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PROGNOSTIC FACTORS, FUNCTIONAL AND ONCOLOGICAL OUTCOMES AFTER RADICAL LAPAROSCOPIC PROSTATECTOMY

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SUMMARY OF DISSERTATION

To award the educational and scientific degree
"DOCTOR"

Scientific supervisor:
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Prof. Dr. Krassimir Prodanov Yanev, MD

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The dissertation contains 295 pages. Illustrated with 13 graphs, 138 tables and 28 figures. The bibliographic reference consists of 214 literary sources, of which 21 are in Cyrillic and 193 are in Latin.

The dissertation work was discussed and directed for defense at a meeting of the Department of Urology at the Sofia University, where Dr. Georgi Ivanov is a full-time doctoral student with the right to defend.

SCIENTIFIC JURY

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The public defense of the dissertation work will take place on 07/04/2023 at 1:00 p.m. in the auditorium of the Clinic of Urology, UMHAT "Alexandrovska", Sofia.

Contents

1. Introduction

Prostate carcinoma (PC) is an oncological disease of particular social importance. PC is estimated to be the second most common cancer in men and the fifth leading cause of death worldwide [1]. This is due to the combination of the general aging of the population, as well as the increasingly sophisticated methods of early detection and diagnosis of the disease [2]. The introduction of the prostate-specific antigen (PSA) as a routine screening marker against PC allowed the disease to be diagnosed early, in its asymptomatic phase, in a large percentage of cases [3]. More and more scientific data are also accumulating regarding the genetic predisposition of the disease and the proof of risk and protective genetic factors [4]. Significant progress in the field of imaging diagnostics, in particular the introduction of modern methods such as multiparametric nuclear magnetic resonance (mNMR) and prostate-specific membrane antigen-mediated positron emission tomography (PSMA PETCT), in turn, allows more and more precise staging and follow-up of the disease [5] [6]. The above-mentioned medical innovations make it possible to diagnose PC most often in its localized form, which allows patients to choose from a number of therapeutic options, each of which provides its own advantages and disadvantages - active surveillance, radical prostatectomy, radiotherapy, focal treatment, androgen deprivation therapy [7]. By itself, operative treatment can be performed in the form of open, laparoscopic and robot-assisted radical prostatectomy [8]. This variety of options can often be confusing and overwhelming for the patient and treating urologist to choose the most appropriate approach in each individual case. This imposes a constant need to accumulate new and up-to-date data regarding the effectiveness and safety of each of the listed therapeutic methods.

Since the first trials by Schuessler and Clayman in 1991 and 1992, laparoscopic radical prostatectomy (LRP) has gradually been proven to be an operative method characterized by excellent oncological and functional results on the background of less blood loss and shorter hospital stay in comparison with the open operative technique [8]. As the surgical practice of LRP advances, new and different techniques are introduced: preservation of the puboprostatic ligaments, preservation of the endopelvic fascia, posterior reconstruction of Danonvilier's fascia, anterior reconstruction, preservation of the bullous neck, anterior reconstruction with hanging suture, preservation of vascular - the nerve bundle, etc. [9] [10] [11]. However, the occurrence of early or late complications or disease recurrence that compromise oncological and functional outcomes after surgery cannot be excluded. In the world literature, high Gleason score (GS), extracapsular spread (pT3a), involvement of the seminal vesicles (pT3b) or positive resection lines (R1) are indicated as main risk factors [12].

Despite the experience gained so far, it can be concluded that modern medicine still faces the challenge of establishing and proving reliable and individualized prognostic factors for each patient who is about to undergo LRP in order to minimize the frequency of possible complications and achieve optimal oncological and functional outcomes. results.

2. Purpose

The purpose of the study is to follow up patients with diagnosed prostate cancer based on preoperative laboratory and imaging studies and to report oncological and functional results, early and late complications after performing laparoscopic radical prostate vesiculectomy.

3. Tasks

1. To follow up the patients undergoing laparoscopic radical prostatectomy by registering the data of the patients' preoperative characteristics, clinical and imaging diagnostic methods.

2. To allocate patients depending on laboratory indicators, clinical and pathological staging and grading.

3. To identify the most frequent intraoperative and early postoperative complications and to determine the factors affecting their occurrence.

4. To follow the patients at the sixth and twelfth postoperative months and to report the rate of late postoperative complications.

5. To follow up the patients on the sixth and twelfth postoperative months and to report the functional and oncological results of the therapy.

6. To study the prognostic influence of preoperative factors on the development of early and late complications and to define the optimal preoperative parameters of patients undergoing laparoscopic radical prostatectomy.

4. Material and methods

4.1 Material. Clinical contingent.

The studied pathological contingent included 100 patients with diagnosed prostate carcinoma and subsequent radical laparoscopic prostate vesiculectomy. The patients were diagnosed, treated and followed up in the Clinic of Urology at the "Alexandrovska" UMBAL for the period 2018-2020.

The mean age of the patients was 64.7 ± 6.52 years, with a range of 53 to 74 years. The distribution by age groups is 50-59 years - 20%; 60-69 years – 55%; 70-79 years - 25%.

4.2 Methods.

4.2.1. Diagnostic methods

4.2.1.1 History and objective condition

A thorough history was taken of each patient. Major attention was paid to the patient's current complaints, the presence of accompanying and past diseases, and family history.

4.2.1.2 Prostate-specific antigen

In each of the patients in the present study, PSA was examined preoperatively as well as during the postoperative follow-up of the patients.

4.2.1.3 Molecular diagnostics.

The author of the present paper was the principal investigator within the Young Researcher project (Contract No. 141/2019 funded by MU-Sofia, FNI), in which polymorphisms in the genes of the androgen receptor and the vitamin D receptor.

Venous blood was drawn from each of the enrolled patients by venipuncture and stored in a tube treated with K2EDTA. DNA isolation of a high-molecular-weight and purified matrix (total DNA) was performed for subsequent analysis from all patients using the AmpliSens DNA isolation kit (Ecoli s.r.o., Slovak Republic). PCR amplification of the target regions of both genes was performed under strictly defined conditions.

4.2.1.4 Digital rectal examination

Digital rectal examination was performed on each of the patients in the present study as part of the initial examination, at the time of prostate biopsy, and before LRP was performed.

4.2.1.5 Transrectal ultrasound

Transrectal ultrasonography of the prostate gland was performed in each of the patients included in the present work - within the framework of transrectal or transperineal fusion biopsy of the prostate gland.

4.2.1.6 MRI

MRI has established itself as the method of choice in PC imaging. MRI provides accurate imaging of carcinoma-suspicious lesions in the prostate – their size, number and location; possible periprostatic spread; involvement of surrounding tissues. mMRI was performed preoperatively in 73 patients (73%).

4.2.1.7 Biopsy of the prostate gland

Transperineal Fusion biopsy under spinal anesthesia was performed in 58 patients of the present sample. Manipulation was performed using the Koelis Trinity apparatus and a Tru-cut Bard Magnum biopsy gun. Patients received perioperative antibiotic prophylaxis with Ceftriaxone 2 g i.v. and postoperative therapy with an oral quinolone or cephalosporin antibiotic.

In 42 patients, a 12-point transrectal biopsy of the prostate gland was performed under ultrasound control. The manipulation was performed under local anesthesia using a Bard Magnum biopsy gun. Oral antibiotic prophylaxis was administered.

4.2.1.8 Histological examination of prostate biopsy material

In the present study, prostate biopsy specimens were placed in individual containers, preserved by treatment with formaldehyde solution, and sent to the histology laboratory in labeled individual containers. For each material, the location in the prostate gland from which it was taken is documented. In the histological laboratory, the proportional presence of PC was noted for each sample. Tumors were graded according to the Gleason score. The pathologist also indicates the percentage involvement of tissue cylinders by carcinoma tissue, as well as the possible presence of various histological features such as perineural invasion, ductal-, cribriform- or mucinous component.

4.2.1.9 Bone scintigraphy

According to the guidelines of the European Association of Urology, bone scintigraphy was performed in all intermediate- or high-risk patients of the present study. LRP was administered as therapy only in patients with a negative test result.

4.2.2 Surgical methods. Surgical technique.

The patient is hospitalized at least one day before the surgical intervention. Consultations are held with an internist and an anesthesiologist, and, if necessary, with other specialists. The patient must familiarize himself with the essence of the surgical intervention and the risks

associated with it, after which he signs an informed consent. The patient does not take liquids and food for a minimum of 6 and 12 hours before the intervention, respectively.

The operation is performed under general intubation anesthesia. Ceftriaxone 2 g intravenously is administered intraoperatively.

LRP was carried out through the following steps:

1. Patient positioning – Trendelenburg, abduction of lower limbs.

2. Surgical access - Hasson's technique.

3. Placement of optical and working trocars.

4. Endopelvic fascia dissection.

5. Ligation of DVC.

6. Incision and dissection of the bladder neck.

7. Liberation and dissection of the seminal vesicles.

8. Dissection of Denonville's fascia and lateral pedicles of the prostate.

9. Preservation of vascular-nerve bundles.

10. Incision of the urethra apically.

11. Reconstruction of a vesicourethral anastomosis and insertion of a urethral catheter.

12. Hemostasis.

13. Specimen extraction.

14. Drain fixation.

15. Extraction of trocars, suturing of the surgical wound.

4.2.3 Histological examination of permanent histological preparation.
To ensure tissue fixation, the material is immersed in a formaldehyde solution for at least 24 hours. The pathologist then notes the status of the surgical margins over the entire surface of the prostate gland. The specimen is cut transversely along the course of the urethra through 3-4 mm. The materials thus obtained are stained and examined microscopically. The pathological result of the material after LRP in each patient is described: histopathological type of the tumor (adenocarcinoma in 95% of cases); pathological staging of the tumor according to the TNM system; status of resection lines; Gleason sum grading; extraprostatic spread; seminal vesicle invasion; multifocality; presence of additional histological variations such as – perineural invasion, lymphovascular invasion, presence of ductal, cribriform, mucinous component and others.

4.2.4 Methods of postoperative follow-up - early postoperative period.

Patients are taken to the intensive care unit and placed under constant monitoring within the first 24 hours postoperatively. Paraclinical indicators are examined immediately postoperatively and at the 24th hour; antibiotic prophylaxis, anticoagulant therapy is carried out; secretion from the drain and diuresis are monitored. Regular dressings of the surgical

wound are performed. The catheter is removed between the 10th and 14th postoperative day. The patient was discharged with a recommendation to take an oral antibiotic for 7 days.

4.2.4.1 Intraoperative and early postoperative complications
When recording the course of the patients' disease in the present work, intraoperative and early postoperative complications are defined as adverse events occurring during radical prostatectomy or in the first month after the intervention. The above include:

• Rectal trauma/lesion

• Hemorrhage – controlled conservatively

• Hemorrhage with the need for revision

• Hematuria

• Leakage of urine from the vesicourethral anastomosis

• Urinary tract infection

• Complications of the surgical wound - suppuration, dehiscence

• Cardiovascular complications – pulmonary thromboembolism, etc.

4.2.4.2 Late postoperative complications, oncological and functional results
In the follow-up of patients after laparoscopic radical prostatectomy, adverse events occurring after the first month of the surgical intervention were defined as late postoperative complications:

• Stricture of the urethra

• Sclerosis in the area of the vesicourethral anastomosis

• Chronic uroinfection

• Erectile dysfunction

• Incontinence

• Biochemical recurrence or progression of prostate carcinoma

• Local recurrence of the disease

• Occurrence of distant metastases

• Complications related to adjuvant therapy

4.2.5. Statistical methods
Data were entered and processed with the statistical package IBM SPSS Statistics 22.0. $p<0.05$ was accepted as a level of significance at which the null hypothesis is rejected.

The following methods were applied:

1. Descriptive analysis – the frequency distribution of the considered signs, broken down by research groups, is presented in tabular form.

2. Analysis of Variance – to assess the central tendency and scatter characteristics of the data.

3. Graphical analysis – for visualization of the obtained results.

4. Alternative analysis – to compare relative shares.

5. Exact test of Fisher's test $\chi 2$ for testing hypotheses about the presence of a relationship between categorical variables.

6. Tests of Perason, Fisher, Spearman, Cramer - to check correlation.

7. Kolmogorov-Smirnov and Shapiro-Wilk tests - to check distributions for normality.

8. Student's t-test for testing hypotheses of difference between two independent samples.

5. Results

5.1 Demographic characteristics of patients.

Table 1 shows the main demographic characteristics of the patients.

Table 1 Distribution of patients according to their demographic characteristics

Characteristic	N=100
Age (Mean ± SD **(Me, IQR)**)[1]	64.700 ± 8.856 **(66.00, 10)**
Height – м (Mean ± SD (**Me, IQR**))	174.680 ± 5.230 **(174.68, 6)**
Weight – кг (Mean ± SD (**Me, IQR**))	86.970 ± 14.435 **(86.97, 17)**
BMI (Mean ± SD (**Me, IQR**))	28.464 ± 4.387 **(28.50, 4.92)**
BMI[2] (number, %)	
Underweight (<18.49)	0 (0.0%)
Normal weight (18.50 – 24.99)	20 (20.0%)
Preobesity (25.00 – 29.99)	51 (51.0%)
Obesity I grade (30.00 – 34.99)	22 (22.0%)
Obesity II grade (35.00 – 39.99)	5 (5.0%)
Obesity III grade (≥ 40.0)	2 (2.0%)
Blood type (number,%)	
0	27 (27.0%)
A	41 (41.0%)
B	11 (11.0%)
AB	8 (8.0%)
N/A	13 (13.0%)
Prior surgery (number, %)	48 (48.0%)
Accompanying diseases (number, %)	75 (75.0%)
one	48 (48.0%)
two	24 (24.0%)
three	1 (1.0%)
four	2 (2.0%)
Family anamnesis for PCa	15%

The distribution of patients according to accompanying diseases is as follows: without PZ - 25%; arterial hypertension – 62%; Diabetes mellitus – 7%; CHD – 6%; COPD – 4%; Gout – 4%; Thrombophlebitis – 2%; Chronic gastritis – 2%; Bronchial asthma – 2%; cerebrovascular disease – 2%; Hashimoto's disease - 2%; Chronic hepatitis B – 2%; Cirrhosis – 1%; HANK – 1%; Chronic atrial fibrillation – 1%,

[1] Средна аритметична величина ± стандартно отклонение **(Медиана, Интерквартилен размах)**
[2] Използвани са нормите за ИТМ според Световната здравна организация (СЗО)

The distribution of patients according to the type of past surgical intervention is as follows: herniotomy – 22%; appendectomy – 17%; limb surgery – 5%; coronary angiography – 3%; nephrectomy – 3%; colon polypectomy – 2%: valve prosthesis – 2%; transurethral resection of bladder – 2%; transurethral resection of the prostate – 2%.

5.2 Correlations of preoperative indicators and prognostic factors

Table 2 Descriptive statistics of the variables

Characteristics	N=100
Prostate-specific antigern (PSA) – ng/ml (Mean ± SD **(Me, IQR)**)	14.813 ± 11.890 **(10.30, 10.59)**
ISUP Grade Group от биопсия (number, %)	
I	16 (16.0%)
II	33 (33.0%)
III	29 (29.0%)
IV	11 (11.0%)
V	4 (4.0%)
N/a	7 (7.0%)
Prostate volume (number, %)	
under 49 cc.	
50 – 99 cc	54 (54%)
Over 100 cc	33 (33%)
N/a	4 (4%)
	9 (95)
ISUP Grade Group от операция (number, %)	
I	4 (4.0%)
II	31 (31.0%)
III	30 (30.0%)
IV	13 (13.0%)
V	22 (22.0%)
MRI - PIRADS (number, %)	
I	0 (0.0%)
II	2 (2.0%)
III	10 (10.0%)
IV	39 (39.0%)
V	22 (22.0%)
N/a	27 (27.0%)
TNM (брой, %)	
pT2	51 (51.0%)
pT3	48 (48.0%)
pT4	1 (1.0%)
Histological variants (Mean ± SD **(Me, IQR)**)	0.98 ± 0.910 **(1.00, 1.00)**
Pathological progression (брой, %)	45 (45.0%)
Positive surgical margins (брой, %)	45 (45.0%)
Prostate capsule penetration (брой, %)	26 (26.0%)

Biochemical reccurence (брой, %)	26 (26.0%)
Local recurrence/metastases (брой, %)	5 (5.0%)

An analysis of the relationships between PSA and a number of other preoperative and postoperative indicators was performed. Summary data are presented in Table 3.

