

# The correlation between the preoperative number of lymphocytes and monocytes and the postoperative outcomes of gastric cancer patients

Irina Balescu<sup>1</sup>, Nicolae Bacalbasa<sup>2,3</sup>, Lucian Pop<sup>4</sup>, Valentin Varlas<sup>2,5</sup>, Andrei Voichituiu<sup>2,4</sup>

<sup>1</sup>Department of Visceral Surgery, Ponderas Academic Hospital, Bucharest, Romania

<sup>2</sup>Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

<sup>3</sup>Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

<sup>4</sup>Department of Obstetrics and Gynecology, "Alessandrescu-Rusescu" National Institute of Mother and Child Care, Bucharest, Romania

<sup>5</sup>Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania

## ABSTRACT

Gastric cancer remains an important health problem worldwide, being associated with poor rates of survival even if radical resection is achieved. Therefore attention was focused on identifying different prognostic markers which might provide a better selection of the patients and a more personalized therapeutic approach. One of the most widely investigated parameters in the last decade is represented by the preoperative hemogram, significant influence being given to the preoperative number of monocytes and lymphocytes. The aim of the current paper is to discuss about the correlation ship which might be established between these parameters and the overall prognostic in gastric cancer patients.

**Keywords:** gastric cancer, lymphocytes, monocytes, outcome

## INTRODUCTION

Gastric cancer remains a significant health problem affecting people worldwide, being still responsible for a significant number of deaths annually [1,2]. This fact was submitted to certain changes in the last decade, significant differences in terms of survival being observed between the eastern and western countries. Therefore, in eastern countries, due to the wide implementation of screening endoscopy, a significant number of patients are diagnosed in early stages of the disease; meanwhile, a particular biological tumoral subtype is encountered in such cases. Due to these reasons, an earlier diagnostic is feasible and meanwhile a radical surgical approach is feasible, maximizing therefore the chances to achieve a long term survival period. In the meantime, in the western countries a significant number of patients is still diagnosed in advanced stages of the disease, a poorer outcome in terms of survival being expected [3-6]. In this respect, attention was focused on identifying different prognostic factors which might pro-

vide a better identification of the patients who are expected to have a poorer outcome and in which a neoadjuvant or specific, adjuvant therapy might improve the long term outcomes. One of the most widely investigated such parameters are represented by the hemogram, particular intention being paid to the circulating number of lymphocytes, monocytes and their ratio [7-9].

The aim of the current paper is to discuss about the modifications encountered in terms of lymphocytes and monocytes number and ratio in gastric cancer patients.

## THE CORRELATION BETWEEN THE PREOPERATIVE LYMPHOCYTE TO MONOCYTE OUTCOMES AND THE EARLY POSTOPERATIVE OUTCOME IN GASTRIC CANCER PATIENTS

Studies conducted so far came to demonstrate that overall, in gastrointestinal tumors, the preoperative value of lymphocyte to monocyte ratio play

*Corresponding author:*

Nicolae Bacalbasa

*E-mail:* nicolae\_bacalbasa@yahoo.ro

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a crucial role in predicting the risk of developing postoperative complications, especially infectious ones [10-12]. This correlation ship has been initially demonstrated in patients with acute ischemic stroke, in such cases a significantly higher rate of pneumonia and urinary tract infections being reported [13]. When it comes to the correlation ship between the lymphocyte to monocyte ratio and the postoperative in early stage gastrointestinal cancer, an interesting study has been published by Shimizu et al in 2020; the study included 323 patients with stage I gastric cancer and 152 cases diagnosed with early stage colon cancer and demonstrated that a lower than 4,2 value of lymphocyte to monocyte ratio was significantly associated with a higher risk of postoperative infectious complications such as pneumonia, cholecystitis pancreatitis, wound infection or urinary tract infection among gastric cancer patients who were further submitted to surgery. Interestingly, when studying the influence of this parameter on the early postoperative outcomes in colorectal cancer, no significant correlation could be established between the lymphocytes to monocytes ratio and the risk of postoperative complications. Moreover, the same study came to demonstrate that the presence of a low lymphocyte to monocyte ratio was a significant predictive factor for death from postoperative infectious complications. In order to diminish the impact of this parameter on the perioperative complications the authors proposed administration of oral nutrients and association of exercise interventions in order to increase the muscle mass [14].

