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PREDICTING THE PROBABILITY OF COMPLICATIONS DURING PROSTATECTOMY IN PATIENTS WITH PROSTATE CANCER USING MACHINE LEARNING METHODS

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ПРОГНОЗИРОВАНИЕ МЕТОДАМИ МАШИННОГО ОБУЧЕНИЯ ВЕРОЯТНОСТИ РАЗВИТИЯ ОСЛОЖНЕНИЙ ПРИ ПРОСТАТЭКТОМИИ У ПАЦИЕНТОВ С РАКОМ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

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Objective. To determine the probabilities of predicting possible complications after surgery in patients with the diagnosis of prostate cancer using artificial intelligence methods.

Materials and methods. Case histories of 701 patients who underwent prostatectomy were analyzed in the study. The anamnesis, findings of clinical, laboratory and instrumental study, as well as objective data of clinical observations were evaluated. The average age was 64.72. On the basis of the set of examination results, patients were selected according to the following inclusion criteria: prostate cancer patients without confirmed metastases with disease stage from T1N0M0 to T3N0M0; absence of previous and concomitant special treatment (immunotherapy or targeted therapy); informed consent to the surgery. Logistic regression, a binary classifier using a sigmoidal activation function on linear combinations of features, was used as a machine learning model.

Results. It was determined that the logistic regression model based on selected parameters (prostate volume, pain syndrome, disease duration), predicts the probability of complications quite well (TPR = 1). The overall accuracy of the model is: Accuracy = 0.98. At the same time, it can be noticed from the agreement matrix that the trained model plays it safe and classifies some cases without complications incorrectly in 5.3 % (FNR = 0.053). However, the model never made an error and did not classify cases with a high risk of complications as those in which such a possibility was unlikely.

Conclusions. The results obtained show that on the basis of just three parameters (prostate volume, pain syndrome, duration of the disease), it is possible to build a fairly good predictive model of the probability of complications after prostatectomy based on such machine learning method as logistic regression.

Keywords. Prostate cancer; prostatectomy; diagnostics; early detection of complications; prediction of complications; logistic regression.

Цель. Определение возможностей прогнозирования вероятности возникновения осложнений после перенесенного оперативного вмешательства у пациентов, поступивших с диагнозом раком предстательной железы, с помощью методов искусственного интеллекта.

Материалы и методы. В исследовании были проанализированы данные историй болезни 701 пациента, которым была выполнена простатэктомия. Проведена оценка анамнеза, данных клинико-лабораторных и инструментальных методов исследования, а также объективных данных клинических наблюдений. Средний возраст пациентов составил 64,72 г. Исходя из комплекса результатов обследования, были отобраны пациенты, соответствующие следующим критериям включения: больные раком предстательной железы без подтвержденных метастазов со стадией заболевания от T1N0M0 до T3N0M0; отсутствие предшествующего и сопутствующего специального лечения (иммунотерапия или таргетная терапия); наличие информированного согласия на проводимое оперативное вмешательство. В качестве модели машинного обучения применялась логистическая регрес-

сия – бинарный классификатор, использующий сигмоидную функцию активации на линейные комбинации признаков.

Результаты. Установлено, что на отобранных параметрах (объем простаты, болевой синдром, длительность заболевания) модель логистической регрессии достаточно хорошо предсказывает вероятность возникновения осложнений ($TPR = 1$). Общая точность модели составляет $Accurasy = 0,98$. При этом из матрицы согласования видно, что обученная модель «перестраховывается» и классифицирует часть случаев без осложнений неправильно – в 5,3 % ($FNR = 0,053$). Однако модель ни разу не ошиблась и не отнесла случаи, в которых высока вероятность возникновения осложнений, к случаям, где такая возможность маловероятна.

Выводы. Полученные результаты показывают, что на основе всего трех параметров (объем простаты, болевой синдром, длительность заболевания) можно построить достаточно хорошую предсказательную модель вероятности возникновения осложнений после простатэктомии на основе такого метода машинного обучения, как логистическая регрессия.

Ключевые слова. Рак предстательной железы, простатэктомия, диагностика, раннее выявление осложнений, прогнозирование осложнений, логистическая регрессия.