Table 3. Correlation of PSA with other variables.

Variable	Point-biserial correlation coefficient	Sig. (2-tailed)	N
Grade Group biopsy	,160	,126	93
Grade Group surgery	,191	,057	100
MRI	,247*	,035	73
TNM	,266**	,008	100
Pathological progression	,146	,159	95
Surgical margins (R+)	,145	,151	100
Capsule penetration	,224*	,025	100
Biochemical recurrence	,247*	,018	91
Local recurrence/meta	,026	,823	76

* Correlation is significant at the 0.05 level

** Correlation is significant at the 0.01 level

Table 4. Distribution of patients according to MRI and PSA findings

MRI	N	PSA (ng/ml)				
		Mean	SD	Me	Min	Max
2	2	8.05	1.054	8.05	7.30	8.79
3	10	13.11	8.318	11.50	4.18	30.00
4	39	12.854	7.923	10.00	4.00	37.00
5	22	19.591	16.322	15.25	5.37	75.00
N/a	27	14.883	13.329	10.00	4.18	62.50

Detailed subgroup analysis did not reveal a statistically significant difference in mean PSA levels (ng/ml) between the four MRI groups (H=4.381, df=3, Sig.=0.223).

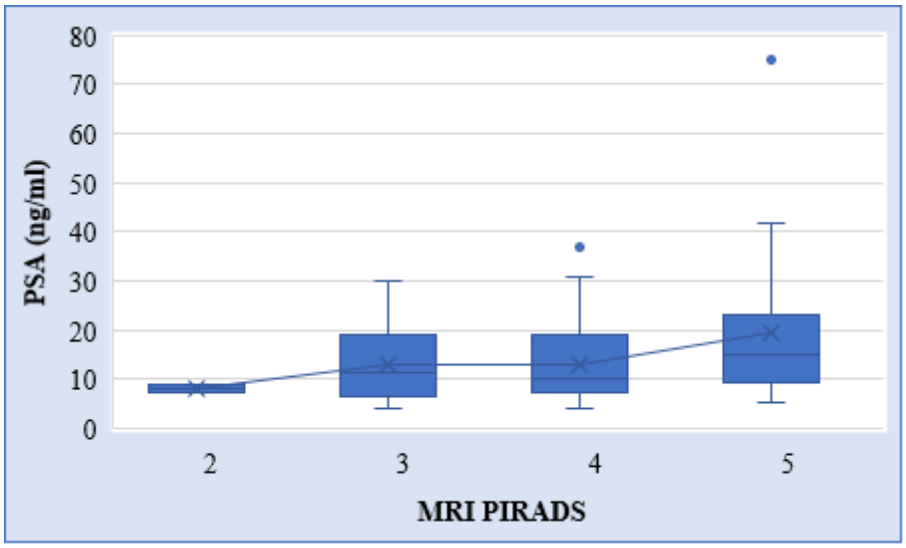


Figure 1 Box-plot diagram – PSA versus MRI finding.

Table 5. Frequency distribution of patients according to PSA and pT stage of PC.

TNM	N	PSA (ng/ml)				
		Mean	SD	Me	Min	Max
pT2	51	12.106	8.051	9.60	4.00	39.00
pT3	48	17.165	14.203	13.57	5.14	75.00
pT4	1	40.000	-	40.00	40.00	40.00
N/a	27	14.883	13.329	10.00	4.18	62.50

There was a statistically significant difference in mean PSA values between the three groups by pT (H=7.786, df=2, Sig.=0.020). After the Kruschkel-Wallis test was statistically significant, multiple Mann-Whitney tests were performed to analyze pairwise differences for groups. A statistically significant difference was found in mean PSA values at pT2 and pT3 (U=894.000, z=-2.311, Sig.=0.021).

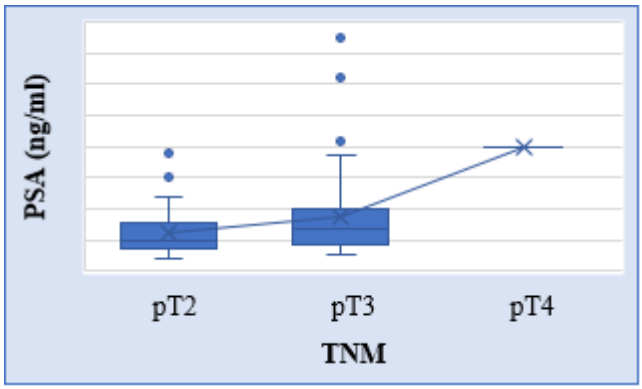


Figure 2 Box-plot diagram – PSA and pT disease stage

Table 6 Analysis of patients according to PSA and prostatic capsule penetration

Prostate capsule penetration	N	PSA (ng/ml)				
		Mean	SD	Me	Min	Max
Yes	26	19.275	14.931	16.25	5.37	74.00
No	74	13.245	10.286	9.75	4.00	62.50
Total	100	14.813	11.890	10.30	4.00	75.00

There was a statistically significant difference in mean PSA values between subjects with and without capsule penetration (U=1302.500, N=100, Sig.=0.007).

Table 7. Frequency distribution of PSA patients and occurrence of biochemical relapse.

Biochemical recurrence	N	PSA (ng/ml)				
		Mean	SD	Me	Min	Max
Yes	26	19.915	4.381	17.50	4.00	62.50
No	65	13.198	11.013	9.60	4.00	75.00
Total	91	15.117	12.369	10.00	4.00	75.00

There was a statistically significant difference in mean PSA values between subjects with and without biochemical recurrence (Figure 6) (U=1114.500, N=91, Sig.=0.018).

Correlation of ISUP Grade group from preoperative biopsy and a number of indicators followed:

Table 8 Correlation of ISUP Grade group from biopsy with other variables

Variable	Correlation coefficient	Statistics	Sig. (2-tailed)	N
MRI	Spearman (r_s)	0.262	0.027	73
TNM	Rank Biserial (r_{rb})	0.252	0.015	93
Histological variants	Biserial (r_b)	0.252	0.015	93
Surgical time /min/	Biserial (r_b)	0.020	0.852	93
Bloodloss /ml/	Biserial (r_b)	0.126	0.228	93
Pathological progression	Rank Biserial (r_{rb})	-0.280	0.007	92
Positive surgical margins	Rank Biserial (r_{rb})	0.089	0.397	93
Capsule penetration	Rank Biserial (r_{rb})	0.387	0.000	93
Biochemical recurrence	Rank Biserial (r_{rb})	0.173	0.110	93
Local recurrence/meta	Rank Biserial (r_{rb})	0.182	0.122	73

Table 8 is interpreted as follows: in the presence of p-values (Sig.) below 0.05, a statistically reliable relationship is established between the two investigated indicators; the higher the correlation coefficient (Correlation coefficient), the more pronounced the degree of correlation. It can be concluded, therefore, that a statistically significant correlation is demonstrated between the ISUP Grade group histological result of the preoperative biopsy and: the MRI finding (r = 0.262; p = 0.027); pT disease stage (r = 0.252; p = 0.015); the presence of histological variations (r = -0.280; p = 0.007); the incidence of prostatic capsule penetration (r = 0.387; p = 0.000).

An analysis of the relationship between the ISUP Grade group result of prostate gland biopsy and the MRI PIRADS finding was performed. The results are shown in Figure 3.

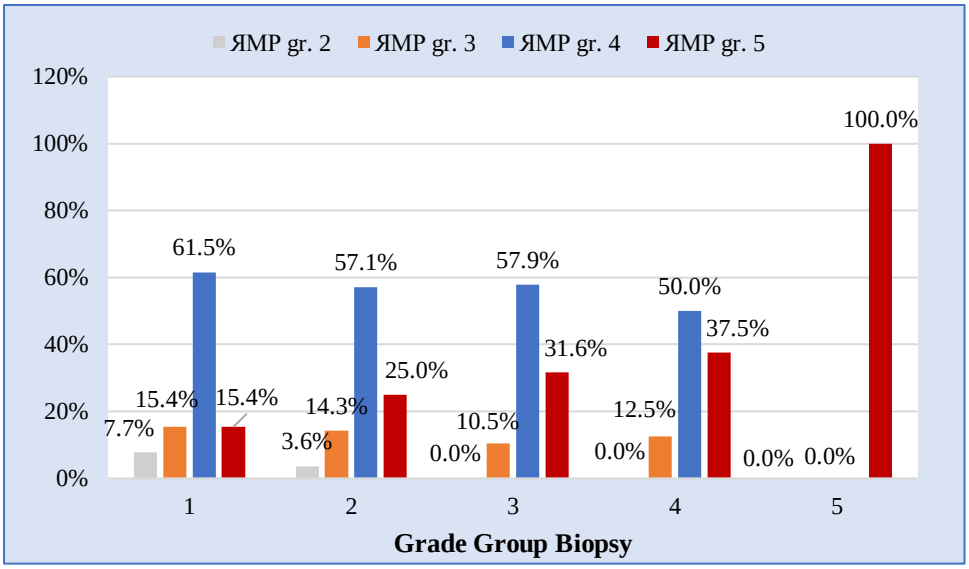


Figure 3. Distribution of Patients by MRI Finding and Biopsy Grade Group (bar chart)

An analysis of the correlation between the ISUP Grade group score of prostate gland biopsy and the TNM stage of the disease after LRP was performed. The results are discussed in Figure 4.

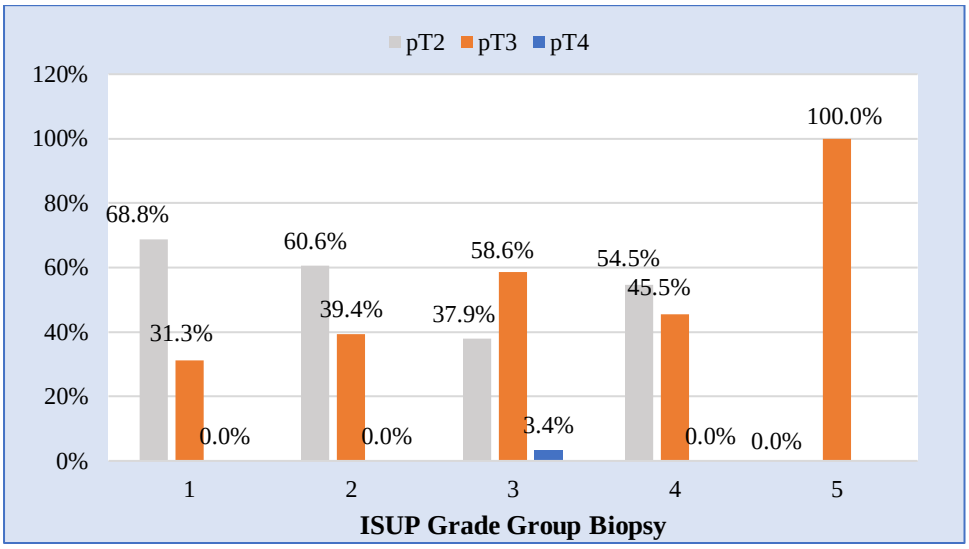


Figure 4. Distribution of patients by biopsy Grade Group and T stage of disease after LRP (bar chart).

The relationship between ISUP Grade group by biopsy and the presence of histological variations is presented in Figure 5.

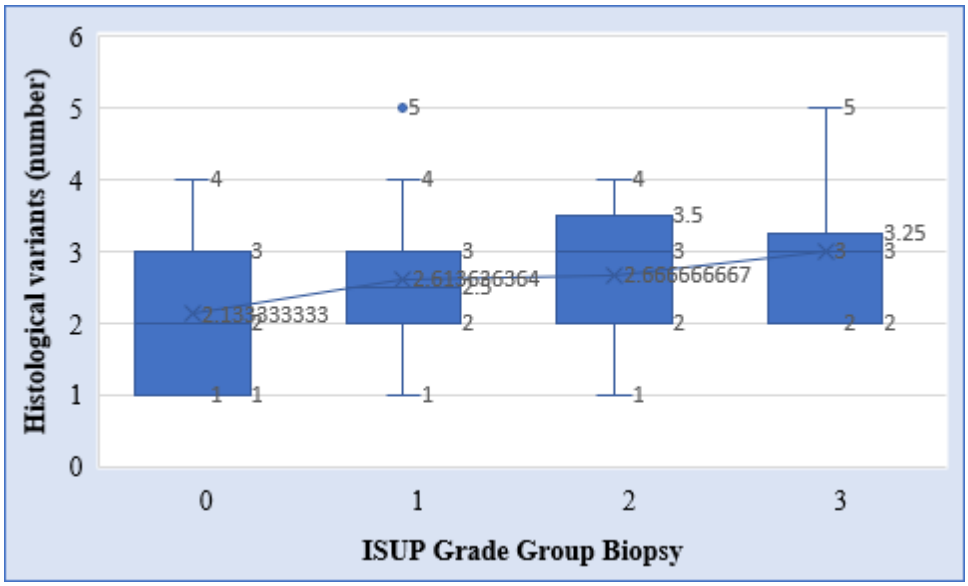


Figure 5. Comparative analysis of the number of histological variations according to the ISUP Grade groups of prostate biopsy results

An increase in the number of histological variations was found with increasing GG, without reaching statistical significance in sub-analysis by group (H=7.813, df=4 N=93, Sig.=0.099).

A comparative analysis of ISUP Grade group data from biopsy preparation and histological progression of the disease was performed. The results are presented in Table 9.

Table 9. Pathological. Progression * Grade Group Biopsy Crosstabulation

Pathol. Progression	Grade Group Biopsy					Total
	1	2	3	4	5	
No	4 (25,0%)	18 (56,3%)	17 (58,6%)	7 (63,6%)	4 (100,0%)	50 (54,3%)
Yes	12 (75,0%)	14 (43,8%)	12 (41,4%)	4 (36,4%)	0 (0,0%)	42 (45,7%)
Total	16 (100,0%)	32 (100,0%)	29 (100,0%)	11 (100,0%)	4 (100,0%)	92 (100,0%)

A statistically significant difference was found in the distribution of patients by Grade Group from biopsy and the establishment of histological progression ($\chi 2$=9.557, df=4, Sig.=0.049).

An analysis of the relationship between penetration of the prostatic capsule and the ISUP Grade Group result of the preoperative biopsy of the prostate gland followed - graph 1.

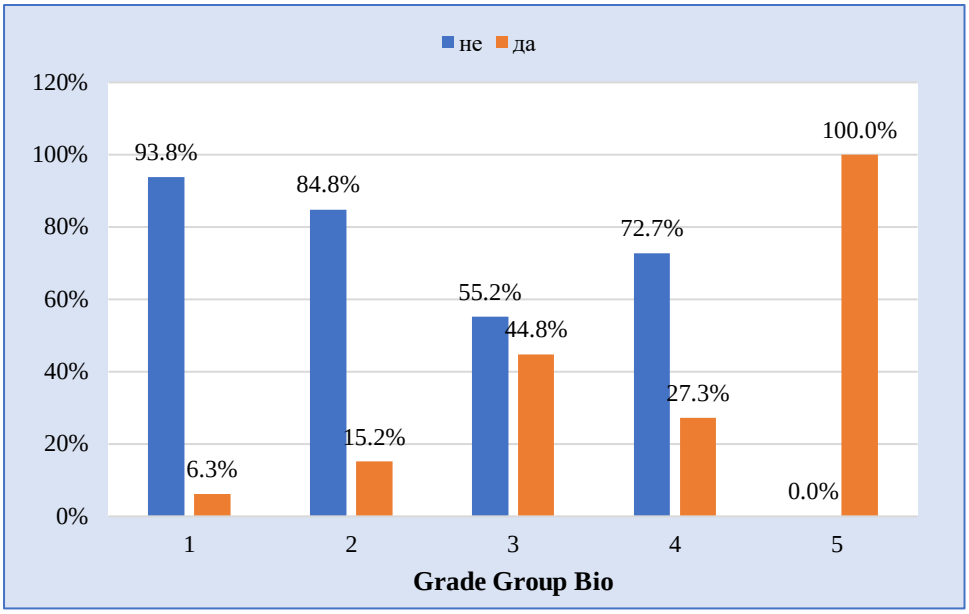


Figure 1. ISUP Grade Group biopsy and capsule penetration

A statistically significant difference was found in the distribution of patients according to ISUP Grade Group - Biopsy according to the frequency of penetration of the prostate capsule ($\chi 2$=20.838, df=4, Sig.=0.000).

