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CAN AST/ALT RATIO PREDICT RETROPERITONEAL LYMPH NODE INVOLVEMENT IN GERM CELL TESTICULAR CANCER?

GERM HÜCRELİ TESTİS KANSERİNDE AST/ALT ORANI RETROPERİTONEAL LENF NODU TUTULUMUNU ÖNGÖREBİLİR Mİ?

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SUMMARY

Introduction: *Testicular cancer is a rare tumour and accounts for 1-2% of cancers in men. Fifteen per cent of seminomas and 30 per cent of NSGCTs may be associated with occult metastatic disease at the time of diagnosis, which may lead to metastatic relapses in retroperitoneal lymph nodes or organs in the future. Although various risk factors are used to predict this risk, there is no definitive marker to predict retroperitoneal lymph node involvement and metastatic disease. The aim of this study was to determine the role of AST/ALT (De Ritis) ratio in predicting retroperitoneal lymph node involvement.*

Materials and Methods: *The data of 50 patients diagnosed with germ cell testicular cancer who underwent inguinal orchiectomy for testicular cancer between January 2009 and July 2019 were retrospectively analysed. Age, preoperative AFP, hCG, LDH, AST and ALT values, pathological and clinical stages, and oncological outcomes were evaluated. Predictive value for AST/ALT ratio was determined by ROC analysis. A p value of p<0.05 was accepted for statistical significance.*

Results: *Using ROC analysis, a value of 0.95 was determined as the predictive value for AST/ALT ratio with 64% sensitivity and 63.6% specificity (AUC:0.667). Patients were divided into 2 groups as AST/ALT ratio <0.95 (Group 1) and ≥0.95 (Group 2). When the data of the two groups were compared, no significant difference was found between the two groups in terms of age, preoperative AST value, tumour type, pathological T stage, N stage, but a significant difference was found between the two groups in retroperitoneal lymph node involvement (p<0.05, OR, 3.150; 95% CI, 0.985-10.077).*

Conclusion: *The use of De Ritis ratio in the diagnosis and prognosis of many malignancies is being investigated. A high De Ritis ratio may be associated with retroperitoneal involvement and metastatic disease. However, the accuracy of this information and which value should be accepted as the limit value is not clear. More studies on this subject are needed.*

ÖZ

Giriş: *Testis kanseri nadir görülen bir tümör olup erkeklerde görülen kanserlerin %1-2'sini oluşturur. Seminomların %15'i, NSGCT'lerin %30'u tanı anında gizli metastatik hastalıkla birlikte bulunabilmekte ve bu durum ileride retroperitoneal lenf nodlarında ya da organlarda metastatik relapslara neden olabilmektedir. Bu riski öngörmede çeşitli risk faktörleri kullanılsa da retroperitoneal lenf nodu tutulumunu ve metastatik hastalığı*

öngörmede kesin bir belirteç bulunmamaktadır. Bu çalışmanın amacı AST/ALT (De Ritis) oranının retroperitoneal lenf nodu tutulumunu öngörmedeki yerini saptamaktır.

Gereç ve Yöntem: *Ocak 2009- Temmuz 2019 yılları arasında testiküler kanser nedeniyle inguinal orşiektomi uygulanan ve germ hücreli testis kanseri tanısı alan 50 hastanın verileri retrospektif olarak incelenmiştir. Hastaların yaş, preoperatif AFP, hCG, LDH, AST ve ALT değerleri, patolojik ve klinik evreleri, onkolojik sonuçları değerlendirilmiştir. AST/ALT oranı için kestirim değeri ROC analizi yardımı ile belirlenmiştir. İstatiksel anlamlılık için p değeri p<0,05 kabul edilmiştir.*

Bulgular: *ROC analizi kullanılarak AST/ALT oranı için %64 sensitivite ve %63,6 spesifite ile 0,95 değeri kestirim değeri olarak belirlenmiştir (AUC:0,667). Hastalar AST/ALT oranı <0,95 (Grup 1) ve ≥0,95 (Grup 2) olarak 2 gruba ayrılmıştır. İki grubun verileri karşılaştırıldığında yaş, preoperatif AST değeri, tümör tipi, patolojik T evresi, N evresi açısından iki grup arasında anlamlı fark bulunamazken, retroperitoneal lenf nodu tutulumunda iki grup arasında anlamlı fark (p<0,05, OR, 3,150; %95 CI, 0,985-10,077) saptanmıştır.*

Sonuç: *De Ritis oranının pekçok malignitede tanı ve prognoz tayininde kullanımı araştırılmaktadır. De Ritis oranı yüksekliği retroperitoneal tutulum ve metastatik hastalık ile ilişkili olabilir. Ancak bu bilginin kesinliği ve hangi değerin sınır değer olarak kabul edilmesi gerektiği konusu netlik kazanmamıştır. Bu konu ile ilgili daha çok çalışmaya ihtiyaç vardır.*

INTRODUCTION

Testicular cancer is a rare tumour and constitutes 1-2% of cancers seen in men. It is the most common cancer in men aged 20-35 years. 95% of them are germ cell tumours (1).