INTRODUCTION

The incidence of prostate cancer (PC) has been rapidly increasing over the last decade in Russia. PC is on the 4th place (6.9 % of tumors of all localizations) after lung cancer, gastric cancer and skin tumors in the structure of malignant neoplasm morbidity among males [1–4]. The number of patients with localized forms of prostate cancer has increased significantly after the implementation of screening programs using prostate specific antigen (PSA) testing [5–7]. A recurrence of PC occurs among 10–30 % of patients after surgical interventions. PC is determined by an increase in PSA level values in the early stages [8–11]. Improvement of the prostatectomy technique proceeds accordingly to the evolution of the study of the anatomy of this area, more accurate understanding of the peculiarities of the location and structure of the fascial layers and functionally important anatomical structures

[12; 13]. Due to the active development of AI, it is possible to create an aid system for making medical decisions on predicting the occurrence of complications of various diseases, including PC. Currently, clinical decision support systems for physician based on retrospective analysis of outpatient charts and clinical history are already being developed and implemented; real-time systems for ICU patients that allow to warn the medical personnel about the onset of critical conditions; wearable systems for monitoring and subsequent retrospective analysis of anamnesis data.

One of the ways of improving the outcomes of post-prostatectomy PC treatment is to identify and predict the postoperative survival rate of patients and the rate of complications at an early stage by using gradient-boosting methods, which will undoubtedly be able to greatly simplify the construction and strategy of treatment.

The aim of the study is to determine the possibilities of predicting the probability

of complications after surgical intervention among patients diagnosed with PC using AI methods.

MATERIALS AND METHODS

The study analyzed data from the clinical histories of 701 patients who had a prostatectomy. The anamnesis, data of the clinical laboratory and instrumental methods of research, as well as objective data of clinical observations were conducted. The average age was 64,72 y. All included in the study patients received a comprehensive examination according to clinical guidelines for diagnosis and treatment of prostate cancer patients. Morphologic examinations of the obtained material (after surgical treatment) was conducted according to the standard technology. The slices colored by hematoxylin and eosin were used in the observational morphological analysis to determine the histological type of the tumor, the degree of differentiation, the severity of secondary changes, and the prevalence of the tumor process according to the WHO classification. eosin were used to determine the histological type of tumor, the degree of differentiation, the intensity of secondary changes and the prevalence of the tumor process according to the WHO classification. Patients were selected according to a set of examination results. They met the following inclusion criteria: cancer patients without confirmed metastases with the disease stage from T1N0M0 to T3N0M0; absence of previous and concomitant special treatment (im-

munotherapy or targeted therapy); informed consent to undergoing surgical intervention and participation in the study. The exclusion criteria were: PC patients with confirmed metastases, previous and concomitant special treatment, and also the presence of exacerbations of chronic diseases. During clinical examination, PSA levels were determined to range from 3.98 to 30.49 ng/mL; the Glisson number was from 3 to 7, and the prostate tumor size ranged from 33.04 to 143.88 cm³.

Logistic regression is a binary classifier that uses a sigmoid activation function on linear combinations of features. It was used as a machine learning model. This machine learning method is the simplest classifier that still shows reasonably good results for certain tasks. At the same time, it allows us to find out the presence of linearly dependent parameters of the dataset.

The following metrics were used here:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

An approval matrix in the form of:

$$\begin{bmatrix} TPR & FNR \\ FPR & TNR \end{bmatrix},$$

where

$$TPR = \frac{TP}{TP + FP}; \quad FPR = \frac{FP}{TP + FP};$$

$$TNR = \frac{TN}{TN + FN}; \quad FNR = \frac{FN}{TN + FN};$$

TPR is the share of patients who had a complication and the model predicted the

complication, out of all patients who had a predicted complication; *FPR* is the share of patients who did not have a complication, but the model predicted a complication, out of all patients who had a predicted complication; *FNR* is the share of patients who had complications but the model did not predict a it, out of all patients who had a predicted absence of complications; *TNR* is the share of patients who did not have a complication and the model predicted the absence of a complication, out of all patients who had a predicted absence of a complication; *TP* is the amount of patients who had a complication and the model predicted the complication; *FP* is the amount of patients who did not have a complication but the model predicted a complication; *FN* is the amount of patients who had complications but the model did not predict a complication; *TN* is the amount of patients who did not have a complication and the model predicted the absence of a complication.