The correlation index of the PIRADS MRI score against a number of other indicators is presented in Table 10 a-c. Detailed correlation analysis and data interpretation are presented with the rest of the intra- and postoperative data.

Table 10 - a

			MRI PIRADS	Grade Group Bio	TNM
Spearman's rho	ЯМР PIRADS	Correlation Coefficient	1,000	,262*	,213
		Sig. (2-tailed)	.	,027	,070
		N	73	71	73

Table 10 - b

		MRI PIRADS	Pathol. Progression	Margins (R+)	Capsule penetration	BCR	Local recurrence/ meta
MRI PIRADS	Biserial	1	-,025	,094	,147	,052	-,029
	Sig. (2-tailed)		,833	,429	,215	,671	,832
	N	73	72	73	73	68	55

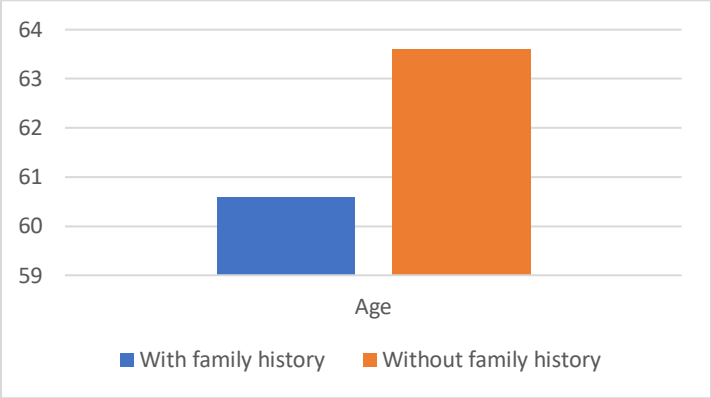
Table 10 - c

	MRI PIRADS	Histol. variants	Surgical time (min.)	Bloodloss (ml)

MRI PIRADS	Pearson Correlation	1	,020	-,180	,012
	Sig. (2-tailed)		,867	,128	,922
	N	73	73	73	73

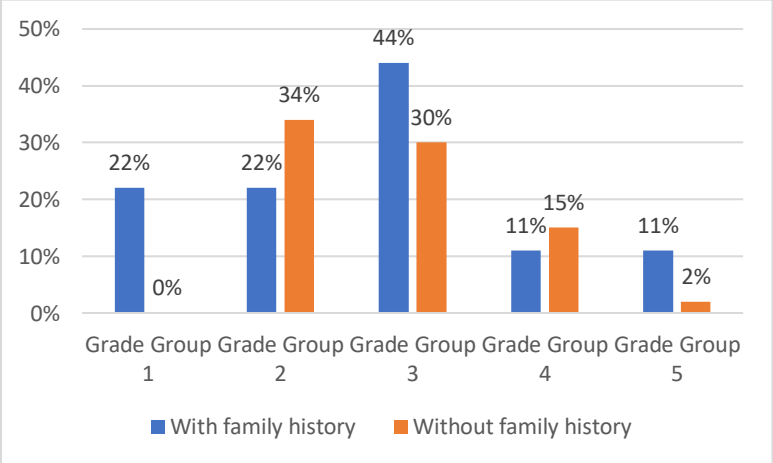
An analysis of the relationships between family history of PK and certain indicators followed.

Graph 2 presents a comparative analysis of the age of patients with and without a family history of PCa.



Graph 2. Comparative analysis between patient age with and without family history of PC.

Graphs 3 and 4 present the frequency distribution of patients by ISUP Grade groups of prostate gland biopsy material and permanent histology material according to the presence or absence of family history.



Graph 3. Frequency distribution of patients by ISUP Grade groups of prostate gland biopsy material according to the presence of family history.

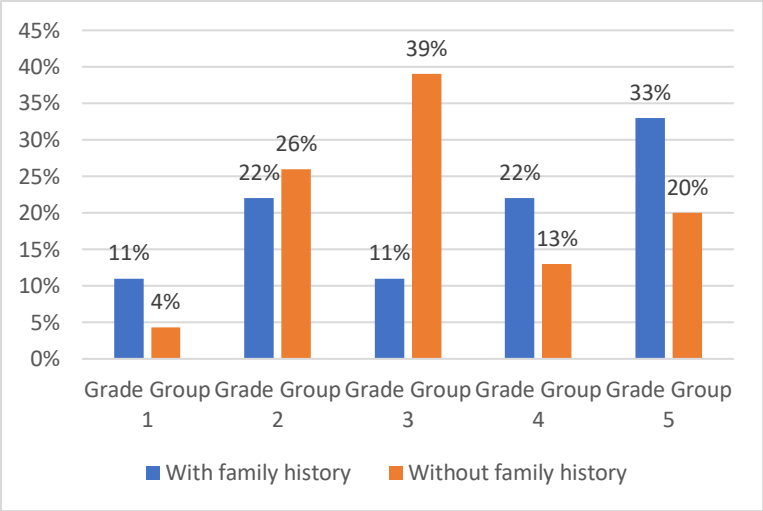
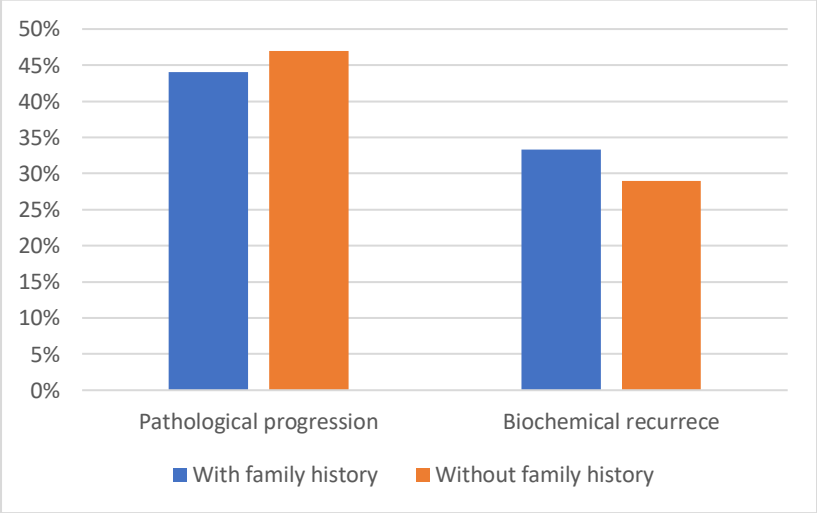


Figure 4. Frequency distribution of patients by ISUP Grade groups of material from a permanent histological preparation of the prostate gland according to the presence of family history.

This was followed by a comparative analysis of the incidence of histological disease progression and the incidence of biochemical relapse of patients according to the presence of a family history of PC. The results are presented in graph 5.



Graph 5. Comparative analysis of patients with and without family history in terms of occurrence of histological disease progression and frequency of biochemical recurrence.

5.3 Genetic markers

In the framework of a scientific project from the competition "Young researcher - 2019" of MU-Sofia AGREEMENT No. D - 141/23.04 2019, PROJECT int. No. 8246/20.11.2018, an analysis of the correlation between clinical and histo-pathological parameters, including polymorphisms in AR (CAG)n and VDR (AT)n genetic markers was performed in 10 patients from the studied sample - due to limited funding of the program.

The studied clinical contingent included 10 men with an average age of 62.9±6.24 years in the interval between 53 and 71. The frequency distribution by age had a normal character (p=0.527). The average value of PSA at the diagnosis of prostate cancer is 20±15.72 ng/ml - in the interval 6 - 62 ng/ml.

The Gleason score (GS) distribution of the preoperative biopsy was: GS 3+3 – 10%; GS 3+4 – 10%; GS 4+3 – 60%; GS 4+4 – 10%; N/a – 10%.

The distribution by GS of the permanent preparation is: GS 3+4 – 2%: GS 4+3 – 40%; GS 4+4 – 10%; GS 4+5 – 20%; GS 5+4 – 10%.

A detailed analysis of the histological features of the preparations after radical prostatectomy showed the presence of capsular invasion in 100% of cases and involvement of the seminal vesicle in 50% (n=5) of cases. Additional histological features of PC have been documented with the following frequency: perineural invasion – 80%; lymphovascular invasion – 30%; angioinvasion – 30%; light cell component – 10%; cribriform component – 20%; ductal component – 30%.

5.3.1. Molecular results in the patient sample

The molecular results regarding the length of the AR(CAG)n repeat are presented by the proven allelic frequencies in Table 10. It is highlighted that a risk allele of AR(CAG)n </= 22 is found in 3 patients (30%) – highlighted in red .

Table 11. Allelic frequencies of the AR(CAG)n repeat in the studied patients

AR (CAG)n=22	6/20	0.3 (30%)
AR (CAG)n=26	2/20	0.1 (10%)
AR (CAG)n=25	4/20	0.2 (20%)
AR (CAG)n=27	2/20	0.1 (10%)
AR (CAG)n=23	6/20	0.3 (30%)
Total sum of the frequencies of all alleles of the gene:		100%

According to literature data, the risk allele AR(CAG)n </= 22 is associated with early occurrence and aggressive course of prostate carcinoma.

The molecular results regarding the Poly A 3' UTR VDR microsatellite marker are presented by the proven allelic frequencies in Table 12 and the reported allelic combinations in Figure 6.

Table 12. Allelic frequencies of "short alleles" (14-17) and "long alleles" (18-24/25 with respect to Poly A 3' UTR VDR

VDR (AT)n =17	8/20	0,4
VDR (AT)n =23	2/20	0,1
VDR (AT)n =24	9/20	0,45
VDR (AT)n =25	1/20	0,05
Total sum of the frequencies of all alleles of the gene:		1

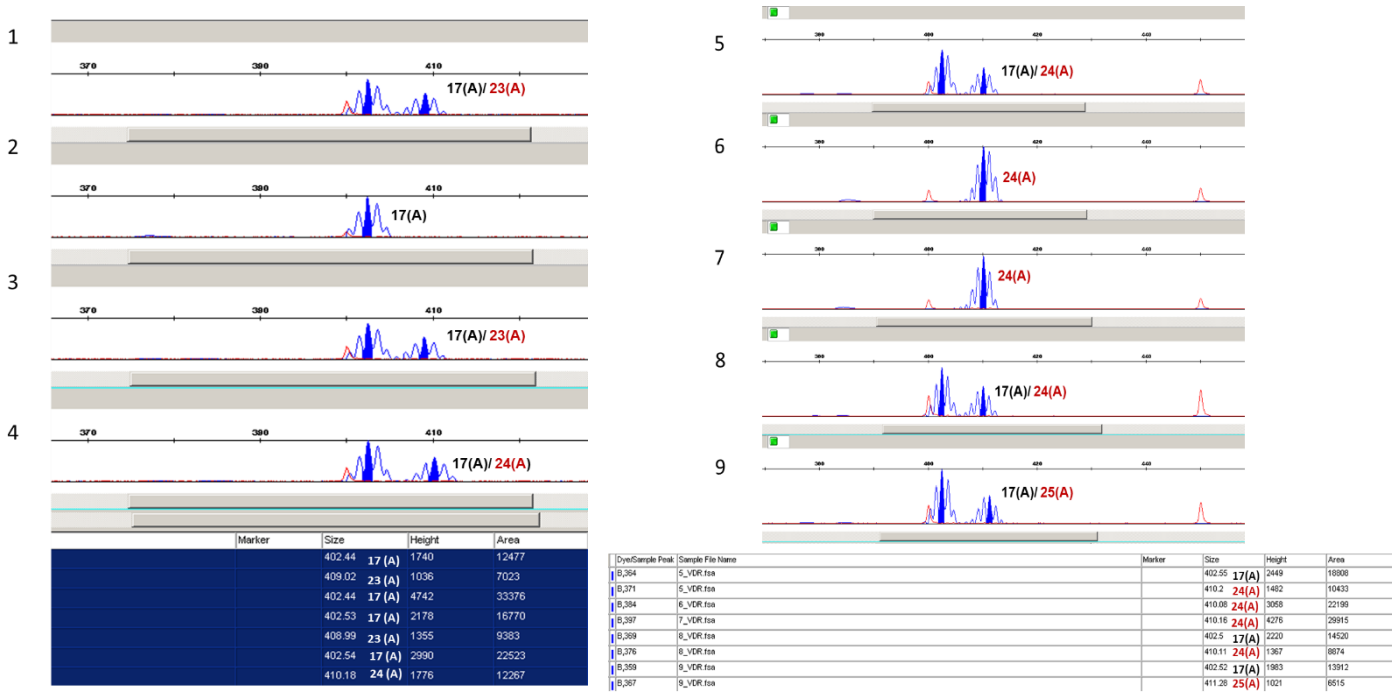


Figure 6. Allelic combinations regarding the Poly A 3'

Genotypic frequencies with respect to the Poly A 3' UTR VDR microsatellite marker are presented in Table 13. SL (60%) and LL (30%) are designated as risk genotypes due to the presence of risk "long alleles" of the Poly A 3' UTR VDR in the heterozygous or homozygous state.

Table 13. Distribution of "short" and "long" alleles in homozygous and heterozygous combination in the studied group of patients

Genotype	**Number of patients**
SS (17/17)	1 (10%)
SL (17/23, 17/24, 17/25)	6 (60%)
LL (23/23, 24/24)	3 (30%)

According to literature data, SL and LL genotypes of VDR(AT)n are associated with early onset and aggressive course of prostate carcinoma.

5.3.2 Correlation between the length of the AR(CAG)n repeat and certain PC characteristics in the studied sample of patients.

First, the relationship between the length of the AR(CAG)n repeat, age and PSA at PC diagnosis was investigated. The results presented in Table 14 show that at-risk patients (AR(CAG)n </=22) have a similar mean age and significantly higher PSA values than those with non-significant, low-risk alleles (AR(CAG)n >22).

Table 14: Comparative analysis of patients with high (AR(CAG)n </=22) and low risk AR(CAG)n >22) by age and PSA.

Variable	*AR*(CAG)n </=22			*AR*(CAG)n >22			P*
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
Age	3	64,33	8,33	7	62,29	5,82	-
PSA	3	35,00	25,24	7	13,57	6,27	-

* statistical significance cannot be calculated due to lack of statistical representativeness of the data /small sample due to limited funding of the project/

Correlation between the length of the AR(CAG)n repeat was performed against the Gleason score (GS) obtained from the preoperative transrectal biopsy of the prostate and the Gleason score (GS) from the histological preparation at the performed radical laparoscopic prostatectomy. The results are presented in Table 15.

Table 15: Comparative analysis of patients with high (AR(CAG)n </=22) and low risk AR(CAG)n >22) according to the indicators GS - biopsy and GS – surgery

Variable	*AR*(CAG)n </=22			*AR*(CAG)n >22			P*
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
GS – biopsy	3	7,33	0,46	6	6,83	0,91	-
GS – surgery	3	8	0,81	7	7,57	0,90	-

The relationship between the length of the AR(CAG)n repeat and the histological features from the final postoperative preparation determining the aggressive course of the disease (perineural invasion, lymphovascular invasion, angioinvasion, clear cell component, ductal component, cribriform component) was analyzed. The results are presented in Table 16.

Table 16: Frequency distribution of patients by AR(CAG)n and histological features

Histological variation	Frequency	*AR*(CAG)n	
		AR(CAG)n </=22	*AR*(CAG)n >22
Perineural invasion	Number	2	6
	%	66,7	85,7
Lymphovascular invasion	Number	1	2
	%	33,3	28,6
Angioinvasion	Number	1	2
	%	33,3	28,6
Ductal component	Number	1	2

	%	33,3	28,6
Cribriform component	Number	0	2
	%	0	28,6
Clearcell component	Number	1	0
	%	33,3	0

From table 16 it is clear that high-risk patients (AR(CAG)n </=22) exceed low-risk patients (AR(CAG)n >22) in terms of their relative proportions to histological features with poor prognosis: Lymphovascular invasion, Angioinvasion, Ductal component and Light cell component, while carriers of low-risk AR(CAG)n alleles have a higher rate of Perineural invasion and Cribriform component. Unfortunately, the small sample size does not allow us to judge whether the conclusions are statistically reliable.

