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PREDICTION OF RECURRENCE IN ENDOUROLOGICAL TREATMENT IN PATIENTS WITH NON-MUSCLE-INVASIVE BLADDER TUMORS

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INTRODUCTION

The main goal of endourologic surgery of bladder tumors is to remove all visible tumors within the limits of healthy tissue. Therefore, the predictability of the surgical outcome depends on the assessment of the factors that might influence the postoperative outcomes (recurrent rate). There is no consensus on which factors are the most important ones in predicting surgery outcome and there is still a lot of disagreement about the choice of surgical method which would be the best for more favorable outcome after surgical interventions.

MATHERIALS AND MHETODS

Study design. This was an analytical prospective clinical study conducted from 2018 to 2022 in a plot of 80 patients (aged between 27–85 years). All underwent surgical treatment in Department of Urology and Surgical Nephrology of the Clinical Republican Hospital "Timofei Mosneaga" the Republic of Moldova was included in this study. All patients underwent a full urologic examination before the surgery. Our study followed the principles of the Declaration of Helsinki and was approved by the Institutional Ethic Committee of the *Nicolae Testemitanu* State University of Medicine and Pharmacy.


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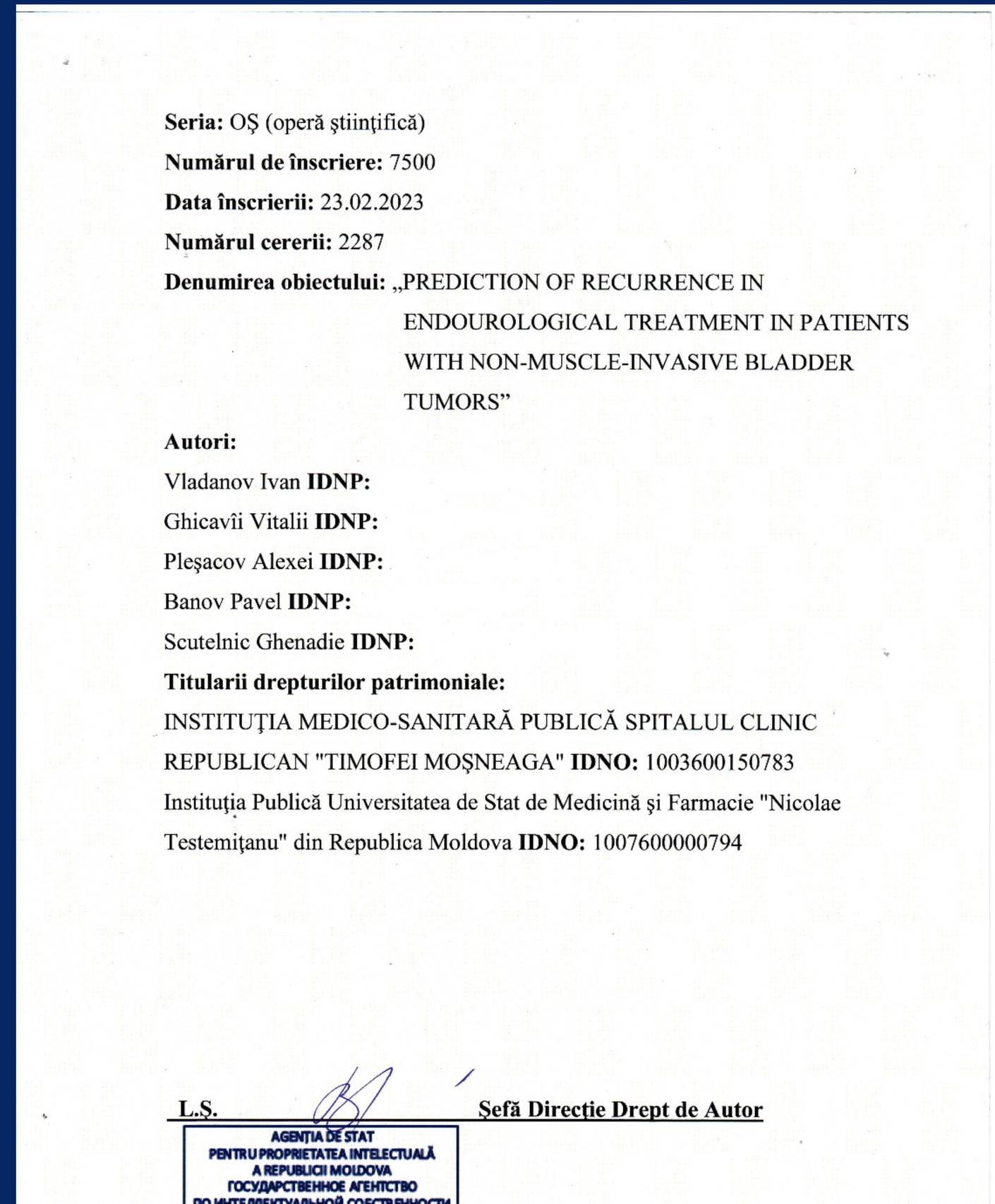
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ГОСУДАРСТВЕННОЕ АГЕНТСТВО ПО ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ РЕСПУБЛИКИ МОЛДОВА