Permission for conducting this study was reflected by the Local Ethical Committee (LEC) of the V.I. Razumovsky Saratov State Medical University (LEC protocol No. 2 of 16.09.2023). The study was conducted in the presence of voluntary informed consent of patients in accordance with the declaration of compliance with international as well as Russian ethical principles and standards (excerpt from Minutes No. 19 of the Bioethics Committee of 26th October, 2018). The study was conducted in accordance with the requirements of the World Medical Association Declaration of Helsinki (revised in 2013).

RESULTS AND DISCUSSION

In addition to TNM staged diagnoses (at the time of hospitalization and after histological confirmation), the collected data set contained the following parameters (*I* – range of values, *m* – average, *s* – standard deviation), shown in Table 1.

Table 1

Parameters of the studied dataset

Name of parameter	Value range	Code
Age, years	<i>I</i> = [50...80] <i>m</i> = 64.73 <i>s</i> = 8.14	AGE
Duration of disease, months	<i>I</i> = [7...120] <i>m</i> = 26.87 <i>s</i> = 19.08	DD
PSA level before surgery, ng/mL'	<i>I</i> = [3.98...30.49] <i>m</i> = 17.21 <i>s</i> = 7.74	PSABS
TNM Glisson score for surgery	<i>I</i> = [3.00...7.00] <i>m</i> = 4.90 <i>s</i> = 1.42	GLISSONFS

Name of parameter	Value range	Code
Prostate ultrasound at the time of hospitalization, cm	$I = [3.00...5.89]$ $m = 4.28$ $s = 0.71$	US1
Prostate ultrasound after surgery, cm	$I = [2.91...8.78]$ $m = 4.23$ $s = 0.83$	US2
Prostate ultrasound at the time of discharge, cm	$I = [2.89...9.70]$ $m = 4.25$ $s = 0.86$	US3
Prostate volume, cm ³	$I = [25.90...180.20]$ $m = 87.84$ $s = 32.05$	PV
Was there residual urine	Yes/No	RU
Infected urine before surgery (All patients had a value of "No". The parameter was excluded from the study)	Yes/No	
Comorbidity	Yes/No	COMORB
Coexisting diseases of the cardiovascular system	Yes/No	CCVD
Coexisting gastrointestinal diseases	Yes/No	GIT
Coexisting diseases of the respiratory system	Yes/No	RS
Surgical history	Yes/No	SH
Surgery type (patients underwent the following surgeries depending on the stage of the tumor process: posterior radical prostatectomy; laparoscopic posterior radical prostatectomy; radical perineal prostatectomy)	Posterior prostatectomy Laparoscopic prostatectomy Perineal prostatectomy	SURT
TNM Glisson score after surgery	$I = [3.00...10.00]$ $m = 6.45$ $s = 2.17$	GLISSONAS
Diagnostic concordance according to the Glisson scale	Yes/No	GLISSONCON
Impurity of blood in urine after surgery	Yes/No	BLOODURINE
Duration of hospitalization after surgery, days	$I = [7.00...41.00]$ $m = 19.69$ $s = 8.34$	HOSPIT
Discharged with a catheter	Yes/No	CATHETER
Blood loss	Yes/No	BLOODL
Demand for blood transfusion	Yes/No	TRANSF
Intraoperative complications	Yes/No	INTEROP
Postoperative complications	Yes/No	POSTOP
Complications which are not directly related to the surgery	Yes/No	COMPLIC
Sluggish urine stream before surgery	Yes/No	SLUGSTREAM
Severe pain syndrome	Yes/No	PAINSYN
Nocturia	Yes/No	NOCT

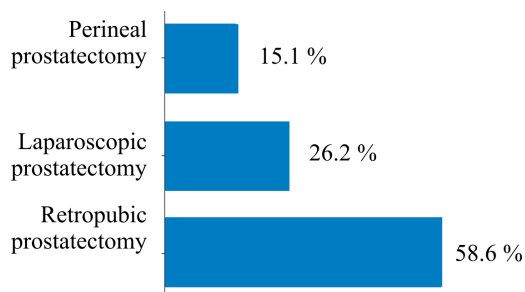


Fig. 1. Percentage of patients by surgery type

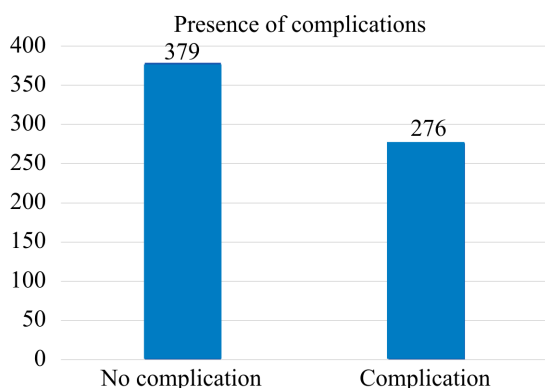


Fig. 2. Patients distribution by presence and absence of complications: 0 – there were no complications, 1 – there were complications