A correlation between AR(CAG)n repeat length and local disease status followed. Invasion of the tumor in the prostate capsule was found in 100% of patients, regardless of the risk according to this indicator. Regarding seminal vesicle involvement, at-risk patients (AR(CAG)n </=22) were found to have a higher incidence of seminal vesicle involvement: 66%, n=2; compared to low-risk patients (AR(CAG)n >22): 42%, n=3. The results are presented in Table 17.

Table 17. Frequency distribution of patients by AR(CAG)n and seminal vesicle invasion (p=1.000)

AR(CAG)n	**Frequency**	**Seminal vesicle invasion**	
		No	**Yes**
***AR*(CAG)n </=22**	Number	1	2
	%	20,0/ 33% от група	40,0/ 66% from group)
***AR*(CAG)n >22**	Number	4	3
	%	80,0/ 58% от група	60,0/ (42%from group)

5.2.3 Analysis of the relationship between the length of the Poly-A 3' UTR VDR and certain PC characteristics in the studied sample.
Patients were divided into three risk groups according to their Poly-A 3' UTR VDR genotype: SS (homozygous combination of "short" alleles [17 repeats]) - low risk; SL (heterozygous combination of "short" and "long" allele) - moderate risk; LL (homozygous combination of "long" alleles [18-24 repeats]) - high risk.

A correlation was made between the molecular profile of the Poly-A 3' UTR VDR marker and age, including PSA value at diagnosis. The results are presented in Table 18.

Table 18. Comparative analysis of patients at low (SS), moderate (SL) and high (LL) risk according to Poly-A 3' UTR VDR genotype by age and PSA

Variable	**SS**	**SL**	**LL**

	n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
Age (years)	1	70,00	0,00	6	61,17	5,38	3	64,00	8,19
PSA	1	6,00	0,00	6	21,50	20,37	3	21,67	9,50

An analysis of the relationship between the Poly-A 3' UTR VDR genotype and the Gleason score (GS) obtained from the preoperative transrectal biopsy of the prostate and the Gleason score (GS) from the histological preparation during the performed radical laparoscopic prostatectomy followed. The results are presented in Table 19.

Table 19. Comparative analysis of patients with low (SS), moderate (SL) and high (LL) risk according to Poly-A 3' UTR VDR by GS - biopsy and GS - surgery indicators

Variable	**Low risk (SS)**			**Intermediate risk (SL)**			**High risk (LL)**		
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
GS – biopsy	1	7,00	0,00	5	7	0,63	3	7,00	0,00
GS – surgery	1	7,00	0,00	6	7,66	0,94	3	8,00	0,81

In the variant of correlation with GS from the final histological preparation after radical prostatectomy, the lowest value was found in the low-risk group (GS=7), a higher average value in the moderate-risk group (GS=7, 66); highest mean in the high-risk group (GS=8). It is important to emphasize that in the high-risk group, the most significant dependence for pathological progression of the disease was also demonstrated - an increase in the average values of GS from 7 to 8.

An analysis of the relationship between the Poly-A 3' UTR VDR profile and the presence of histological features from the final postoperative preparation determining an aggressive course of the disease (perineural invasion, lymphovascular invasion, angioinvasion, clear cell component, ductal component, cribriform component) was performed. The results are presented in Table 20.

Table 20. Frequency distribution of patients according to VDR (AT)n and histological features

Histological variation	**Frequency**	***VDR* (AT)n Genotype**		
		Low risk (SS)	**Intermediate risk (SL)**	**High risk (LL)**
Perineural invasion	Number	1	5	2
	%	100,0	83,3	66,7
Lymphovascular invasion	Number	0	2	1
	%	0	33,3	33,3
Angioinvasion	Number	0	3	0
	%	0	50,0	0
Ductal component	Number	0	2	1

	%	0	33,3	33,3
Cribriform component	Number	0	2	0
	%	0	33,3	0
Clearcell component	Number	0	1	0
	%	0	16,7	0

It can be seen that the most histological features associated with an aggressive course of the disease are observed in patients with the SL genotype according to VDR (AT)n in the moderate risk group. We recorded a single case of perineural invasion among the low-risk patients (genotype SS).

A correlation was made between a molecular profile of Poly-A 3' UTR VDR and local disease status. Invasion of the tumor in the prostate capsule was found in 100% of patients, regardless of the risk according to this indicator. Results regarding seminal vesicle engagement are presented in Table 21.

Table 21. Frequency distribution of VDR (AT)n patients and seminal vesicle invasion

***VDR* (AT)n Genotype**	**Frequency**	**Seminal vesicle invasion**	
		No	**Yes**
Low risk (SS)	Брой	0	1
	%	0,0/ 0%	20,0/ 100% of subgroup
Intermediate risk (SL)	Брой	4	2
	%	80,0/ 66%	40,0/ 33% of subgroup
High risk (LL)	Брой	1	2
	%	20,0/ 33%	40,0/ 66% of subgroup

5.4 Intraoperative indicators

The mean operative time for the patients was 183.2 ± 41 minutes. Preservation of vascular-nerve bundles was performed in 49% of cases. The average blood loss during LRP was 174 ml (50 - 550 ml). Blood loss is graphically expressed in Figure 14. Intraoperative hemotransfusion of 1 bag of Er-mass was performed in 11% of patients (Figure 15.). In the remaining 89% of patients, hemotransfusion was not performed. Intraoperative complications were reported in 6% of patients. Their type and fair distribution are as follows: peritoneum lesion - 2%; need for extended plasty of the cystic cervix – 1%; conversion – 1%; difficult course of the operation due to a pronounced middle part - 1%; overcoming adhesions to the hernioplasty cloth - 1%.

An analysis of the relationship of intraoperative blood loss with a number of other indicators was performed. The summarized data are shown in Table 22. The table is followed by a detailed analysis and interpretation of the data.

Table 22. Correlation dependence of intraoperative blood loss.

Variable		Bloodloss (ml)	Age	Accompanying diseases	BMI	(PSA) ng/ml
Bloodloss (ml)	Pearson Correlation	1	-,102	-,113	-,087	-,060
	Sig. (2-tailed)		,313	,261	,389	,552
	N	100	100	100	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Table 23. – Comparative analysis of patients according to intraoperative blood loss and BMI.

Variable		n	Bloodloss	
			Mean ± SD	Me (Min, Max)
BMI		**100**	**174,800 ± 94,114**	**150 (50, 550)**
	Normal weight	20	182,500 ± 87,772	150 (50, 400)
	Preobesity	51	171,569 ± 99,627	150 (50, 550)
	Obesity I gr	22	177,273 ± 98,473	150 (50, 350)
	Obesity II gr	5	186,000 ± 54,589	150 (100, 250)
	Obesity III gr	2	125,000 ± 106,066	125 (50, 200)

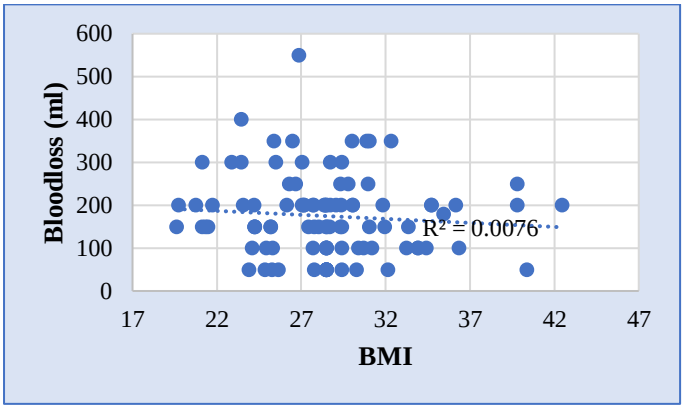


Figure 7. Distribution of patients according to intraoperative blood loss and BMI.

Table 24 presents a comparative analysis of intraoperative blood loss according to the presence or absence of at least one previous operative disease in the patients.

Table 24

Variable	n	Bloodloss	
		Mean ± SD	Me (Min, Max)
Prior surgery	**100**	**174,800 ± 94,114**	**150 (50, 550)**
yes	48	184,375 ± 99,01	150 (50, 550)
no	52	165,965 ± 89,40	150 (50, 400)

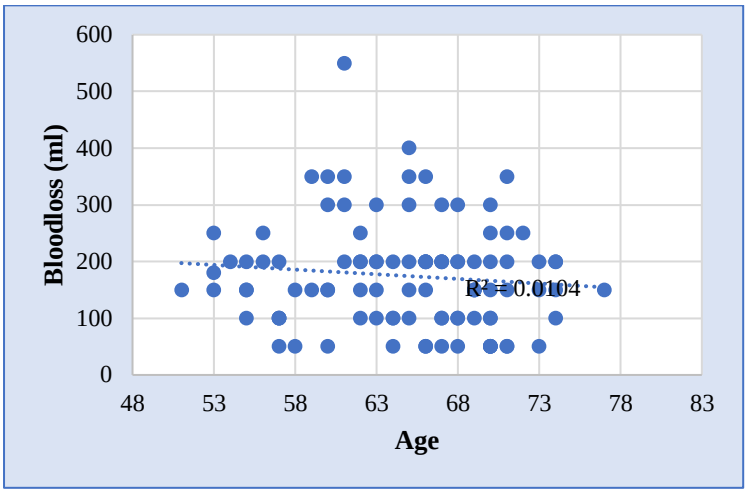


Figure 8. Distribution of patients according to intraoperative blood loss and age.

A comparative analysis of the patients' blood loss according to the value of the preoperative PSA (below and above 10 ng/ml) was performed - table 25. The results indicate higher values of blood loss in the patients with a PSA below 10 ng/ml - 187.6 ml against 162 ml.

Table 25

Variable	n	Bloodloss	
		Mean ± SD	Me (Min, Max)
PSA групи	**100**	**174,800 ± 94,114**	**150 (50, 550)**
< 10 ng/ml	50	187,600 ± 114,972	190 (50, 550)
> 10 ng/ml	50	162,000 ± 65,900	150 (50, 350)

A statistically significant correlation was found between blood loss (ml) and TNM (r=0.228, N=100, p=0.017). The results of the analysis showed that high blood loss was observed with increased values of Grade Group - biopsy, Grade Group - surgery, TNM, MRI and Nerve sparing. A detailed look at the data and dependencies follows.

In a comparative analysis of the data of intraoperative blood loss and the preoperative histological result of the patients according to ISUP Grade groups (table 26), it was found that

the greatest blood loss was in the patients with Grade group 4 - 227,273 ± 84,746 ml. Second, in patients with Grade group 5, a blood loss of 187,500 ± 25,000 ml was documented.

Table 26

Variable	n	Bloodloss	
		Mean ± SD	Me (Min, Max)
ISUP Grade Group - biopsy	**93**	**172,903 ± 93,954**	**150 (50, 550)**
1	16	151,875 ± 84,001	150 (50, 350)
2	33	180,303 ± 116,552	150 (50, 550)
3	29	153,448 ± 71,877	150 (50, 300)
4	11	227,273 ± 84,746	200 (100, 400)
5	4	187,500 ± 25,000	200 (150, 200)

In a comparative analysis of the patients' intraoperative blood loss and according to the result of the permanent histological preparation according to ISUP Grade groups (table 27). the greatest blood loss is reported in patients with Grade group 4 - 200,000 ± 95,743 ml. Patients with Grade Group 2 from the permanent histological preparation had the second largest average blood loss – 196,129 ± 124,490 ml.

Table 27

Variable	n	Bloodloss	
		Mean ± SD	Me (Min, Max)
ISUP Grade Group - surgery	**100**	**174,800 ± 94,114**	**150 (50, 550)**
1	4	100,000 ± 70,711	75 (50, 200)
2	31	196,129 ± 124,490	180 (50, 550)
3	30	153,333 ± 71,840	150 (50, 350)
4	13	200,000 ± 95,743	200 (50, 400)
5	22	172,727 ± 61,193	200 (50, 300)

Table 28 shows a comparative analysis of blood loss in patients after LRP according to pT stage of the disease from the permanent histological preparation. A statistically significant correlation was demonstrated between increasing T-stage and increasing intraoperative bleeding: Mean blood loss pT2 vs pT3 vs pT4 - 154,510 ± 108,154 vs 194,792 ± 72,376 vs 250,000 ml.

Table 28

Variable		n	Bloodloss	
			Mean ± SD	Me (Min, Max)
TNM		**100**	**174,800 ± 94,114**	**150 (50, 550)**
	pT2	51	154,510 ± 108,154	150 (50, 550)
	pT3	48	194,792 ± 72,376	200 (50, 400)
	pT4	1	250,000 ± NA	250 (250, 250)

No statistically significant correlation was found between PIRADS MRI findings and the amount of intraoperative blood loss in LRP - table 29.

Table 29.

Variable		n	Bloodloss	
			Mean ± SD	Me (Min, Max)
ЯМР PIRADS		**73**	**170,274 ± 93,422**	**150 (50, 550)**
	2	2	300,000 ± NA	300 (300, 300)
	3	10	108,000 ± 58,462	100 (50, 200)
	4	39	180,769 ± 103,629	150 (50, 550)
	5	22	168,182 ± 73,266	200 (50, 300)

Table 30 depicts an analysis of the relationship between prostate gland volume and mean intraoperative blood loss.

Table 30.

Variable		n	Bloodloss	
			Mean ± SD	Me (Min, Max)
Prostate volume		**91**	**170,274 ± 93,422**	**150 (50, 550)**
	Under 49 cc	54	182,286 ± 97,626	200 (50, 550)
	50 – 99 cc.	33	177,272 ± 94,448	180 (50, 350)
	Over 100 cc	4	137,500 ± 47,871	125 (100, 200)

Table 31 presents a comparative analysis of patients according to the preservation of vascular-nerve bundles and their intraoperative blood loss.

Table 31.

Variable	n	Bloodloss	
		Mean ± SD	Me (Min, Max)
Nerve sparing	**100**	**170,274 ± 93,422**	**150 (50, 550)**
yes	49	178,571 ± 110,867	150 (50, 550)
no	51	171,176 ± 75,568	180 (50, 400)

Table 32 presents the statistical relationship between the need for intraoperative hemotransfusion and a number of indicators. A detailed analysis and interpretation of the data was performed after tabulation.

Table 32.

		Intraoperative hemotransfusion	BMI	Accompanying diseases	Age	(PSA) ng/ml
Intraoperative hemotransfusion	Point-biserial	1	-,104	,123	,067	-,146
	Sig. (2-tailed)		,302	,223	,505	,147
	N	100	100	100	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Tables 33, 34 and 35 present the data regarding the need for intraoperative hemotransfusion and their correlation with the patients' body mass index, presence of prior surgery and accompanying diseases.

Table 33.

Variable		Intraoperative hemotransfusion		
		yes	no	Total
BMI		**11 (100,0%) / (% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
	Normal weight	3 (27,3%); (15%)	17 (19,1%)	20 (20,0%)
	Preobesity	5 (45,5%); (9,8%)	46 (51,7%)	51 (51,0%)
	Obesity I gr	3 (27,3%); (13,6%)	19 (21,3%)	22 (22,0%)
	Obesity II gr	0 (0,0%); (0%)	5 (5,6%)	5 (5,0%)
	Obesity III gr	0 (0,0%); (0%)	2 (2,2%)	2 (2,0%)

Table 34.

Variable	Intraoperative hemotransfusion		
	yes	**no**	**Total**
Accompanying diseases	**11 (100,0%)/(% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
yes	9 (81,8%); (12%)	66 (74,2%)	75 (75,0%)
no	2 (18,2%); (8%)	23 (25,8%)	25 (25,0%)

Table 35. (брой, %)

Variable	Intraoperative hemotransfusion		
	yes	**no**	**Total**
Prior surgery	**11 (100,0%)/(% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
yes	7 (63,6%); (14,5%)	41 (40,4%)	48 (48,0%)
no	5 (36,3%); (9,62%)	47 (46,7%)	52 (52,0%)

Table 36 provides a comparative analysis of patient data according to the need for intraoperative transfusion and their distribution by age group.

