes defined as lower disease free intervals. However, the overall survival was not significantly influenced by the pretreatment levels of neutrophil to lymphocyte ratio [14].

CONCLUSIONS

Initially considered as a valuable prognostic marker for evolution of sever inflammatory or septic disorders, the neutrophil to lymphocyte ratio also seem to give important information regarding the existence of an aggressive ovarian tumor which might be associated with poor disease free intervals and even with poor survival rates. Depending to the values of this parameter and to their dynamics new therapeutic strategies might be offered and might offer the premise of creating new guidelines in ovarian cancer patients.

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