

The prognostic role of preoperative platelet count in gallbladder cancer

Irina BALESCU¹, Nicolae BACALBASA^{2,3,4}, Mihaela VILCU^{2,5}, Claudia Stoica^{6,7},
Tarig MASSAWI⁸, Sorin PETREA^{2,5}, Cristina MARTAC⁹, Adriana CIUVICA^{10,11},
Andrei VOICHITOIU^{10,11}, Victor CAUNI¹², Bogdan GASPAR^{2,13}, Iulian BREZEAN^{2,5}

¹Doctoral School, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

²Department of Surgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

³"Dan Setlacec" Center of Visceral Surgery and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania

⁴Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

⁵Department of Surgery, "Ion Cantacuzino" Clinical Hospital, Bucharest, Romania

⁶Department of Anatomy, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁷Department of Surgery, Ilfov County Emergency Hospital, Bucharest, Romania

⁸Department of Obstetrics and Gynecology, Ilfov County Emergency Hospital, Bucharest, Romania

⁹Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

¹⁰Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

¹¹Department of Obstetrics and Gynecology National Institute of Mother and Child Care „Alessandrescu-Rusescu“, Bucharest, Romania

¹²Department of Urology, Colentina Clinical Hospital, Bucharest, Romania

¹³Department of Visceral Surgery, Floreasca Clinical Emergency Hospital, Bucharest, Romania

ABSTRACT

Gallbladder cancer represents the most commonly encountered malignancy of the biliary tract which becomes symptomatic only in advanced stages of the disease when, in most cases, local invasion in unresectable structures is already present. Another significant problem regarding this pathology is related to the fact a positive diagnostic is difficult to be established preoperatively. The aim of the current paper is to discuss about the possible relationship between the preoperative number of circulating platelets and the overall prognosis in gallbladder cancer patients.

Keywords: gallbladder cancer, platelet count, prognostic, survival

INTRODUCTION

Primary gallbladder carcinoma represents the most commonly encountered malignancy of the biliary tract which is usually associated with poor prognosis due to the high capacity of spread via multiple ways such as lymphatic, hematogenous, perineural pathway and

even due to direct extension to the liver [1-3]. Moreover, gallbladder carcinoma remains asymptomatic for a long period of time and in a significant number of cases intraoperatively unresectable disease is found, in such cases only palliative procedures being taken in consideration. As expected, in such cases the overall survival is very poor and surgery should not be performed only

Corresponding author:

Nicolae Bacalbasa

E-mail: nicolaebacalbasa@gmail.com

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if local complications are present. Therefore, in unresectable cases oncological therapies remain the only chance to improve the long term outcomes [4].

In order to improve the outcomes of oncological patients, different prognostic factors have been studied so far, special attention being given to inflammatory and procoagulant markers such as platelet count, fibrinogen or interleukines. The aim of the current paper is to investigate the possible correlation ship between preoperative number of circulating platelets and the overall prognosis of gallbladder cancer patients [3-6].

STUDIES CONDUCTED SO FAR ON THIS ISSUE

One of the first studies conducted on this issue was published by Ong et al in 2008 and included 73 cases of patients diagnosed with gallbladder cancer; among these patients there were 23 cases submitted to surgery with curative intent, 28 cases were submitted to surgery but intraoperatively unresectable lesions were found and the remaining 22 cases were considered as having an unresectable lesion based on the preoperative imagistic findings. The survival analysis reported a median survival rate of 12,4 months, cases submitted to surgery with curative intent reporting a significantly higher survival when compared to cases in which resection was not feasible and respectively cases in which surgery was not taken in consideration [based on the preoperative imagistic findings]. When analyzing the preoperative characteristics of these patients, the authors came to demonstrate that cases submitted to surgery with curative intent had a significantly lower level of the preoperative platelet count, of the white cell count, of bilirubin and respectively alkaline phosphatase when compared to cases in which resection was tempted but was not possible and respectively when compared to cases in which resection was contraindicated based on the radiological findings. When analyzing the receiving operating curve, a cut off value for the preoperative platelet count was established at 345.000/microl; furthermore, the authors underlined the fact that cases with preoperative suspicion of gallbladder cancer and a higher than 345.000/microl level of circulating platelets should be rather submitted to systemic therapies than to surgery even if the radiological findings did not describe elements of unresectable disease [6]. In this respect, the authors proposed that the preoperative number of circulating platelets should be considered as part of the preoperative criteria for proposing patients for surgery or for systemic therapy.

In the study published by Wang et al in 2015 the authors included 223 patients diagnosed with gallbladder cancer; the cut off value for the number of circulating platelets was established at 178.000. The authors

came to demonstrate that patients with higher numbers of circulating platelets had a poorer biological status, a more advanced stage of the disease and a higher amount of lymph node metastases. When analyzing the impact on the overall survival, the authors demonstrated that tumor location, tumor differentiation, TNM stage, the presence of lymph node metastases and preoperative number of circulating platelets were significant predictors for the long term outcomes. Moreover, when performing a multivariate analysis, lymph node metastases, TNM stage, tumor location and platelet number were independent prognostic factors for predicting the long term outcomes [4].

All these data enable us to consider that the preoperative count of platelets should be included as a prognostic marker in order to better orientate the patients with gallbladder cancer suspicion [6-9]. Therefore, cases with lower preoperative numbers of platelets should be rather submitted to surgery while cases with higher levels should be submitted to per primam systemic therapy; this observation is particularly important in cases in which radiology shows no sign of nonresectable lesions and laparotomy is performed. Furthermore, Ong et al demonstrated that these patients are expected to have an overall survival lower when compared to cases submitted to per primam systemic therapy [6].

One of the latest studies conducted on this issue was published by Cao et al and was published in 2021 in BMC Gastroenterology. The study included 58 patients with gallbladder cancer, 60 patients with cholesterol polyps and 60 healthy volunteers and demonstrated that preoperative levels of fibrinogen and platelet count could be considered as reliable biomarkers in order to distinguish between the three categories, to identify patients with possible infiltrative or metastatic disease and to predict the postsurgical outcomes. Moreover, the authors underlined the fact that in cases diagnosed with malignant disease should benefit from anticoagulant therapies in order to control the progression of the disease. Therefore, the authors demonstrated that both fibrinogen level and platelet number present significantly higher levels among patients with gallbladder cancer when compared to those with cholesterol polyps and respectively to healthy subjects. When it comes to the cut off values of the platelet count, a value of 300.000/microl was agreed. Meanwhile, a significant correlation ship was described between the preoperative levels of fibrinogen and respectively the preoperative number of platelets demonstrating the utility of combining the two parameters and using them as prognostic markers [10].

Once these correlations are widely accepted, it is easily to understand why in such cases anticoagulant and antiaggregant therapies might be efficient. Therefore, the presence of a high number of circulating plate-

lets is expected to associate increased levels of released cytokines, chemokines, proteases and procoagulant molecules. In this respect, association of any antiagregant or anticoagulant therapy is considered to be beneficial in such cases [10-15].

CONCLUSIONS

Preoperative platelet count seem to be a promising prognostic marker in order to better identify patients

who are potential candidates for surgery with curative intent and to exclude from surgery cases without clear radiological findings of unresectable lesions. Therefore, in this respect an improved overall survival is to be expected due to the fact that unnecessary surgical procedures are expected to be avoided and a more specific systemic therapy will not be delayed.

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