Table 36

Variable	Intraoperative hemotransfusion		
	да	**не**	**Total**
Age	**11 (100,0%)/ (% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
50 - 60 y.o.	3 (27,3%); (12%)	22 (24,7%)	25 (25,0%)
60 - 70 y.o	4 (36,4%); (6,67%)	56 (62,9%)	60 (60,0%)
70 - 80 y.o	4 (36,4%); (26,6%)	11 (12,4%)	15 (15,0%)

Table 37 reflects the statistical correlation between the need for intraoperative hemotransfusion and the MRI finding, as well as a number of histological parameters. This is followed by a detailed frequency distribution of the determined indicators and a detailed analysis and interpretation of the data.

Table 37

		Intraoperative hemotransfusion	Grade Group Biopsy	Grade Group Surgery	TNM	MRI PIRADS
Intraoperative hemotransfusion	Rank-biserial	1	-,019	-,106	-,092	,182
	Sig. (2-tailed)		,856	,295	,361	,124
	N	100	93	100	100	73

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 38 presents the frequency distribution of patients according to PSA and ISUP Grade groups from the preoperative biopsy and permanent histological preparation after LRP according to the need for intraoperative hemotransfusion.

Table 38

Variable	Intraoperative hemotransfusion		
	yes	**no**	**Total**
PSA group	**11 (100,0%)/ (% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
< 10 ng/ml	7 (63,6%); (14%)	43 (48,3%)	50 (50,0%)
> 10 ng/ml	4 (36,4%); (8%)	46 (51,7%)	50 (50,0%)
ISUP Grade Group biopsy	**9 (100,0%)**	**84 (100,0%)**	**93 (100,0%)**
1	1 (11,1%); (6,2%)	15 (17,9%)	16 (17,2%)
2	5 (55,6%); (15,5%)	28 (33,3%)	33 (35,5%)
3	2 (22,2%); (6,9%)	27 (32,1%)	29 (31,2%)
4	0 (0,0%) (0%)	11 (13,1%)	11 (11,8%)
5	1 (11,1%) (25%)	3 (3,6%)	4 (4,3%)
ISUP Grade Group surgery	**11 (100,0%)**	**89 (100,0%)**	**100 (100,0%)**
1	1 (9,1%); (25%)	3 (3,4%)	4 (4,0%)
2	5 (45,5%); (16,1%)	26 (29,2%)	31 (31,0%)
3	2 (18,2%); (6,67%)	28 (31,5%)	30 (30,0%)
4	1 (9,1%); (7,69%)	12 (13,5%)	13 (13,0%)
5	2 (18,2%); (9,09%)	20 (22,5%)	22 (22,0%)

Table 39 provides a comparative analysis of patient data according to intraoperative blood transfusion and pT stage of the disease from the permanent histological preparation.

Table 39

Variable	Intraoperative hemotransfusion		
	да	не	Total
TNM	**11 (100,0%)/ (% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
pT2	7 (63,6%); (13,7%)	44 (49,4%)	51 (51,0%)
pT3	4 (36,4%); (8,3%)	44 (49,4%)	48 (48,0%)
pT4	0 (0,0%); (0%)	1 (1,1%)	1 (1,0%)

Table 40 shows the frequency distribution of patients according to the need for intraoperative blood transfusion and PIRADS MRI lesion type.

Table 40

Variable	Intraoperative hemotransfusion		
	Yes	No	Total
MRI PIRADS	**5 (100,0%)/ (% of subgroup)**	**68 (100,0%)**	**73 (100,0%)**
2	0 (0,0%); (0%)	2 (2,9%)	2 (2,7%)
3	0 (0,0%); (0%)	10 (14,7%)	10 (13,7%)
4	2 (40,0%); (5,1%)	37 (54,4%)	39 (53,4%)
5	3 (60,0%); (13,6%)	19 (27,9%)	22 (30,1%)

A comparative and correlational analysis of the patients was carried out according to the same indicator and the preservation of the vascular-nerve bundles - table 41 a-b. The frequency of intraoperative hemotransfusion was 16.3% in patients with Nerve sparing and 5.8% in patients without SNS preservation. However, the dependence did not reach statistical significance.

Table 41 – a

Variable	Intraoperative hemotransfusion		
	да	не	Total
Nerve sparing	**11 (100,0%)/ (% of subgroup)**	**89 (100,0%)**	**100 (100,0%)**
yes	8 (72,7%); (16,3%)	41 (46,1%)	49 (49,0%)

Variable	Intraoperative hemotransfusion		
	да	не	Total
no	3 (27,3%); (5,8%)	48 (53,9%)	51 (51,0%)

Table 41 - b Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2,784[a]	1	,095	,118	,088	
Continuity Correction[b]	1,820	1	,177			
Likelihood Ratio	2,869	1	,090	,118	,088	
Fisher's Exact Test				,118	,088	
Linear-by-Linear Association	2,757[c]	1	,097	,118	,088	,066
N of Valid Cases	100					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 5,39.

b. Computed only for a 2x2 table

c. The standardized statistic is 1,660.

Table 42 presents a comparative analysis of patients according to the volume of the prostate gland and the need for intraoperative transfusion.

Table 42. (брой, %)

Variable	Intraoperative hemotransfusion		
	Yes	**No**	**Total**
Prostate volume	**11 (100,0%)/ (% of subgroup)**	**80 (100,0%)**	**91 (100,0%)**
Under 49 cc	5 (45,5%); (9.2%)	49 (61,3%)	54 (59,3%)
50 – 99 cc	6 (55,5%); (18,1%)	27 (33,7%)	33 (36,2%)
Over 100 cc	0 (0,0%); (0%)	4 (5%)	4 (4,4%)

Table 43 and Table 44 reflect the correlation between the incidence of intraoperative complications and a number of other indicators. The frequency distribution and interpretation of the data is presented in the subsequent tables and text.

Table 43

		Intraoperative complications	BMI	ASA	Accompanying diseases	Age	(PSA) ng/ml
Intraoperative complications	Point-biserial	1	-,079	,182	-,102	-,034	,009
	Sig. (2-tailed)		,432	,090	,311	,740	,928
	N	100	100	88	100	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Table 44

		Intraoperative complications	Grade Group Biopsy	Grade Group Surgery	TNM	MRI PIRADS
Intraoperative complications	Rank-biserial	1	-,146	,011	-,055	-,115
	Sig. (2-tailed)		,162	,910	,584	,331
	N	100	93	100	100	73

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

In Table 45, a comparative analysis of patient data, the presence or absence of accompanying and past diseases and the occurrence of intraoperative complications, was performed.

Table 45. (брой, %)

Variable	**Intraoperative complications**		
	no	**yes**	**Total**
Accompanying diseases	**94 (100,0%)**	**6 (100,0%)/ (% of subgroup)**	**100 (100,0%)**
yes	69 (73,4%)	6 (100%); (8%)	75 (75,0%)
no	25 (26,6%)	0 (0%); (0%)	25 (25,0%)
Prior surgery	**94 (100,0%)**	**6 (100,0%)**	**100 (100,0%)**
yes	45 (47,8%)	3 (50%); (6.2%)	48 (48,0%)
no	49 (52,2%)	3 (50%); (5,7%)	52 (52,0%)

An analysis of the data regarding the age distribution of patients and the frequency of intraoperative complications is presented in Table 46.

Table 46.

Variable		Intraoperative complications		
		no	yes	Total
Age groups		**94 (100,0%)**	**6 (100,0%)/ (% of subgroup)**	**100 (100,0%)**
	50 - 60 y.o	24 (25,5%)	1 (16,6%) / (4%)	25 (25,0%)
	60 - 70 y.o	55 (58,5%)	5 (83,4%) / (8,3%)	60 (60,0%)
	70 - 80 y.o	15 (16%)	0 (0%) / (0%)	15 (15,0%)

In Table 47, a comparative analysis of the data according to the occurrence of an intraoperative complication and the preoperative PSA value, as well as the MRI finding according to PIRADS, was performed.

Table 47. (брой, %)

Variable		Intraoperative complications		
		No	Yes	Total
PSA group		**94 (100,0%)**	**6 (100,0%)/ (% of subgroup)**	**100 (100,0%)**
	< 10 ng/ml	48 (51%)	2 (33,3%) / (4%)	50 (50,0%)
	> 10 ng/ml	46 (49%)	4 (66,7%) / (8%)	50 (50,0%)
MRI PIRADS		**67 (100,0%)**	**6 (100,0%)**	**73 (100,0%)**
	2	2 (2,9%)	0 (0,0%) / (0%)	2 (2,7%)
	3	10 (14,9%)	0 (0%) / (0%)	10 (13,7%)
	4	35 (52,2%)	4 (66,7%) / (10,2%)	39 (53,4%)
	5	21 (31,3%)	2 (33,3%) / (9%)	22 (30,1%)

Data analysis according to the histological result of the preoperative biopsy and permanent histological preparation by ISUP Grade groups and the frequency of intraoperative complications is presented in Table 48.

Table 48. (брой, %)

Variable	Intraoperative complications		
	No	Yes	Total
ISUP Grade Group biopsy	**87 (100,0%)**	**6 (100,0%)/ (% of subgroup)**	**93 (100,0%)**
1	14 (16%)	2 (33,3%) / (12,5%)	16 (17,2%)
2	31 (35,6%)	2 (33,3%) (6%)	33 (35,5%)
3	28 (32,1%)	1 (16,6%) / (3,45%)	29 (31,2%)
4	10 (11,4%)	1 (16,6%) / (9%)	11 (11,8%)
5	4 (4,6%)	0 (0,0%) / (0%)	4 (4,3%)
ISUP Grade Group surgery	**94 (100,0%)**	**6 (100,0%)**	**100 (100,0%)**
1	4 (4,2%)	0 (0%) / (0%)	4 (4,0%)
2	30 (31,9%)	1 (16,6%) / (3,23%)	31 (31,0%)
3	26 (27,6%)	4(66,67%)/ (13,3%)	30 (30,0%)
4	12 (12,7%)	1 (16,6%) / (7,6%)	13 (13,0%)
5	22 (23,4%)	0 (0%) / (0%)	22 (22,0%)

Table 49 reflects the frequency distribution of patients according to the incidence of intraoperative complication and the pT stage of the disease from the permanent histological preparation.

Table 49. (брой, %)

Variable	Intraoperative complications		
	No	Yes %/ (% of subgroup)	Total
TNM	**94 (100,0%)**	**6 (100,0%)**	**100 (100,0%)**
pT2	49 (52,13%)	2 (33,33%) / (3,9%)	51 (51,0%)
pT3	44 (46,8%)	4 (66,67%) / (8,3%)	48 (48,0%)
pT4	1 (1,2%)	0 (0,0%) / (0%)	1 (1,0%)

Table 50 a-b depicts the frequency distribution of patients according to the occurrence of an intraoperative complication and the performance of preservation of vascular-nerve bundles.

Table 50 - a. (брой, %)

Variable	Intraoperative complications		
	No	**Yes %/ (% of subgroup)**	**Total**
Nerve sparing	**94 (100,0%)**	**6 (100,0%)**	**100 (100,0%)**
yes	46 (49%)	3 (50%) / (6,1%)	49 (49,0%)
no	48 (51%)	3 (50%) / (5,8%)	51 (51,0%)

Table 50 – b. Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1,150[a]	1	,284	,390	,217	
Continuity Correction[b]	,615	1	,433			
Likelihood Ratio	1,165	1	,280	,390	,217	
Fisher's Exact Test				,390	,217	
Linear-by-Linear Association	1,138[c]	1	,286	,390	,217	,131
N of Valid Cases	100					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 6,86.

b. Computed only for a 2x2 table

c. The standardized statistic is -1,067.

Table 51 presents a comparative analysis of patients according to the history of previous operative interventions and their age relative to the average operative time

Table 51

Variable	Surgery duration		
	n	**Mean ± SD**	**Me (Min, Max)**
Prior surgery	**100**	**183,250 ± 41,914**	**180 (120, 360)**
yes	48	183,125 ± 41,458	180 (120, 270)
no	52	183,365 ± 42,734	180 (120, 360)
Age groups	**100**	**183,250 ± 41,914**	**180 (120, 360)**
50 - 60 y.o.	25	178,200 ± 35,175	180 (120, 270)

Variable		Surgery duration		
		n	Mean ± SD	Me (Min, Max)
	60 - 70 y.o.	60	186,750 ± 44,805	180 (120, 360)
	70 - 80 y.o	15	177,667 ± 41,355	180 (120, 270)

Table 52 presents an analysis of the relationship between patients' body mass index and operative time.

Table 52

Variable		Surgery duration (min)		
		n	Mean ± SD	Me (Min, Max)
BMI		**100**	**183,25 ± 41,914**	**180 (120, 360)**
	Normal weight	20	176,25 ± 27,042	173 (140, 240)
	Preobesity	51	180,78 ± 42,289	170 (120, 270)
	Obesity Gr I	22	187,955 ± 52,160	180 (120, 360)
	Obesity Gr II	5	197,000 ± 28,196	210 (165, 230)
	Obesity Gr III	2	230,000 ± 56,569	230 (190, 270)

Table 53 shows a comparative analysis of the groups of patients with a preoperative PSA value below or above 10 ng/ml against the mean operative time.

Table 53

Variable		Surgery duration (min)		
		n	Mean ± SD	Me (Min, Max)
PSA groups		**100**	**183,250 ± 41,914**	**180 (120, 360)**
	< 10 ng/ml	50	180,600 ± 40,891	170 (120, 270)
	> 10 ng/ml	50	185,900 ± 43,162	180 (120, 360)

Table 54 reflects the frequency distribution of patients according to their ISUP Grade histological result of the preoperative biopsy and persistent histology patient versus mean operative time.

Table 54

Variable	Surgery duration (min)		
	n	Mean ± SD	Me (Min, Max)
ISUP Grade Group biopsy	**93**	**182,957 ± 42,741**	**180 (120, 360)**
1	16	191,563 ± 43,921	178 (140, 270)
2	33	175,455 ± 36,622	180 (120, 270)
3	29	180,862 ± 39,485	170 (120, 240)
4	11	204,091 ± 65,796	190 (120, 360)
5	4	167,500 ± 8,660	165 (160, 180)
ISUP Grade Group surgery	**100**	**183,250 ± 41,914**	**180 (120, 360)**
1	4	200,00 ± 54,773	195 (140, 270)
2	31	177,419 ± 30,683	180 (120, 240)
3	30	188,000 ± 43,184	180 (120, 270)
4	13	188,462 ± 67,342	180 (120, 360)
5	22	178,864 ± 34,189	168 (130, 255)

Analysis of the relationship between pT-stage of PK and operative time and presented in Table 55.

Table 55

Variable		Surgery duration (min)		
		n	Mean ± SD	Me (Min, Max)
TNM		**100**	**183,250 ± 41,914**	**180 (120, 360)**
	pT2	51	188,235 ± 46,774	180 (120, 360)
	pT3	48	178,646 ± 36,066	180 (120, 270)
	pT4	1	150 ± NA	150 (150, 150)

The correlation between the volume of the prostate gland and the average operative time is presented in Table 56.

Table 56

Variable	Surgery duration (min)		
	n	Mean ± SD	Me (Min, Max)
Prostate volume	**91**	**184,315 ± 42,909**	**180 (120, 360)**
Under 49 cc	54	173,97 ± 45,21	180 (120, 250)
50-99 cc	33	192,58 ± 50,20	180 (150, 360)
Over 100 cc.	4	197,14 ± 34,53	195 (175, 250)

5.5 Postoperative indicators

The distribution of patients according to the histological result by ISUP Grade groups is presented in figure 9. It is noteworthy that 31% of the patients fall into Grade group 2 (GS 3+4=7 from the permanent histological preparation) - 31%, and the second more frequent are the patients who fall into Grade group 3 (GS 4+3=7) – 30%.

