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CLINICAL STUDY

Neutrophil-to-lymphocyte ratio as a predictor of preoperative tumor staging in testicular germ cell tumors

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ABSTRACT

OBJECTIVES: The aim of our study was to evaluate associations of elevated preoperative neutrophil-to-lymphocyte ratio (NLR) with testicular germ cell tumors (GCT) characteristics other than cancer specific survival (CSS) and progression free survival (PFS).

BACKGROUND: NLR was recently presented as a widely available and inexpensive marker of poor prognosis in several types of solid tumors. Previous study showed no predictive value of NLR for CSS and PFS in testicular GCT.

METHODS: Association of high NLR with histological type of tumor, presence of metastatic disease preoperatively and worse than T1 stadium in TNM classification preoperatively was analyzed in 103 patients who underwent radical orchiectomy for testicular GCT.

RESULTS: No statistically significant difference in the prevalence of seminomas and non-seminomas neither in the group with NLR≥4 (p=0.6698) nor in the group with NLR<4 (p=0.9115) was detected. Similarly, no statistically significant difference in the prevalence of metastatic and non-metastatic disease in the group with NLR≥4 (p=0.2008), however statistically significant higher prevalence of non-metastatic disease in the group with NLR<4 (p=0.0001) was found. There was a statistically significant higher number of patients with worse than T1 stadium in patients with NLR≥4 (p=0.0105), but not significant difference in the group with NLR<4 (p=0.0956).

CONCLUSION: The results of our study showed that NLR lower than 4 predicts non-metastatic disease and NLR higher or equal 4 predicts worse than T1 stadium *(Tab. 3, Ref. 12)*. Text in PDF *www.elis.sk.*

KEY WORDS: neutrophil-to-lymphocyte ratio, testicular neoplasms, germ cell and embryonal neoplasms, neoplasm staging.

Introduction

Testicular cancer is a relatively rare disease affecting mainly young men. Its incidence in developed countries is rising, with age-adjusted incidence of 5.8 cases per 100,000 and mortality rate of 0.4 in European countries (2012 estimate) according to European Cancer Observatory (1, 2). The average age-adjusted incidence (between 1993 and 2002) in Slovak republic was 6.2/100,000, mortality 0.5/100,000 of males (3). The majority of testicular tumors (90–95%) are germ cell tumors (GCT) (4). The mortality of these tumors is relatively low, but this type of cancer affects predominantly young men, causing unpleasant psychological, social and economic problems. Neutrophil-to-lymphocyte ratio (NLR) was recently presented as a widely available and inexpensive marker of poor prognosis in several types of solid tumors (5). According to our findings, only one study has evaluated the prognostic value of preoperative NLR in testicular GCT so far, showing preoperative NLR not to be a useful tool to predict the prognosis of these tumors – cancer specific survival (CSS) and progression-free survival (PFS) showed no statistically significant relation to elevated NLR (6). The aim of our study was to evaluate other associations of elevated preoperative NLR with testicular GCT.

Materials and methods

Retrospectively we collected data of all patients, who underwent radical orchiectomy at our department for testicular cancer between 2010 and 2016. We included into our study all patients with histologically proven testicular germ cell tumors, with peripheral blood count collected and examined preoperatively in our hospital (all specimens examined in one laboratory, including at least neutrophil and lymphocyte count) and preoperative CT scan with described TNM stadium (according to Union for International Cancer Control – 8th edition TNM (7)). We excluded patients with other types of testicular cancer; we also excluded all patients with other diseases causing increased an inflammatory response (e.g. ulcerative colitis) or hematologic diseases affecting blood count. Informed consent was obtained from all the patients. Neutrophil-to-lymphocyte ratio was defined as an absolute neutrophil count divided by an absolute lymphocyte count. The cut-off value for

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high NLR was set at 4.0, based on median cut-off value in studies that proved prognostic impact of NLR (5). Statistical significance was set at p value of < 0.05. We analyzed the association of high NLR with histological type of tumor, the presence of metastatic disease preoperatively and worse than T1 stadium preoperatively (worse than T1, N1 or worse, M1 or worse stadium in TNM classification). Observed and expected frequencies were compared using chi-square tests.

Results

Inclusion criteria were met by 103 male patients aged 20 to 68 years with the median age 36 and the average age 36.7 years. There were 22 patients with NLR equal or higher than 4. The prevalence of histological tumor types is described in Table 1. There was no statistically significant difference in the prevalence of seminomas and non-seminomas either in the group with NLR ≥ 4 (p = 0.6698) or in the group with NLR < 4 (p = 0.9115). The prevalence of non-metastatic and metastatic disease (according to TNM staging – any N or M) is described in Table 2. There was no statistically significant difference in numbers of non-metastatic and metastatic diseases in the group with NLR ≥ 4 (p = 0.2008), however, a statistically significant higher prevalence of non-metastatic disease was found in the group with NLR < 4 (p = 0.0001). We also investigated the prevalence of disease worse than T1 stadium (in TNM classification) in both groups; results are shown in Table 3. There was a statistically significant higher number of patients with worse than T1 stadium in patients with NLR ≥ 4 (p = 0.0105), but not significant difference in the group with NLR < 4 (p = 0.0956).

Discussion

The cause of an increased NLR for advanced tumors is poorly understood (5). It is thought that activated neutrophils are suppressing lymphocytes causing a lower anti-tumor activity of lymphocytes (8, 9) resulting in worse prognosis (10). Many studies showed that elevated NLR predicted worse mortality rates (11) or disease severity (12, 13) also in non-oncologic diseases. The results of our study showed that NLR lower than 4 predicted non-metastatic disease and NLR higher or equal 4 predicted worse than T1 stadium. Worse than T1 stadium in TNM classification means that the cancer has spread to blood or lymph vessels near the tumor, or the tunica vaginalis (7) – it signals an increased malignant potential. Although our study describes a relatively small number of patients, it shows NLR to be a useful tool to predict TNM staging in patients with testicular germ cell tumors. According to the study of Bolat et al., NLR was not a useful tool for prediction of cancer specific survival and progression free survival (6) – it is possible, that TNM staging preoperatively is not connected to worse CSS or PFS, but we also have to take into account even fewer patients enrolled in the study (53 patients) with a lower statistical power. NLR is widely available and an inexpensive marker with proven predictive value in many solid tumors, so further statistical survey in testicular GCT is necessary. It can be used preoperatively for identification of patients eligible to deferred radical orchiectomy after chemotherapy in the absence of staging CT preoperatively.

Tab. 1. Prevalence of histological tumor types.

	Patients with NLR<4	Patients with NLR≥4
Seminoma	41	10
Non-seminoma	40	12
Two-tailed P value	p = 0.9115	p = 0.6698

Tab. 2. Prevalence of metastatic disease.

	Patients with NLR<4	Patients with NLR≥4
Metastatic	13	8
Non-metastatic	68	14
Two-tailed P value	p = 0.0001	p = 0.2008

Tab. 3. Prevalence of TNM stadium worse than T1.

	Patients with NLR<4	Patients with NLR≥4
T1	33	5
Worse than T1	48	17
Two-tailed P value	o = 0.0956	p = 0.0105

Learning points

Neutrophil-to-lymphocyte ratio was recently presented as a widely available and inexpensive marker of poor prognosis in several types of solid tumors.

No proven predictive value – cancer specific survival and progression free survival in testicular germ cell tumors.

Neutrophil-to-lymphocyte ratio can be a useful tool to predict TNM staging in patients with testicular germ cell tumors.

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