$$P = \frac{1}{1+e^{-(-1,722+(-1,548)*\text{ Procedure}+(0.947)*\text{Lateral wall}+(1.558)*\text{Posterior wall}+((1.869)*\text{Anterior wall}+(-3.931)*\text{Bladder dome}}}$$

where p – probability of recurrence, e (exponential) – constant equal to 2.71828 **Formula 1**

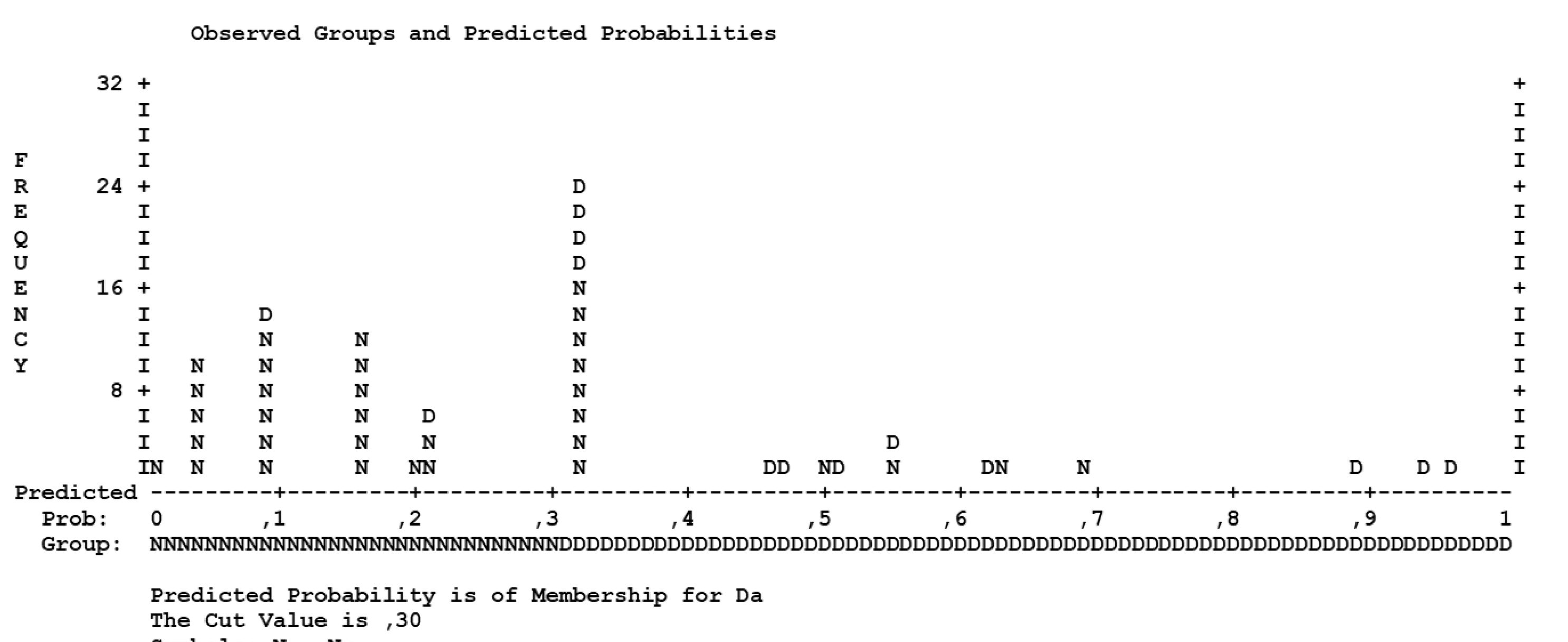

Figure 1. The classification chart for the predictive model of the probability of recurrence in patients with non-muscle invasive bladder tumors depending on the location of the tumor process and the surgical method of treatment.