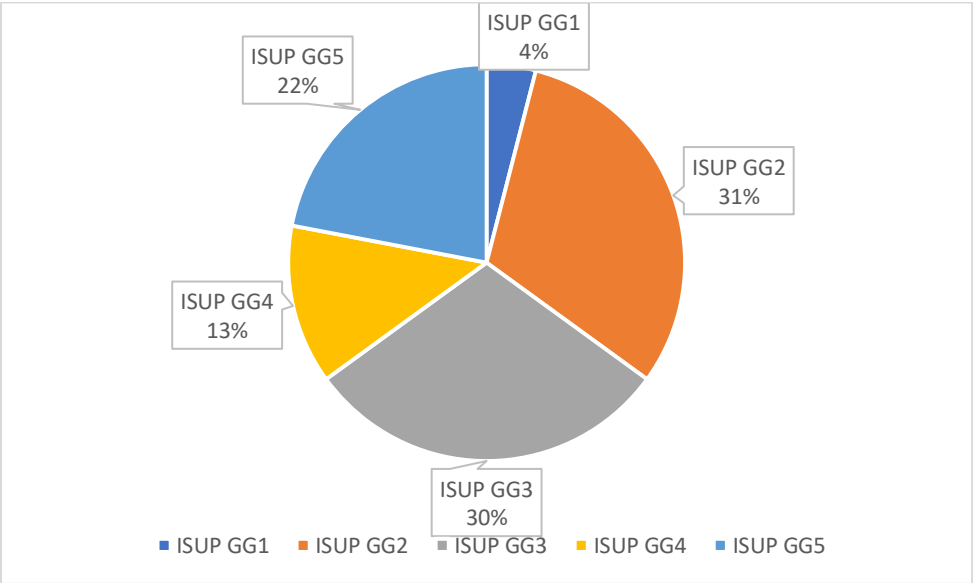


Fig. 9.

Histological progression of the disease - an increase in the histological stage according to the ISUP Grade group from the permanent histological preparation compared to the baseline value from the preoperative biopsy was reported in 47% of the patients.

The distribution of patients according to the pT stage of the disease is presented in Figure 10. 38% of the patients demonstrated pT2c stage disease on the permanent histological preparation. In second and third place in terms of frequency are patients with disease stage pT3b and pT3a, respectively - 23% and 19%.

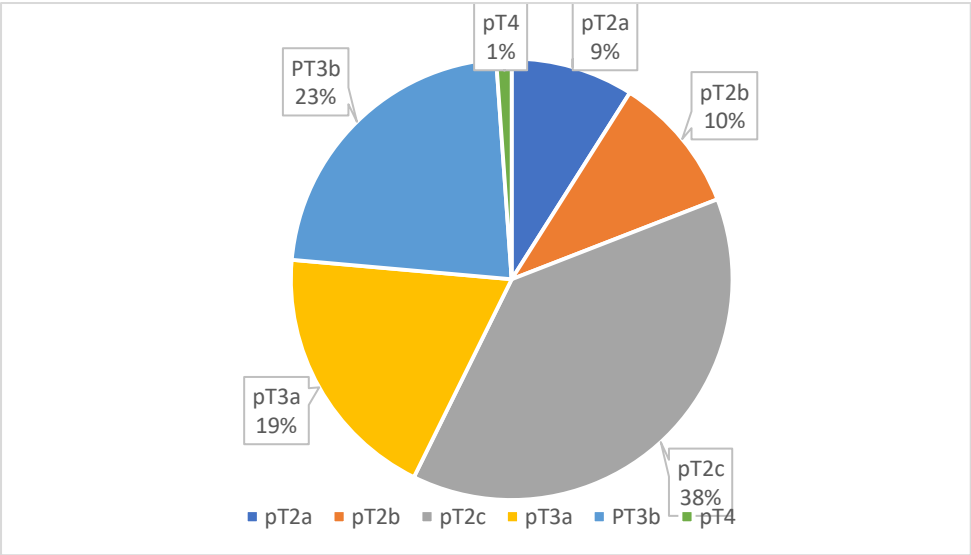
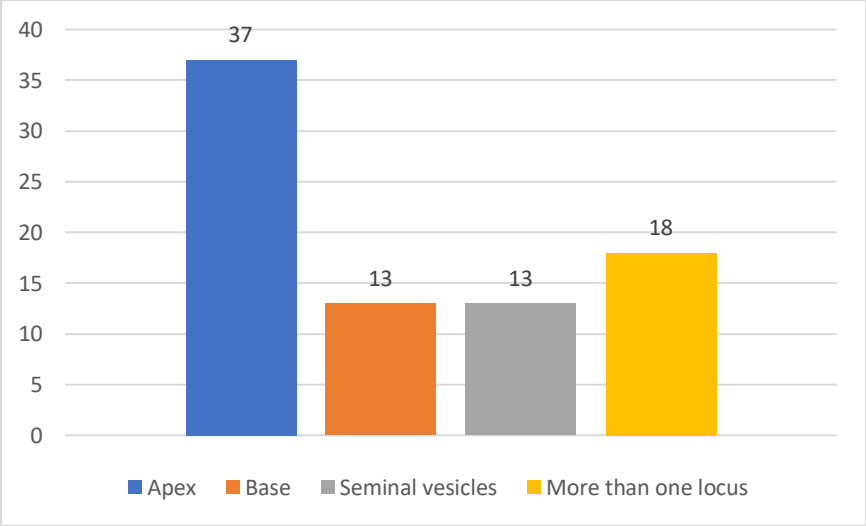


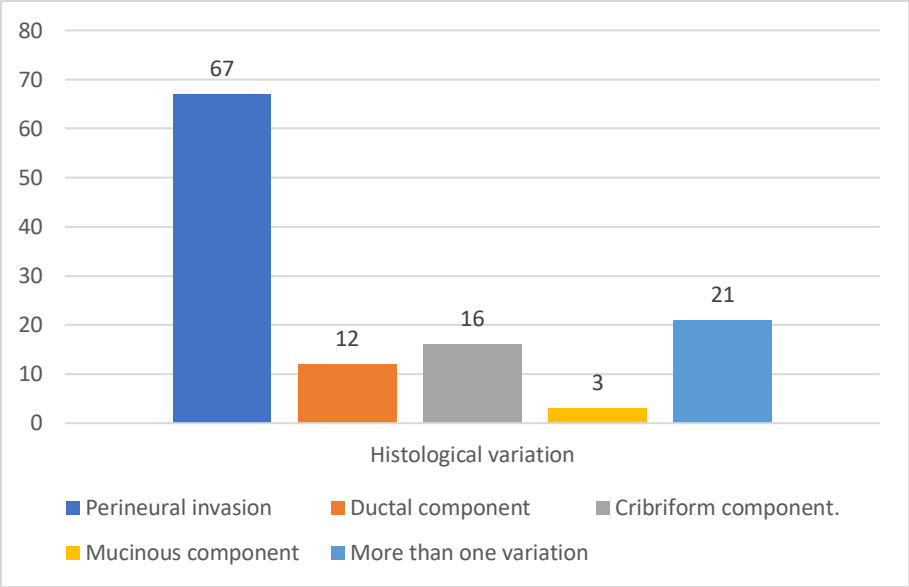
Fig. 10.

Positive surgical margins were demonstrated in 45% of patients. Their distribution by locus is presented in graph 6. Penetration of the prostatic capsule was reported in 26% of patients.



Graph 6.

Histologic features such as cribriform component, ductal component, mucinous component, clear cell component, and perineural invasion were reported in 68 of the patients. The distribution is presented in graph 7.



Graph. 7.

Table 56 presents the correlation between the histological result by Grade Group from the permanent histological preparation and a number of other indicators. The frequency distribution of the data and interpretation are presented in the subsequent tables and text.

Table 56.

		Postoperative complications	Grade Group Biopsy	Grade Group Surergy	TNM	MRI PIRADS
Grade Group Surgery	Rank-biserial	,021	,530**	1	,368**	,204
	Sig. (2-tailed)	,832	,000		,000	,084
	N	100	93	100	100	73
	N	73	71	73	73	73

Table 57 analyzes the data according to the finding of the permanent histological preparation by ISUP Grade groups and pT stage of the disease. A statistically significant relationship was demonstrated between an increase in GG from a durable preparation and the pT stage of the disease (r = 0.368; p = 0.000).

Table 57

	ISUP Grade Group Surgery					
	1	**2**	**3**	**4**	**5**	**Total**
TNM	**4 (100,0%)**	**31 (100,0%)**	**30 (100,0%)**	**13 (100,0%)**	**22 (100,0%)**	**100 (100,0%)**
pT2	4 (100,0%)	21 (67,7%)	16 (53,3%)	4 (30,8%)	6 (27,3%)	51 (51,0%)
pT3	0 (0,0%)	10 (32,3%)	14 (46,7%)	8 (61,5%)	16 (72,7%)	48 (48,0%)

pT4	0 (0,0%)	0 (0,0%)	0 (0,0%)	1 (7,7%)	0 (0,0%)	1 (1,0%)

The frequency distribution of patients by ISUP Grade groups of the permanent histological preparation according to the occurrence of histological progression of the disease is demonstrated in Table 76. The data indicate that an increase in the ISUP Grade group was present in 48.1% of patients with GG3, 53.8% of GG4 patients and 81% of GG5 patients.

Table 58

	ISUP Grade Group Surgery					
	1	**2**	**3**	**4**	**5**	**Total**
Pathological progression	**4 (100,0%)**	**30 (100,0%)**	**27 (100,0%)**	**13 (100,0%)**	**21 (100,0%)**	**95 (100,0%)**
yes	0 (0,0%)	8 (26,7%)	13 (48,1%)	7 (53,8%)	17 (81,0%)	45 (47,4%)
no	4 (100,0%)	22 (73,3%)	14 (51,9%)	6 (46,2%)	4 (19,0%)	50 (52,6%)

Table 59 shows the frequency distribution of patients according to ISUP Grade groups of permanent histological preparation according to the presence of positive surgical margins, as well as penetration of the capsule of the prostate gland.

Table 59

	ISUP Grade Group Surgery					
	1	**2**	**3**	**4**	**5**	**Total**
Pos. Sur. margins (R+)	**4 (100,0%)**	**31 (100,0%)**	**30 (100,0%)**	**13 (100,0%)**	**22 (100,0%)**	**100 (100,0%)**
yes	0 (0,0%)	11 (35,5%)	16 (53,3%)	5 (38,5%)	13 (59,1%)	45 (45,0%)
no	4 (100,0%)	20 (64,5%)	14 (46,7%)	8 (61,5%)	9 (40,9%)	55 (55,0%)
Prostate capsule penetration	**4 (100,0%)**	**31 (100,0%)**	**30 (100,0%)**	**13 (100,0%)**	**22 (100,0%)**	**100 (100,0%)**
yes	0 (0,0%)	3 (9,7%)	8 (26,7%)	6 (46,2%)	9 (40,9%)	26 (26,0%)
no	4 (100,0%)	28 (90,3%)	22 (73,3%)	7 (53,8%)	13 (59,1%)	74 (74,0%)

Table 60 reflects the correlation between the histological result according to ISUP Grade groups of the durable preparation and the probability of occurrence of biochemical and clinical recurrence of PCa.

Table 60.

	ISUP Grade Group surgery					
	1	2	3	4	5	Total
Biochemical recurrence	**3 (100,0%)**	**26 (100,0%)**	**29 (100,0%)**	**12 (100,0%)**	**21 (100,0%)**	**91 (100,0%)**
yes	1 (33,3%)	4 (15,4%)	8 (27,6%)	4 (33,3%)	9 (42,9%)	26 (28,6%)
no	2 (66,7%)	22 (84,6%)	21 (72,4%)	8 (66,7%)	12 (57,1%)	65 (71,4%)
Local recurrence/ Meta	**2 (100,0%)**	**22 (100,0%)**	**24 (100,0%)**	**12 (100,0%)**	**16 (100,0%)**	**76 (100,0%)**
yes	0 (0,0%)	0 (0,0%)	2 (8,3%)	0 (0,0%)	3 (18,8%)	5 (6,6%)
no	2 (100,0%)	22 (100,0%)	22 (91,7%)	12 (100,0%)	13 (81,3%)	71 (93,4%)

Table 61 shows the distribution of patients according to the histological pT stage of the disease and the frequency of pathological progression, as well as the frequency of positive surgical margins and penetration of the prostatic capsule.

Table 61.

Variable		TNM			
		pT2	pT3	pT4	Total
Pathol. progression		**48 (100,0%)**	**46 (100,0%)**	**1 (100,0%)**	**95 (100,0%)**
	no	27 (56,3%)	23 (50,0%)	0 (0,0%)	50 (52,6%)
	yes	21 (43,8%)	23 (50,0%)	1 (100,0%)	45 (47,4%)
Pos. Surg. Margins (R+)		**51 (100,0%)**	**48 (100,0%)**	**1 (100,0%)**	**100 (100,0%)**
	no	38 (74,5%)	16 (33,3%)	1 (100,0%)	55 (55,0%)
	yes	13 (25,5%)	31 (66,7%)	1 (100%)	45 (45,0%)
Prostate capsule penetration		**51 (100,0%)**	**48 (100,0%)**	**1 (100,0%)**	**100 (100,0%)**
	no	48 (94,1%)	26 (54,2%)	0 (0,0%)	74 (74,0%)
	yes	3 (5,9%)	22 (45,8%)	1 (100,0%)	26 (26,0%)

Table 62 reflects the relationship between the rate of biochemical recurrence as well as the rate of local recurrence/distant metastasis and pT stage from the permanent histological preparation.

Table 62.

Variable		TNM			
		pT2	pT3	pT4	Total

Biochemical recurrence		**45 (100,0%)**	**45 (100,0%)**	**1 (100,0%)**	**91 (100,0%)**
	no	32 (71,1%)	33 (73,3%)	0 (0,0%)	65 (71,4%)
	yes	13 (28,9%)	12 (26,7%)	1 (100,0%)	26 (28,6%)
Local recurrence/ Meta		**37 (100,0%)**	**38 (100,0%)**	**1 (100,0%)**	**76 (100,0%)**
	no	35 (94,6%)	35 (92,1%)	1 (100,0%)	71 (93,4%)
	yes	2 (5,4%)	3 (7,9%)	0 (0,0%)	5 (6,6%)

Table 63 presents the frequency distribution of patients according to the average number of histological variations and pT stage of the disease.

Table 63.

		TNM			
		pT2	**pT3**	**pT4**	**Total**
Histological variations (quantity)	N	51	48	1	100
	Mean	,706	1,292	,000	,980
	Standard Deviation	,782	,944	NA	,910

In a comparative analysis of the data in relation to the hospital stay and the body mass index of the patients; age of the patients, preoperative PSA and MRI, histological parameters; intraoperative blood loss and complications – no statistically significant correlation between indicators was demonstrated.

5.6 Early postoperative complications

Early postoperative complications were reported in 12% of patients. Their distribution is as follows: bleeding – 2%; urine leakage – 1%: uroinfection – 7%; hematuria – 1%; hematoma of the scrotum – 1%.

Hemotransfusion was performed in two patients (2%) in a volume of 2 bags of erythrocyte mass and 1 bag of erythrocyte mass, respectively. The mean preoperative hemoglobin was 151 ± 12.9 g/L, and the mean postoperative hemoglobin was 131.2 ± 12.74 g/L. A mean drop in hemoglobin of 19.8 ± 9.71 g/l was reported in patients after LRP.

Table 64 presents the frequency distribution of patients according to their body mass index and anesthetic risk versus the presence or absence of early postoperative complications.

Table 64.

Variable	Early postoperative complications		
	yes	no	Total
Индекс на телесна маса	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**
Normal weight	1 (8,3%) / (5%)	19 (21,6%)	20 (20,0%)
Preobesity	9 (75,0%) / (17%)	42 (47,7%)	51 (51,0%)
Obesity Gr I	1 (8,3%)/ (4,5%)	21 (23,9%)	22 (22,0%)
Obesity Gr II	1 (8,3%)/ (20%)	4 (4,5%)	5 (5,0%)
Obesity Gr III	0 (0,0%)/ (0%)	2 (2,3%)	2 (2,0%)
ASA	**10 (100,0%)**	**78 (100,0%)**	**88 (100,0%)**
2	6 (60,0%)/ (17%)	28 (35,9%)	34 (38,6%)
3	4 (40,0%)/ (8,1%)	45 (57,7%)	49 (55,7%)
4	0 (0,0%)/ (0%)	5 (6,4%)	5 (5,7%)

Table 65 reflects the frequency distribution of patients according to the indicator of early postoperative complications and its dependence on the presence or absence of accompanying and past surgical diseases, as well as on the age group of the patients.