Various tumour markers are used in the diagnosis, prognosis and follow-up of testicular tumours. For this purpose, alphafetoprotein (AFP), hCG and LDH are used. AFP and hCG are elevated in half of non-seminamatous germ cell tumours (NSGCT). In approximately one third of seminoma patients, elevated hCG can be detected at the time of diagnosis (2,3). LDH is not a specific tumour marker and has been found to be associated with high tumour volume (3).

Fifteen percent of seminomas and 30 per cent of NSGCTs may be found with occult metastatic disease at the time of diagnosis and this may lead to metastatic relapses in retroperitoneal lymph nodes or organs in the future (4,5). Although various risk factors are used to predict this risk, there is no definite marker to predict retroperitoneal lymph node involvement and metastatic disease. The aim of this study was to determine the role of AST/ALT (De Ritis) ratio in the prediction of retroperitoneal lymph node involvement.

MATERIALS AND METHODS

Approval for our study was obtained from the ethics committee of Izmir Bozyaka Training and Research Hospital with decision number 2023/08 on 25.01.2023. The data of 50 patients who underwent inguinal orchiectomy for testicular cancer between January 2009 and July 2021 were retrospectively analysed. Age, preoperative AFP, hCG, LDH, AST and ALT values, pathological and clinical stages, and oncological results were evaluated. The 2009 TNM classification was used for testicular cancer classification. Preoperative lymph node involvement and metastasis status were evaluated by contrast-enhanced computed tomography. AST and ALT values were analysed in blood samples taken within 1 week before the operation.

Statistical analysis was performed using SPSS ver. 18 (SPSS Inc., Chicago, IL, USA) statistical analysis software was used. AST/ALT ratio was evaluated using receiver operating characteristics (ROC) analysis and the area under the curve with 95% confidence interval, sensitivity and specificity values were indicated. Again with the help of ROC analysis, the cut-off value for AST/ALT ratio was determined. Patients were divided into two groups according to the cut-off value. Chi-square test was used to determine the relationship between categorical variables. Kolmogorov Smirnov test was used to determine the suitability for normal distribution. Mean and standard deviation values were used for the groups conforming to normal distribution, median and minimum and maximum value ranges were used for the groups not conforming to normal distribution. Statistical significance was based on $p<0.05$.

RESULTS

The mean age of the patients was 36.32± 12.16 years. The mean preoperative AST and ALT values were 24.28±11.46 and 26.09±16.83, respectively. AST/ALT ratio was found to be 1.12±0.55 in all patients. Other clinical data are summarised in Table 1. Using ROC analysis, a cut-off value of 0.95 was determined for AST/ALT ratio with 64% sensitivity and 63.6% specificity (Fig.1, AUC:0.667). Patients were divided into 2 groups as AST/ALT ratio <0.95 (Group 1) and ≥0.95 (Group 2). When the data of the two groups were compared, no significant difference was found between the two groups in terms of age, preoperative AST value, tumour type, pathological T stage, N stage, whereas a significant difference (p<0.05, OR, 3.150; 95% CI, 0.985-10.077) was found between the two groups in retroperitoneal lymph node involvement (Table 2).

Table 1. Clinical Data of The Patients

Age			36,32 ± 12,16
Preoperative AST (U/L)			24,28 ± 11,46
Preoperative ALT (U/L)			26,09 ± 16,83
Preoperatif AFP (ng/ml)			4,6 (1,13-3000)
Preoperative LDH (U/L)			223,5 (134-1434)
Preoperative bHCG (mU/ml)			6,09 (0-5161)
Preoperative AST/ALT			1,12 ± 0,55
Tumor Type	Seminoma		29 (58%)
	Non-Seminoma		6 (12%)
	Mix Germ Cell		15 (30%)
Pathological T Stage	T1		39 (78%)
	T2		9 (18%)
	T3		2 (4%)
	T4		0 (0%)
Retroperitoneal Lymph Node Involvement	Positive		28 (56%)
	Negative		22 (44%)
N Stage	N0		26 (52%)
	N1		12 (24%)
	N2		7 (14%)
	N3		5 (10%)
M Stage	M0		46 (92%)
	M1a		3 (6%)
	M1b		1 (2%)
Non-Regional Lymph Node Metastasis	Pozitive		2 (4%)
	Negative		48 (98%)
Organ Metastasis	Lung Metastasis	Pozitive	3 (6%)
		Negative	47 (94%)
	Extrapulmonary Organ Metastasis	Pozitive	1 (2%)
		Negative	49 (98%)