### **THE IMPACT OF THE PREOPERATIVE VALUE OF LYMPHOCYTE TO MONOCYTE RATIO ON THE OVERALL SURVIVAL AFTER GASTRECTOMY FOR GASTRIC CANCER**

When it comes to the impact of the preoperative lymphocytes to monocytes ratio on the long term outcomes, Shimzu et al came to demonstrate a significant association between a lower value of this parameter and a significantly poorer overall survival [14]. Another interesting study conducted on this issue was published by Okuno et al in Langenbecks Archives of Surgery in 2021; the authors investigated the correlation ship between eight markers of inflammation (white blood cell count, neutrophil count, monocyte count, platelet count, total lymphocyte count, lymphocyte to monocyte ratio, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio) and the long term outcomes in gastric cancer patients. Among all these inflammatory markers the authors came to demonstrate that the most suitable one for predicting the long term outcomes was represented by the lymphocyte to monocyte ratio, cases with lower values than 4,6 of this parameter pre-

senting a significantly poorer five year survival rate when compared to cases presenting a higher value of this ratio; moreover, this parameter proved to be statistically significant also in multivariate analysis, correlation ship which failed to demonstrated for all the other seven investigated parameters [15]. This aspect was widely explained through the fact that a lower value of circulating lymphocytes is usually associated with a decreased systemic antitumoral response while a higher number of monocytes is usually associated with the presence of tumor associated macrophages , cells which promote angiogenesis, tumorigenesis and tumoral spread [16-19].

Maybe the most relevant study conducted on this issue was conducted by Ma et al and was published in 2018; this paper was in fact a meta-analysis of the studies conducted so far on this issue; therefore, the authors included in this meta-analysis six studies containing 4908 patients diagnosed with different stages of gastric cancer and demonstrated that a lower value of lymphocytes to monocytes ratio was significantly associated with decreased survival rates but not with the disease free interval. Meanwhile the authors underlined the fact that this ratio was also significantly corelated with patients' age, sex, serum value of carcinoembryonic antigen, stage at diagnostic, tumor dimension and presence of lymphatic or distant metastases [8]. Therefore, these data represented another proof that in gastric cancer patients the lymphocyte to monocyte ratio plays a crucial role in identifying patients who are expected to achieve a long term survival after curative intent maneuvers [8].

### **THE CORRELATION BETWEEN THE PRETREATMENT VALUE OF LYMPHOCYTE TO MONOCYTE RATIO AND THE RESPONSE TO SYSTEMIC THERAPY IN ADVANCED STAGE OR RELAPSED GASTRIC CANCER**

Another significant information which seems to be given by the value of lymphocyte to monocyte ratio regards the possibility of achieving a good clinical response to monoclonal antibodies therapies. Therefore, in the study conducted by Tokumaru et al and published in 2021 in Oncology journal, the authors came to demonstrate that patients with a low value of lymphocyte to monocyte ratio at two weeks after the initiation of nivolumab treatment was associated with a significantly longer overall survival rate and therefore this value should be considered as an important prognostic tool for patients with unresectable advanced stage or recurrent gastric cancer [20]. A similar study conducted by Chen et al and published in 2021 aimed to investigate the correlation ship between the lymphocyte to monocyte ratio and the overall survival among advanced gastric cancer

patients treated with immune checkpoint inhibitors. The study included 139 patients submitted to this type of treatment and demonstrated that lymphocyte to monocyte ratio at baseline and at week six were significantly correlated with the progression free and overall survival rate [21]. These data enabled the authors to consider that the lymphocyte to monocyte ratio represents a significant tool in order to provide a specific identification of patients who could benefit most from the administration of immune checkpoint inhibitors [21].

## CONCLUSIONS

Studies published so far came to demonstrate that the pretreatment value of the lymphocyte to monocyte ratio play a crucial role in predicting the response to surgery or systemic treatment in both primary and relapsed gastric cancer. Therefore, this parameter should be further investigated in order to increase the efficacy of the process of patients' selection and to maximize the long term survival rates.

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