Table 65

Variable	Early postoperative complications		
	yes	no	Total
Accompanying diseases	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**
yes	8 (66,7%)/ (10%)	67 (76,1%)	75 (75,0%)
no	4 (33,3%)/ (16%)	21 (23,9%)	25 (25,0%)
Prior surgery	12 (100%)	88 (100%)	100 (100%)
yes	6 (50%)/ (12,5%)	42 (47,7%)	48 (48%)
no	6 (50%)/ (11,5%)	46 (52,3%)	52 (52%)
Age groups	**12 (100,0%)**	**88 (100,0%)**	**100 (100,0%)**
50 - 60 y.o.	3 (25,0%)/ (12%)	22 (25,0%)	25 (25,0%)
60 – 70 y.o.	6 (50,0%)/ (10%)	54 (61,4%)	60 (60,0%)
70 - 80 y.o.	3 (25,0%)/ (20%)	12 (13,6%)	15 (15,0%)

Table 66 presents the frequency distribution of patients according to the preoperative PSA value and the occurrence of early postoperative complications.

Table 66.

Variable	Early postoperative complications		
	да	не	Total
PSA	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**
< 10 ng/ml	8 (66,7%)/ (16%)	42 (47,7%)	50 (50,0%)
> 10 ng/ml	4 (33,3%)/ (8%)	46 (52,3%)	50 (50,0%)

Analysis of the data relative to ISUP Grade group histological outcome of the preoperative biopsy and permanent histological preparation and the incidence of early postoperative complications is shown in Table 67.

Table 67.

Variable	Early postoperative complications		
	yes	no	Total
ISUP Grade Group Biopsy	**11 (100,0%)/ (% of subgroup)**	**82 (100,0%)**	**93 (100,0%)**
1	2 (18,2%)/ (12%)	14 (17,1%)	16 (17,2%)
2	6 (54,5%)/ (18%)	27 (32,9%)	33 (35,5%)
3	1 (9,1%)/ (3,4%)	28 (34,1%)	29 (31,2%)
4	1 (9,1%)/ (9%)	10 (12,2%)	11 (11,8%)
5	1 (9,1%)/ (25%)	3 (3,7%)	4 (4,3%)
ISUP Grade Group Surgery	**12 (100,0%)**	**88 (100,0%)**	**100 (100,0%)**
1	0 (0,0%)/ (0%)	4 (4,5%)	4 (4,0%)
2	6 (50,0%)/ (19%)	25 (28,4%)	31 (31,0%)
3	0 (0,0%)/ (0%)	30 (34,1%)	30 (30,0%)
4	3 (25,0%)/ (23%)	10 (11,4%)	13 (13,0%)
5	3 (25,0%)/ (13%)	19 (21,6%)	22 (22,0%)

Table 68 reflects the relationship between the pT stage of the permanent histological preparation and the incidence of early postoperative complications in the sample.

Table 68.

Variable	Early postoperative complications		
	yes	no	Total
TNM	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**

Variable	Early postoperative complications		
	yes	no	Total
pT2	8 (66,7%)/ (15%)	43 (48,9%)	51 (51,0%)
pT3	4 (33,3%)/ (8,3%)	44 (50,0%)	48 (48,0%)
pT4	0 (0,0%)/ (0%)	1 (1,1%)	1 (1,0%)

An analysis of the frequency distribution of patients according to the preoperative PIRADS MRI finding and the frequency of early postoperative complications is expressed in Table 69.

Table 69.

Variable	Early postoperative complications		
	yes	no	Total
MRI PIRADS	**10 (100,0%)/ (% of subgrouop)**	**63 (100,0%)**	**73 (100,0%)**
2	1 (10,0%)/ (50%)	1 (1,6%)	2 (2,7%)
3	1 (10,0%)/ (10%)	9 (14,3%)	10 (13,7%)
4	5 (50,0%)/ (12%)	34 (54,0%)	39 (53,4%)
5	3 (30,0%)/ (13%)	19 (30,2%)	22 (30,1%)

Table 70 presents the relationship between the volume of the prostate gland and the frequency of early postoperative complications.

Table 70.

Variable	Early postoperative complications		
	yes	no	Total
Prostate volume	**10 (100,0%)/ (% of subgroup)**	**82 (100,0%)**	**92 (100,0%)**
Under 49 cc	5 (50,0%)/ (10%)	41 (50%)	46 (50%)
50 – 99 cc	5 (50,0%)/ (15%)	28 (34,5%)	33 (35,9%)
Over 100 cc	0 (0%)/ (0%)	4 (4,8%)	4 (4,3%)

Table 71 (a-b) presents the frequency distribution of patients according to the performance of preservation of vascular-nerve bundles and the occurrence of early postoperative complications.

Table 71 - a

Variable	Early postoperative complications		
	yes	no	Total
Nerve sparing	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**
yes	8 (66,7%)/ (16%)	41 (46,6%)	49 (49,0%)
no	4 (33,3%)/ (7,8%)	47 (53,4%)	51 (51,0%)

Table 71-b Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1,703[a]	1	,192	,230	,159	
Continuity Correction[b]	,994	1	,319			
Likelihood Ratio	1,729	1	,189	,230	,159	
Fisher's Exact Test				,230	,159	
Linear-by-Linear Association	1,686[c]	1	,194	,230	,159	,107
N of Valid Cases	100					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 5,88.

b. Computed only for a 2x2 table

c. The standardized statistic is 1,298.

The frequency distribution of patients according to intraoperative blood loss and the frequency of early postoperative complications is depicted in Table 72

Table 72.

Variable	Early postoperative complications		
	yes	no	Total
Bloodloss	**12 (100,0%)/ (% of subgroup)**	**88 (100,0%)**	**100 (100,0%)**
50 - 150 ml	7 (58,3%)/ 13%	45 (51,1%)	52 (52,0%)
150 - 250 ml	3 (25,0%)/ 9%	30 (34,1%)	33 (33,0%)
250 - 350 ml	2 (16,7%)/ 15%	11 (12,5%)	13 (13,0%)
350 - 450 ml	0 (0,0%/ 0%	1 (1,1%)	1 (1,0%)
450 - 550 ml	0 (0,0%)/ 0%	1 (1,1%)	1 (1,0%)

The correlation index between the incidence of early postoperative complications and the indicators listed above is presented in Tables 73 and 74.

Table 73.

		Early complications	ASA	Grade Group Biopsy	Grade Group Surgery	TNM	MRI PIRADS
Early postoperative complications	Rank-biserial	1	-,167	-,050	,021	-,118	-,060
	Sig. (2-tailed)		,119	,636	,832	,241	,616
	N	100	88	93	100	100	73

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

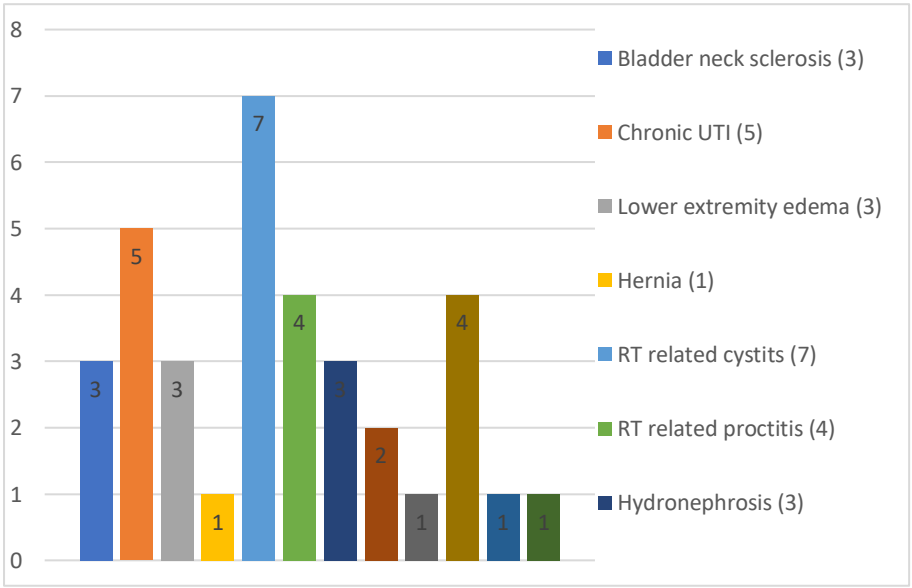
Table 74.

		Early complications	BMI	Accompanying diseases	AGE	(PSA) ng/ml	Bloodloss (ml)
Early postoperative complications	Point-biserial	1	-,035	-,031	-,007	-,157	-,032
	Sig. (2-tailed)		,728	,761	,942	,119	,751
	N	100	100	100	100	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

5.7 Late postoperative complications

Late postoperative complications were defined as events occurring after the first postoperative month. The incidence of late postoperative complications was 39% in the present sample. The distribution of complications by type is presented in graph 8.



Graph 8.

Exitus lethalis was registered in three patients (3%), occurring at the 7th, 14th and 17th postoperative months, respectively. The reasons for the occurrence of exitus lethalis are - COVID 19, diverticulitis and ileus, Pulomary embolism.

Table 75 reflects the frequency distribution of patients according to a number of histological indicators in relation to the occurrence or not of late postoperative complications.

Table 75.

		Late complications					
		no		yes		Total	
Grade Group biopsy		**54**	**(100,0%)**	**34**	**(100,0%)/ (% of subgroup)**	**88**	**(100,0%)**
	1	10	(18,5%)	6	(17,6%)/ 37%	16	(18,2%)
	2	21	(38,9%)	9	(26,5%)/ 30%	30	(34,1%)
	3	13	(24,1%)	14	(41,2%)/ 51%	27	(30,7%)
	4	8	(14,8%)	3	(8,8%)/ 27%	11	(12,5%)
	5	2	(3,7%)	2	(5,9%)/ 50%	4	(4,5%)
Grade Group surgery		**58**	**(100,0%)**	**37**	**(100,0%)**	**95**	**(100,0%)**
	1	1	(1,7%)	3	(8,1%)/75%	4	(4,2%)
	2	17	(29,3%)	11	(29,7%)/ 39%	28	(29,5%)
	3	20	(34,5%)	10	(27,0%)/ 33%	30	(31,6%)
	4	8	(13,8%)	4	(10,8%)/ 33%	12	(12,6%)
	5	12	(20,7%)	9	(24,3%)/ 42%	21	(22,1%)
TNM		**58**	**(100,0%)**	**37**	**(100,0%)**	**95**	**(100,0%)**
	pT2	31	(53,4%)	16	(43,2%)/ 34%	47	(49,5%)
	pT3	27	(46,6%)	20	(54,1%)/ 42%	47	(49,5%)
	pT4	0	(0,0%)	1	(2,7%)/ 100%	1	(1,1%)
Pos. Surgical margins (R+)		**58**	**(100,0%)**	**37**	**(100,0%)**	**95**	**(100,0%)**
	yes	26	(44,8%)	18	(48,6%)/ 40%	44	(46,3%)
	no	32	(55,2%)	19	(51,4%)/ 37%	51	(53,7%)
Prostate capsule penetration		**58**	**(100,0%)**	**37**	**(100,0%)**	**95**	**(100,0%)**
	yes	14	(24,1%)	12	(32,4%)/ 46%	26	(27,4%)
	no	44	(75,9%)	25	(67,6%)/ 36%	69	(72,6%)

Table 76 presents an analysis of preoperative PSA data and MRI findings relative to the detection of late postoperative complications.

Table 76.

		Late complications					
		no		**yes**		**Total**	
PSA		**58**	**(100,0%)**	**37**	**(100,0%)/ (% of subgroup)**	**95**	**(100,0%)**
	< 10 ng/	31	(53,4%)	16	(43,2%)/ 34%	47	(49,5%)
	> 10 ng/	27	(46,6%)	21	(56,8%)/ 43%	48	(50,5%)
MRI PIRADS		**48**	**(100,0%)**	**22**	**(100,0%)**	**70**	**(100,0%)**
	2	1	(2,1%)	1	(4,5%)/ 50%	2	(2,9%)
	3	8	(16,7%)	0	(0,0%)/ 0%	8	(11,4%)
	4	24	(50,0%)	14	(63,6%)/ 36%	38	(54,3%)
	5	15	(31,3%)	7	(31,8%)/ 31%	22	(31,4%)

Table 77 reflects the frequency distribution of late operative complications in relation to the preservation of vascular-nerve bundles in patients.

Table 77.

		Late complications					
		no		**yes**		**Total**	
Nerve sparing		**58**	**(100,0%)**	**37**	**(100,0%)/ (% of subgroup)**	**95**	**(100,0%)**
	yes	30	(51,7%)	16	(43,2%)/ 34%	46	(48,4%)
	no	28	(48,3%)	21	(56,8%)/ 42%	49	(51,6%)

Table 78 presents the relationship between administration of adjuvant therapy and the occurrence of late postoperative complications.

Table 78.

		Late complications					
		no		**yes**		**Total**	
Adjuvant therapy		**56**	**(100,0%)**	**33**	**(100,0%)/ (процент от подгрупата)**	**89**	**(100,0%)**
	yes	38	(67,9%)	29	(87,9%)/ 43%	67	(75,3%)
	no	18	(32,1%)	4	(12,1%)/ 18%	22	(24,7%)

Table 79 presents the frequency distribution of patients according to intraoperative blood loss, age and body mass index in relation to the occurrence of late postoperative complications.

Table 79.

		Late complications		
		No	**Yes**	**Total**
Bloodloss (ml)	Count	58	37	95
	Mean	182,414	177,027	180,316
	Standard Deviation	104,501	73,214	93,176
BMI	Count	58	37	95
	Mean	28,677	28,271	28,519
	Standard Deviation	4,238	4,874	4,476
Age	Count	58	37	95
	Mean	64,948	64,054	64,600
	Standard Deviation	5,874	5,850	5,850

5.8 Functional Results

A validated questionnaire - IIEF (International index of erectile function) and in particular - its abbreviated and simplified version (IIEF - 5) was used to assess the erectile function of the patients. According to the total number of points achieved, patients were divided into 5 groups: 22 - 25 points - without erectile dysfunction - group 5; 17 – 21 points – mild erectile dysfunction – group 4; 12 – 16 points – mild to moderate erectile dysfunction – group 3; 8 – 11 points – moderate erectile dysfunction – group 2; 5 – 7 points severe erectile dysfunction - group 1. We defined as preserved erectile function groups 4 and 5. Patients were evaluated preoperatively, at the 6th and at the 12th postoperative month.

The preoperative distribution of patients according to IIEF 5 is presented in Figure 11.