RESULTS, DISCUSSION AND CONCLUSION

In order to identify the potential predictors a correlation analysis wasapplied. It revealed significant associations between the location of tumor process and the surgical method of treatment in patients with non-muscle invasive bladder tumors. The elaboration of a prognostic score for determining the probability of developing a relapse was carried out through multivariate analysis (logistic regression). To estimate the predictive potential, the following characteristics were taken into account: coefficient of determination (Nagelkerke R Square), calibration indicators (Hosmer–Lemeshow test and classification graph), discrimination indicators (specificity, sensitivity, area under the ROC curve with optimization of sensitivity/specificity relations by changing the critical point (cut-off)), evaluating the stability of the models (resampling by bootstrapping). The obtained results were described according to the requirements recommended in the literature about statistical analytics.

The main result is the development of the predictive model for determining the probability of recurrence in patients with non-muscle invasive bladder tumors depending on the location of the tumor process and the treatment method (Figure 1).

The indicator of determination, Nagelkerke R Square, showed a value of 0.302 (30.2%). Compared to the Model it means that one third of the variance of the variable of interest was explained/covered by the covariates in the modified Model.

The calibration indicator (Hosmer–Lemeshow test) demonstrated an insignificant value, $\chi 2 = 4.435$, df = 6, p = 0.618, the results being faithful in the sense of predicting the results obtained over the entire range of predicted scores.

The area under the ROC curve for the predictive model was 0.777, with a 95% confidence interval (0.664 and 0.891) and with a significant difference from the value of 0.5 (p = 0.000) (figure 2).

The model included constant (B = -1.601) procedure value (B = -1.522), lateral wall (B = 0.892), posterior wall (B = 1.468), anterior wall (B = 1.780), bladder trigone/neck (B = -0.335) and the bladder dome (B = -3.755), having the appropriate, logical signs in front of the coefficients (Table 1, step 1a). Analysis of the stability by resampling of the model developed alternatively for the probability of relapses, the bootstrapping method (1000 samples) showed that the coefficients are stable, evidently is the significance of the parameters, the small amplitude of the confidence intervals and keeping the signs in front of the coefficients in the equation (Table 1, step 2a).

Taking into account the mentioned coefficients, the elaborated model has the following mathematical expression (Formula 1).

The modified Step 2 score components showed the following effects. The value of the Procedure showed a positive association with the probability for decreasing the risk almost 5 times (OR = 0.213 (95% CI 0.058, 0.786)) for each tumor of the given region. In the case of the lateral wall, the risk of recurrence increases by 2.5 hours (OR = 2.577 (95% CI 1.216, 5.460)) for each tumor in the given region. The posterior wall risk increases 4.7 times (OR = 4.748 (95% CI 1.124, 20.047)) for each tumor of the given region. The anterior wall increases the risk by 6.5 (OR = 6.481 (95% CI 1.062, 39.560)). Bladder dome was assessed (OR = 0.02 (95% CI 0.00, 1.691)) for each tumor of the given region.

The discrimination indicators mentioned in the classification, namely specificity and sensitivity, were equal to 64.4% and 76.2%, respectively, the summary (global) percentage was valued at 67.5%. The results of these characteristics were obtained at the critical point 0.5.

The predictive model can determinate the probability of recurrence in patients with non-muscle invasive bladder tumors depending on the location of the tumor process and the treatment method. In addition, these models need to be validated using an independent sample in the following studies. Finally, the proposed strategy, in our opinion, has perspectives in order to have an efficient instrument to determinate the probability of recurrence.

Table 1. The variables in the equation of the predictive model of the probability of recurrence in patients with non-muscle invasive bladder tumors depending on the location of the tumor process and the surgical method of treatment.

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper.
Step 1ª	Procedure	-1,522	,668	5,195	1	,023	,218	,059	,808
	Lateral wall	,892	,408	4,777	1	,029	2,440	1,096	5,431
	Posterior wall	1,468	,767	3,666	1	,056	4,342	,966	19,518
	Anterior wall	1,780	,945	3,548	1	,060	5,931	,930	37,804
	Bladder trigone/neck	-,335	,905	,137	1	,712	,716	,121	4,221
	Bladder dome	-3,755	2,310	2,641	1	,104	,023	,000	2,168
	Constant	-1,601	,638	6,296	1	,012	,202		
Step 2ª	Procedure	-1,548	,667	5,384	1	,020	,213	,058	,786
	Lateral wall	,947	,383	6,105	1	,013	2,577	1,216	5,460
	Posterior wall	1,558	,735	4,493	1	,034	4,748	1,124	20,047
	Anterior wall	1,869	,923	4,101	1	,043	6,481	1,062	39,560
	Bladder dome	-3,931	2,274	2,989	1	,084	,020	,000	1,691
	Constant	-1,722	,549	9,837	1	,002	,179		