Figure 1 shows the percentage of patients according to the type of surgery, figure 2 shows the distribution of patients according to age.

According to the data of Fig. 1, the information set is unbalanced by the type of performed operation. The majority of patients (58.6 %) had a retropubic prostatectomy. Laparoscopic prostatectomy was conducted for 26.2 % of patients and perineal prostatectomy for 15.1 %. At the same time, the amount of patients with and without complications was approximately the same, as can be seen from Fig. 2.

For further study, parameters with values that were either unique or the

same for all patients were removed. As a result, the following parameters remained: “AGE” (age of the patients), “DD” (duration of disease (in months)), “TNM.T” (tumor size according to TNM classification), “TNM.N” (stages with lymph node involvement according to TNM classification), “PSABS” (preoperative PSA level, ng/mL), “GLISSONFS” (TNM Glisson score for surgery), “US1” (prostate ultrasound at the time of hospitalization, cm), “US2” (prostate ultrasound after surgery, cm), “US3” (prostate ultrasound at the time of discharge, cm), “PV” (prostate volume, cm³), “RU” (was there residual urine), “CCVD” (coexisting diseases of the cardiovascular system), “GIT” (coexisting gastrointestinal diseases), “RS” (coexisting diseases of the respiratory system), “SH” (surgery history), “SURT” (surgery type (patients underwent the following surgeries depending on the stage of the tumor process: posterior radical prostatectomy; laparoscopic posterior radical prostatectomy; radical perineal prostatectomy)), “GLISSONAS” (TNM Glisson score after surgery), “gTNM.T” (histologic verification of tumor according to TNM classification), “GLISSONCON” (diagnostic concordance according to the Glisson scale), “BLOODURINE” (impurity of blood in urine after surgery), “CATHETER” (discharged with a catheter), “BLOODL” (blood loss), “TRANSF” (demand for blood transfusion), “PAINSYN” (severe pain syndrome), “NOCT” (nocturia). Target variable for predicting “POSTOP” (postoperative complications).

Logistic regression was used to identify the significance of the remaining linearly independent parameters that were linearly dependent parameters are summarized in Table 2. The calculation results of

Table 2

Calculation results of the importance of the remaining independent parameters

Model	Logit		Method		MLE	
Dependent Variable:	AS		Pseudo R-squared:		0.853	
Date:	2024-03-29 20:26		AIC:		186.4373	
No. Observations:	701		BIC:		291.1450	
Df Model:	22		Log-Likelihood:		-70.219	
Df Residuals:	678		LL-Null:		-478.59	
Converged:	1.0000		LLR p-value:		1.6073e-158	
No. Iterations:	11.0000		Scale:		1.0000	
	Coef.	Std.Err.	z	P > z	[0.025	0.975]
AGE	-0.0220	0.0270	-0.8158	0.4146	-0.0750	0.0309
DD	-0.0204	0.0091	-2.2558	0.0241	-0.0382	-0.0027
TNM.T	-0.0465	0.6236	-0.0745	0.9406	-1.2688	1.1759
TNM.N	0.0198	1.9323	0.0102	0.9918	-3.7674	3.8069
PSABS	0.0146	0.0320	0.4565	0.6480	-0.0480	0.0772
GLISSONFS	-0.1571	0.1754	-0.8955	0.3705	-0.5009	0.1867
US1	-0.0702	0.3461	-0.2028	0.8393	-0.7486	0.6082
US2	-0.4671	0.2545	-1.8349	0.0665	-0.9659	0.0318
US3	-0.0195	0.2300	-0.0850	0.9323	-0.4704	0.4313
PV	-0.0148	0.0073	-2.0188	0.0435	-0.0292	-0.0004
RU	0.0001	0.0329	0.0018	0.9985	0.0645	0.0646
CCVD	-1.0520	1.1430	-0.9204	0.3574	-3.2923	1.1883
GIT	-0.6683	0.5550	-1.2041	0.2286	-1.7560	0.4195
RS	1.1087	1.5938	0.6956	0.4866	-2.0150	4.2324
SH	1.0268	0.9198	1.1163	0.2643	-0.7760	2.8297
SURT	0.3699	0.4353	0.8499	0.3954	-0.4832	1.2231
GLISSONAS	-0.0891	0.1207	-0.7381	0.4605	-0.3256	0.1475
gTNM.T	1.1078	0.8687	1.2752	0.2022	-0.5948	2.8104
GLISSONCON	-0.0751	0.5762	-0.1303	0.8963	-1.2044	1.0542
BLOODURINE	0.0498	1.4686	0.0339	0.9730	-2.8286	2.9281
CATHETER	-0.9088	0.7519	-1.2087	0.2268	-2.3824	0.5649
BLOODL	-0.0786	1.4563	-0.0539	0.9570	-2.9329	2.7758
PAINSYN	10.4449	1.5913	6.5636	0.0000	7.3259	13.5638