Table 2. AST/ALT ratios according to age, TNM stage and retroperitoneal lymph node involvement

		AST/ALT < 0,95	AST/ALT ≥ 0,95	P Value
Age		34,29 ± 9,83	38,19 ± 13,9	0,261
Preoperative AST (U/L)		25,91 ± 12,95	22,76 ± 9,91	0,337
Preoperative ALT (U/L)		36 ± 17,79	16,94 ± 9,1	<0,05
Tumor Type	Seminoma	13 (54,2%)	16 (61,5%)	0,862
	Non-Seminoma	3 (12,5%)	3 (11,5%)	
	Mix Germ Cell	8 (33,3%)	7 (26,9%)	
Pathological T Stage	T1	19 (79,2%)	20 (76,9%)	0,357
	T2	5 (20,8%)	4 (15,4%)	
	T3	0 (0%)	2 (7,7%)	
	T4	0 (0%)	0 (0%)	
N Stage	N0	15 (62,5%)	11 (42,3%)	0,305
	N1	6 (25%)	6 (23,1%)	
	N2	2 (8,3%)	5 (19,2%)	
	N3	1 (4,2%)	4 (15,4%)	
Retroperitoneal Lymph Node Involvement	Pozitive	10 (41,7%)	18 (69,2%)	<0,05
	Negative	14 (58,3%)	8 (30,8%)	

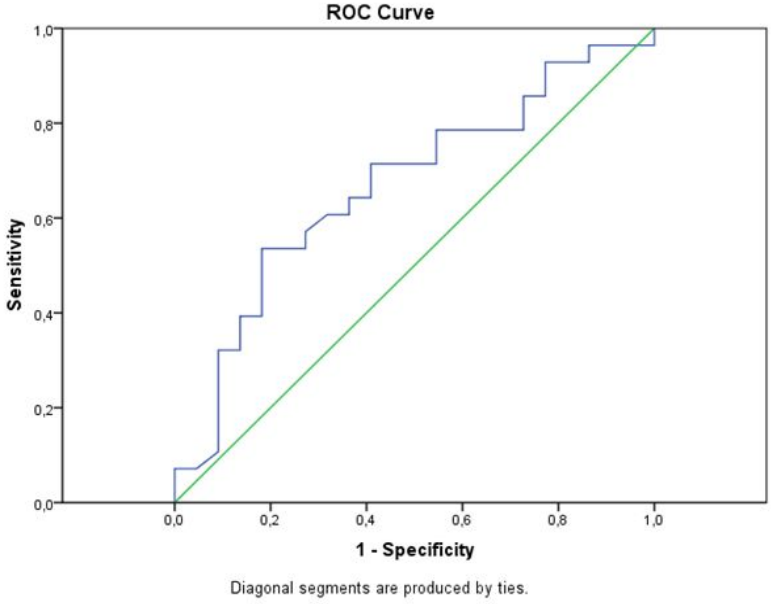


Figure 1. Using ROC analysis, a cut-off value of 0.95 was determined for AST/ALT ratio with 64% sensitivity and 63.6% specificity

DISCUSSION

A relationship was found between AST/ALT ratio and retroperitoneal lymph node involvement. It was observed that retroperitoneal lymph node involvement was significantly higher when the AST/ALT ratio was 0.95 and above (Table 2). The use of this ratio in the prognosis and clinic of malignancies has been on the agenda for a long time. Although there are not enough studies on its use in testicular cancer, in a recent study, the cut-off value was determined as 1.3 and retroperitoneal lymph node involvement was found to be significantly higher above this value.

In our study, the preoperative ALT value was found to be significantly lower in the patient group with retroperitoneal lymph node involvement and found to be compatible with the literature (6). The reason for the increase in AST/ALT ratio in retroperitoneal lymph node involvement is that the ALT value is significantly lower in patients with lymph node involvement.

The main limitation of the study is that it was retrospective. Insufficient number of patients is the second reason. In addition, AST and ALT values may be affected by liver diseases and medications. Liver metastasis was detected in one patient, but AST and ALT values were within the normal range and the patient was not excluded from the study.

CONCLUSION

The use of De Ritis ratio in the diagnosis and prognosis of many malignancies is being investigated. In urological malignancies, data are very limited. Publications on its use in testicular cancer are based on the last few years. A high de Ritis rate may be associated with retroperitoneal involvement and metastatic disease. However, the accuracy of this information and which value should be accepted as the cut-off value is not clear. More studies on this subject are needed.

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