

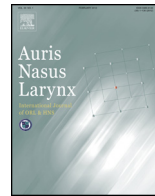


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The prognostic value of pretreatment platelet count in patients with head and neck squamous cell carcinoma

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ABSTRACT

Objective: Thrombocytosis is commonly observed in patients with solid tumors. This study aimed to evaluate the prognostic role of circulating pretreatment platelet count in a large series of patients with head and neck squamous cell carcinoma (HNSCC).

Methods: We retrospectively studied 824 patients with HNSCC treated at a single institution from 2000 to 2012. Disease-specific survival and local, regional, and distant recurrence-free survival were analyzed according to the distribution of the platelet count.

Results: By defining the platelet count $250.05 \times 10^9/L$ as a cut-off point with the best predictive capacity, we classified the patients into two groups: those with a high platelet count ($n = 378$, 45.9%), and those with a low platelet count ($n = 446$, 54.1%). On univariate analysis, there were significant differences in disease-specific survival depending on pretreatment platelet count ($P = 0.001$). The 5-year specific survival rates were 74.1% (CI 95%: 69.8–78.4%) and 61.6% (CI 95%: 56.4–66.8%) for patients with a low and high platelet count, respectively. According to the results of a multivariate analysis, patients with a high count of platelets had a tendency to a lower disease-specific survival, but the hazard ratio did not reach statistically significant differences (HR 1.24, CI 95%: 0.97–1.61, $P = 0.085$).

Conclusion: Platelet count was significantly associated with survival in univariate analysis. However, in a multivariate analysis it lost its prognostic capacity, limiting its utility as a prognostic marker in patients with HNSCC. Considering separately each primary tumor location, patients with hypopharyngeal cancer and a high platelet count had a significant decrease of disease-specific survival.

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1. Introduction

Thrombocytosis is commonly observed in patients with solid tumors. Paraneoplastic thrombocytosis appears to involve

a feedback loop, in which malignant tumors produce cytokines such as IL-6 that stimulate thrombocytosis [1], and in turn platelets promote tumor progression [2]. Several studies have found a link between increased platelet count and a worse prognosis in patients with lung [3], esophageal [4], gastric [5], colorectal [6], breast [7] or gynecologic cancers [8,9].

Numerous studies have analyzed the prognostic power of pretreatment platelet count on disease control in patients with head and neck squamous cell carcinoma (HNSCC), reaching

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contradictory conclusions. While some authors have found a significant relationship between a high platelet count and a decrease in overall survival [10–12], others showed that high or decreased platelet count compared to the normal ranges correlated with a poor prognosis [13,14]. Finally, some authors did not find statistically significant correlation between the number of circulating platelets and tumor control [15].

The aim of our study is to evaluate the prognostic role of circulating platelet count in a large series of patients with HNSCC treated at a single institution.

2. Patients and methods

2.1. Patient selection

The clinical data used in this study were obtained retrospectively from a database that collects prospectively epidemiological, treatment-related, and follow-up data of all patients with HNSCC treated at our institution from 1985 [16]. We initially included 1189 patients with a histologically confirmed squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx diagnosed at our hospital between January 2000 and December 2012. We collected retrospectively hematological parameters from routine laboratory measurements. We only included those patients for whom we obtained the platelet count within the 4 weeks prior to the start of treatment. Exclusion criteria were the lack of pretreatment platelet count records or an interval of more than 4 weeks between the blood test and the start of treatment. Thus, a total of 824 patients were analyzed in this study. Table 1 shows the characteristics of the patients included in the study.

We ascertained retrospectively HPV status in patients with an oropharyngeal carcinoma. We tested for the presence of HPV-DNA on all available tissue blocks using SPF-10 PCR and DNA enzyme immunoassay (DEIA), as they did in other studies [17]. The HPV genotyping was performed using a PCR-reverse hybridization line probe assay (LiPA25_v1) on all samples testing positive for viral DNA.

All procedures were reviewed and approved by the Institutional Review Board at Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. The investigation conforms to the principles outlined in the Declaration of Helsinki. Due to the retrospective type of the study, no formal consent was required.

2.2. Data analysis

We evaluated the relationship between the absolute values of platelet count and variables such as age, sex, smoking habits, alcohol consumption, primary tumor site, local and regional extension, and histological grade. We categorized the platelet count value according to the median value. We carried out a multivariate analysis, considering the platelet count category (below vs. above the median) as the dependent variable, the clinical-pathologic characteristics of the patients being the independent variables.

Considering the disease-specific survival as the dependent variable, we defined the platelet count value which appeared to have the best predictive capacity. We determined the

Table 1
Characteristics of the patients included in the study.

	N	%
Age (mean/standard deviation), years	62.2/11.1	
Sex		
Male	717	87.0%
Female	107	13.0%
Tobacco		
No	93	11.3%
<50 pack-years	140	17.0%
≥50 pack-years	591	71.7%
Alcohol		
No	199	24.2%
<80 g/day	340	41.3%
≥80 g/day	285	34.6%
Location		
Oral cavity	119	14.4%
Oropharynx	203	24.6%
Hypopharynx	82	10.0%
Larynx	420	51.0%
T		
T1	199	24.2%
T2	235	28.5%
T3	244	29.6%
T4	146	17.7%
N		
N0	456	55.3%
N1	98	11.9%
N2	234	28.4%
N3	36	4.4%
Grade		
Well differentiated	101	12.3%
Moderately differentiated	642	77.9%
Poorly differentiated	81	9.8%
Treatment		
Palliative	35	4.2%
Surgery ± radiotherapy	268	32.5%
Radiotherapy ± chemotherapy	521	63.2%

disease-specific survival, and the local, regional, and distant recurrence-free survival according to the platelet count category.

We conducted a multivariate study considering the disease-specific survival as the dependent variable. The primary tumor site, the local extension (T1–2 vs. T3–4), the regional extension (N0 vs. N+), the histological grade, and the platelet count category (low vs. high) were entered as independent variables.

Finally, we repeated the multivariate analysis considering separately each primary tumor location. We treated the disease-specific survival as the dependent variable, and local extension, regional extension, and categories of platelet count as independent variables.

2.3. Statistical study

We used Student *t*-test and one-way ANOVA to compare the platelet count with the clinical variables. A multivariate analysis was performed using Cox's proportional hazard regression analysis and a logistic regression model. We determined the cut-off point of platelet count with the best prognostic capacity through a ROC analysis. We calculated survival curves according to Kaplan–Meier method. Differences in survival

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