Note: Constant - value of the equation constant, B - coefficients B, S.E. - standard errors, Wald - Wald statistic, df - degrees of freedom, Sig. - statistical significance, Exp (B) - odds ratio (OR) values, 95% C.I.for EXP(B) - confidence interval for odds ratio

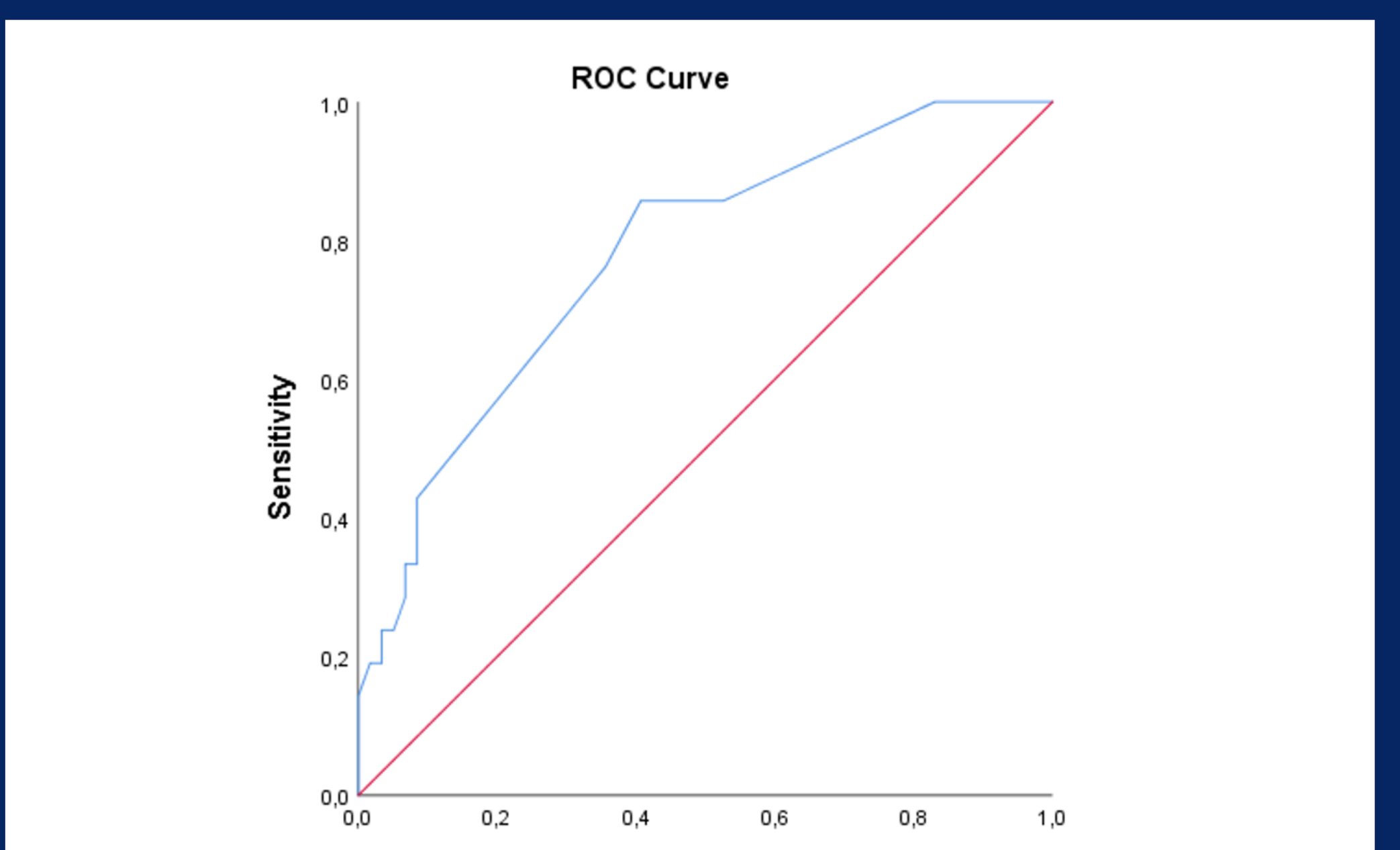

Figure 2. The ROC curve of the predictive model of the probability of recurrence in patients with non-muscle invasive bladder tumors depending on the location of the tumor process and the surgical method of treatment.

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