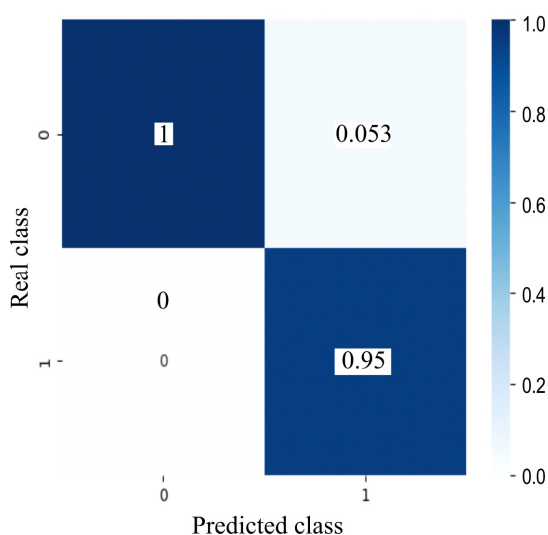


Fig. 3. Approval matrix

As we can see from the data presented in Table 2, the most important parameters determining the likelihood of complications are prostate volume (PV, $p = 0.0435$), pain syndrome (PAINSYN, $p = 0.0000$), and disease duration (DD, $p = 0.0241$).

Then, logistic regression was trained on these parameters to determine the probability of complications.

The original data set was divided in the proportion of 70 %/30 % for training and metrics calculation such that the distributions of the target variable (AS) were statistically indistinguishable in the training and variation metrics.

The Accuracy metric was 0.98 as a result of testing the trained model on the validation sample. The concordance matrix is shown in Fig. 3. As it can be seen, the share of patients who had complications and among patients to whom the model predicted complications was $TPR = 1$. The

model never made an error and did not categorize patients with complications to patients without complications ($FPR = 0$). In this case, the model “reinsured” and it predicted the occurrence of complications for 5.3 % of patients, although they did not get a complication ($FNR = 0.053$ and $TNR = 0.95$).

It is necessary to mention that the certificate of state registration of computer programs “System of prediction of complications prediction during prostatectomy for prostate cancer” (No. 2024613673)1 has also been obtained to date.

CONCLUSIONS

As can be seen from the obtained metrics, the logistic regression model predicts the probability of complications reasonably well ($TPR = 1$) on the selected parameters (prostate volume (PV), pain syndrome (PAINSYN), duration of disease (DD)). The overall accuracy of the model is 0.98. However, as can be seen from the concordance matrix, the model “reinsures” and classifies a part of cases without complications incorrectly. Thus, 5.3 % ($FNR = 0.053$) were misclassified as cases with a high likelihood of complications. At the same time, the model never made an error in categorizing cases in which there was a high probability of complications to cases where such a possibility was low.

Thus, the obtained results show that on the basis of only three parameters

(prostate volume (PV), pain syndrome (PAINSYN), duration of disease (DD)), it is possible to build a reasonably good predictive model of the probability of complications after prostatectomy based on such a machine learning method as logistic regression. If the model metrics need to be improved, further the patient sample can be increased and the model can be trained using more sophisticated machine learning and AI methods.

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