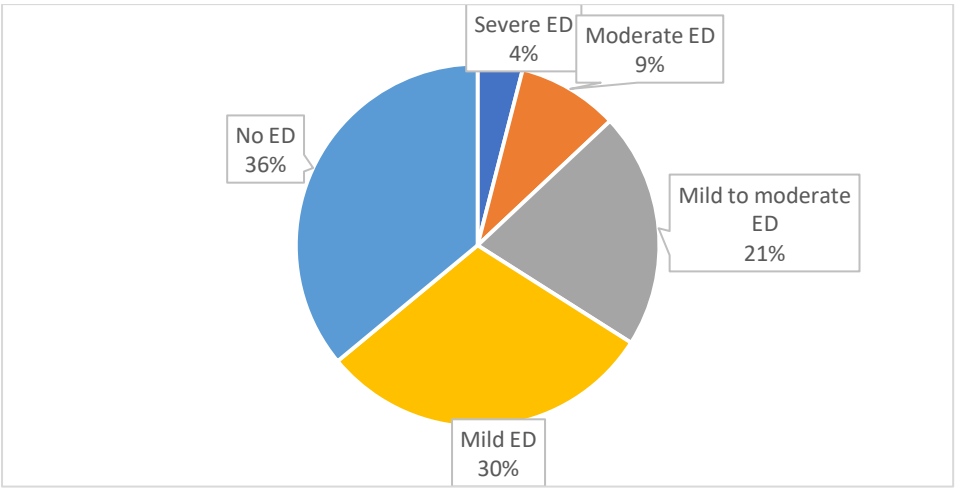
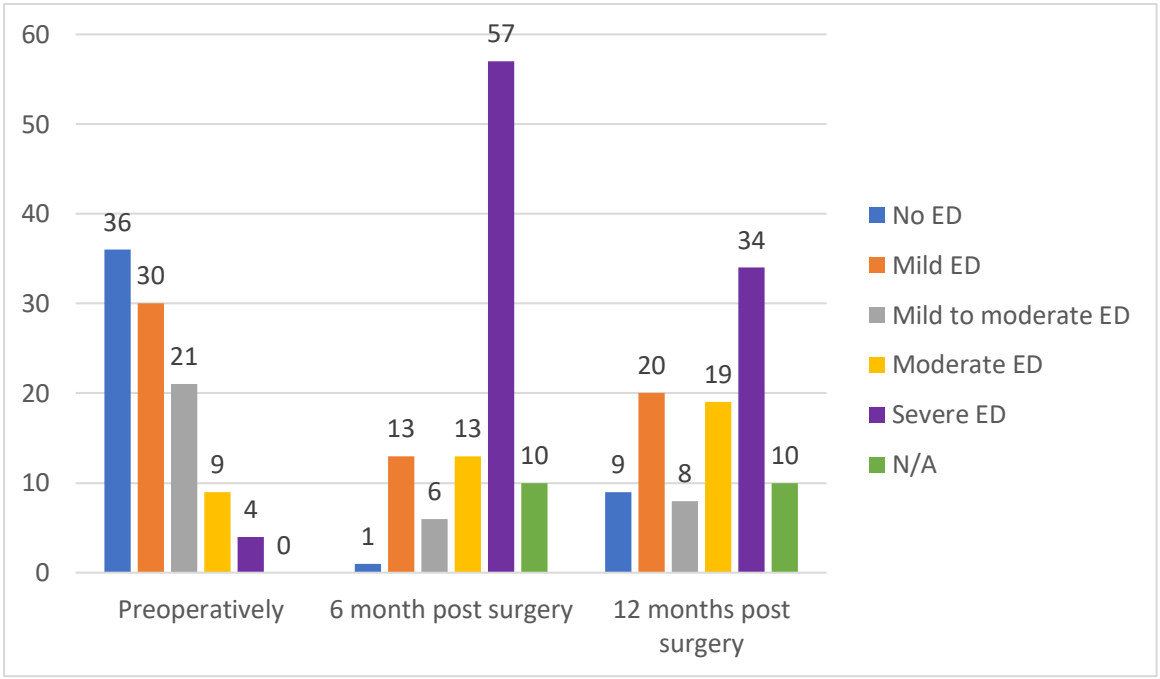


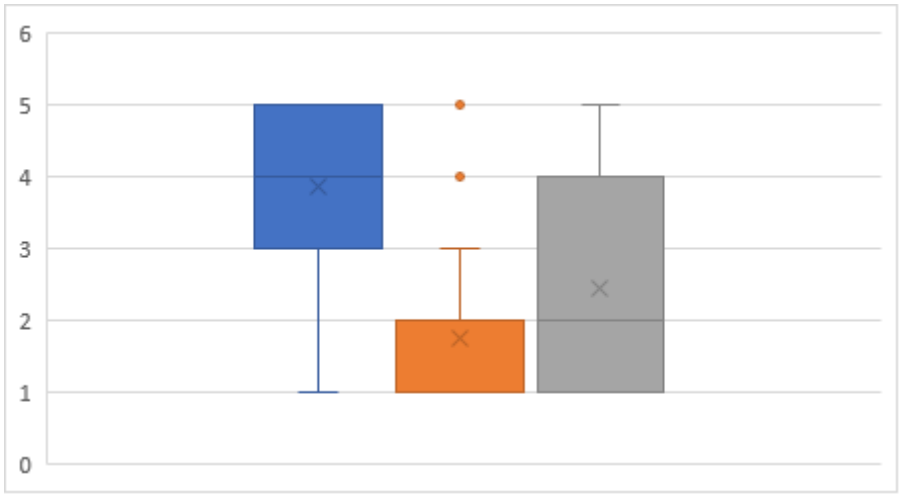
Figure 11.

The distribution of patients according to IIEF preoperatively, at 6 months, and at 12 months postoperatively is shown in Graph. 9.



Graph 9.

An average drop of 2.18 points was found for patients by group of erectile function preoperatively at the 6th postoperative month. The average decline of patients by group of erectile function preoperatively at the 12th postoperative month was 1.48 points. The data demonstrated a significant improvement in erectile function at 12th postoperative month compared to 6th postoperative month. The results are presented in Figure 12.



F

igure 12. Mean score by IIEF groups: preoperatively (blue), at 6th postoperative month (orange), at 12th postoperative month (grey).

The correlation between a number of histological indicators and the erectile function of patients is expressed in table 80.

Table 80.

		IIEF 6 м					
		1	2	3	4	5	Total
Grade Group Biopsy		**54(100,0%)**	**12(100,0%)**	**6(100,0%)**	**12(100,0%)**	**1(100,0%)**	**85(100,0%)**
	1	6 (11,1%)	2 (16,7%)	1(16,7%)	6 (50,0%)	1(100,0%)	16(18,8%)
	2	14(25,9%)	4 (33,3%)	5(83,3%)	4 (33,3%)	0(0,0%)	27(31,8%)
	3	23(42,6%)	4 (33,3%)	0(0,0%)	1 (8,3%)	0(0,0%)	28(32,9%)
	4	7 (13,0%)	2 (16,7%)	0(0,0%)	1 (8,3%)	0(0,0%)	10(11,8%)
	5	4 (7,4%)	0 (0,0%)	0(0,0%)	0 (0,0%)	0(0,0%)	4 (4,7%)
Grade Group Surgery		**57(100,0%)**	**13(100,0%)**	**6(100,0%)**	**13(100,0%)**	**1(100,0%)**	**90(100,0%)**
	1	1 (1,8%)	0 (0,0%)	0(0,0%)	2 (15,4%)	0(0,0%)	3 (3,3%)
	2	9 (15,8%)	6 (46,2%)	5(83,3%)	5 (38,5%)	0(0,0%)	25(27,8%)
	3	20(35,1%)	4 (30,8%)	0(0,0%)	4 (30,8%)	1(100,0%)	29(32,2%)
	4	9 (15,8%)	1 (7,7%)	0(0,0%)	2 (15,4%)	0(0,0%)	12(13,3%)
	5	18(31,6%)	2 (15,4%)	1(16,7%)	0 (0,0%)	0(0,0%)	21(23,3%)
TNM		**57(100,0%)**	**13(100,0%)**	**6(100,0%)**	**13(100,0%)**	**1(100,0%)**	**90(100,0%)**
	pT2	22(38,6%)	6 (46,2%)	3(50,0%)	12(92,3%)	1(100,0%)	44(48,9%)
	pT3	34(59,6%)	7 (53,8%)	3(50,0%)	1 (7,7%)	0(0,0%)	45(50,0%)
	pT4	1 (1,8%)	0 (0,0%)	0(0,0%)	0 (0,0%)	0(0,0%)	1 (1,1%)
R-status (R+)		**57(100,0%)**	**13(100,0%)**	**6(100,0%)**	**13(100,0%)**	**1(100,0%)**	**90(100,0%)**
	да	32(56,1%)	6 (46,2%)	2(33,3%)	0 (0,0%)	1(100,0%)	41(45,6%)
	не	25(43,9%)	7 (53,8%)	4(66,7%)	13(100,0%)	0(0,0%)	49(54,4%)
Prostate capsule penetration		**57(100,0%)**	**13(100,0%)**	**6(100,0%)**	**13(100,0%)**	**1(100,0%)**	**90(100,0%)**
	да	20(35,1%)	4 (30,8%)	2(33,3%)	0 (0,0%)	0(0,0%)	26(28,9%)
	не	37(64,9%)	9 (69,2%)	4(66,7%)	13(100,0%)	1(100,0%)	64(71,1%)

Table 81 a-b Reflects the relationship between the preservation of vascular-nerve bundles and erectile function at the 6th postoperative month.

Table 81 – a

		IIEF 6 м					
		1	2	3	4	5	Total
Nerve sparing		**57 (100,0%)**	**13 (100,0%)**	**6 (100,0%)**	**13 (100,0%)**	**1 (100,0%)**	**90 (100,0%)**
	yes	15 (26,3%)	9 (69,2%)	6 (100,0%)	13 (100,0%)	1 (100,0%)	44 (48,9%)
	no	42 (73,7%)	4 (30,8%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	46 (51,1%)

Table 81- b

		IIEF 6 м					
		1	2	3	4	5	Total
Nerve sparing		**57**	**13**	**6**	**13**	**1**	**90**
	yes	15 (34%)	9 (21%)	6 (14%)	13 (29%)	1 (2%)	44 (100%)
	no	42 (91%)	4 (9%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	46 (100%)

The relationship between patients' preoperative erectile function and 6th postoperative month erectile function is depicted in Table 82.

Table 82.

		IIEF 6 м					
		1	2	3	4	5	Total
IIEF preoperatively		**57 (100,0%)**	**13 (100,0%)**	**6 (100,0%)**	**13 (100,0%)**	**1 (100,0%)**	**90 (100,0%)**
	1	3 (5,3%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	3 (3,3%)
	2	6 (10,5%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	6 (6,7%)
	3	17 (29,8%)	1 (7,7%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	18 (20,0%)
	4	16 (28,1%)	4 (30,8%)	5 (83,3%)	4 (30,8%)	0 (0,0%)	29 (32,2%)
	5	15 (26,3%)	8 (61,5%)	1 (16,7%)	9 (69,2%)	1 (100,0%)	34 (37,8%)

The relation of the administration of adjuvant therapy to the erectile function of the patients at the 6th postoperative month is presented in table 83 a-b.

Table 83-a.

		IIEF 6 м					
		1	2	3	4	5	Total
Adjuvant therapy		**57(100,0%)**	**13(100,0%)**	**6(100,0%)**	**13(100,0%)**	**1(100,0%)**	**90(100,0%)**
	yes	53(93,0%)	12(92,3%)	3(50,0%)	0 (0,0%)	0(0,0%)	68(75,6%)
	no	4 (7,0%)	1 (7,7%)	3(50,0%)	13(100,0%)	1(100,0%)	22(24,4%)

Table 83-b

		IIEF 6 м					
		1	2	3	4	5	Total
Adjuvant therapy		**57**	**13**	**6**	**13**	**1**	**90**
	yes	53(77,0%)	12(17,6%)	3(4,4%)	0 (0,0%)	0(0,0%)	68(100%)
	no	4 (18,3%)	1 (4,5%)	3(13,7%)	13(59,0%)	1(4,5%)	22(100%)

The correlation of a number of other indicators with the erectile function of patients at the 6th postoperative month is presented in table 84.

Table 84.

		IIEF 6 м					
		1	2	3	4	5	Total
Bloodloss (ml)	Count	57	13	6	13	1	90
	Mean	176,842	165,385	208,333	173,077	100,000	175,889
	Standard Deviation	92,566	89,872	115,830	103,311	.	93,951
BMI	Count	57	13	6	13	1	90
	Mean	28,641	29,449	29,578	27,111	28,501	28,598
	Standard Deviation	5,013	3,663	3,256	3,331	.	4,495
Age	Count	57	13	6	13	1	90
	Mean	64,509	61,385	65,167	66,385	57,000	64,289

		IIEF 6 м					
		1	**2**	**3**	**4**	**5**	**Total**
	Standard Deviation	6,339	4,992	4,916	3,618	.	5,858
Accompanying dieseases	Count	57	13	6	13	1	90
	Mean	0,982	1,154	1,000	1,077	0,000	1,011
	Standard Deviation	,744	,689	,632	1,115	NA	0,786

The frequency distribution of patients according to important histological features and erectile function at the 12th postoperative month and presented in Table 85.

Table 85.

		IIEF 12M					
		1	**2**	**3**	**4**	**5**	**Total**
Grade Group biopsy		**31(100,0%)**	**19(100,0%)**	**8(100,0%)**	**18(100,0%)**	**9(100,0%)**	**85(100,0%)**
	1	4 (12,9%)	2 (10,5%)	2(25,0%)	3 (16,7%)	5(55,6%)	16(18,8%)
	2	8 (25,8%)	4 (21,1%)	2(25,0%)	11(61,1%)	2(22,2%)	27(31,8%)
	3	12(38,7%)	9 (47,4%)	3(37,5%)	3 (16,7%)	1(11,1%)	28(32,9%)
	4	3 (9,7%)	4 (21,1%)	1(12,5%)	1 (5,6%)	1(11,1%)	10(11,8%)
	5	4 (12,9%)	0 (0,0%)	0(0,0%)	0 (0,0%)	0(0,0%)	4 (4,7%)
Grade Group surgery		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	1	1 (2,9%)	0 (0,0%)	0(0,0%)	0 (0,0%)	2(22,2%)	3 (3,3%)
	2	6 (17,6%)	1 (5,3%)	3(37,5%)	13(65,0%)	2(22,2%)	25(27,8%)
	3	12(35,3%)	7 (36,8%)	2(25,0%)	4 (20,0%)	4(44,4%)	29(32,2%)
	4	3 (8,8%)	6 (31,6%)	0(0,0%)	2 (10,0%)	1(11,1%)	12(13,3%)
	5	12(35,3%)	5 (26,3%)	3(37,5%)	1 (5,0%)	0(0,0%)	21(23,3%)
PSA groups		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	< 10 ng/	14(41,2%)	6 (31,6%)	5(62,5%)	15(75,0%)	6(66,7%)	46(51,1%)
	> 10 ng/	20(58,8%)	13(68,4%)	3(37,5%)	5 (25,0%)	3(33,3%)	44(48,9%)

		IIEF 12M					
		1	2	3	4	5	Total
TNM		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	pT2	12(35,3%)	7 (36,8%)	6(75,0%)	11(55,0%)	8(88,9%)	44(48,9%)
	pT3	22(64,7%)	11(57,9%)	2(25,0%)	9 (45,0%)	1(11,1%)	45(50,0%)
	pT4	0 (0,0%)	1 (5,3%)	0(0,0%)	0 (0,0%)	0(0,0%)	1 (1,1%)
R-status (R+)		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	yes	20(58,8%)	11(57,9%)	4(50,0%)	5 (25,0%)	1(11,1%)	41(45,6%)
	no	14(41,2%)	8 (42,1%)	4(50,0%)	15(75,0%)	8(88,9%)	49(54,4%)
Prostate capsule penetration		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	yes	14(41,2%)	6 (31,6%)	2(25,0%)	4 (20,0%)	0(0,0%)	26(28,9%)
	no	20(58,8%)	13(68,4%)	6(75,0%)	16(80,0%)	9(100,0%)	64(71,1%)

The relationship between the erectile function on the 12th postoperative month and the preservation of vascular-nerve bundles is presented in table 86 a-b.

Table 86 -a.

		IIEF 12M					
		1	2	3	4	5	Total
Nerve sparing		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	yes	7 (20,6%)	4 (21,1%)	4(50,0%)	20(100,0%)	9(100,0%)	44(48,9%)
	no	27(79,4%)	15(78,9%)	4(50,0%)	0 (0,0%)	0(0,0%)	46(51,1%)

Table 86-b

		IIEF 12M					
		1	2	3	4	5	Total
Nerve sparing		**34**	**19**	**8**	**20**	**9**	**90**
	yes	7 (15%)	4 (9,5%)	4(9,5%)	20(45%)	9(20%)	44(100%)
	no	27(58%)	15(33%)	4(9%)	0 (0,0%)	0(0,0%)	46(100%)

The ratio of preoperative erectile function to erectile function at the 12th postoperative month is presented in Table 87.

Table 87.

		IIEF 12M					
		1	2	3	4	5	Total
IIEF group preoperatively		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	1	2 (5,9%)	1 (5,3%)	0(0,0%)	0 (0,0%)	0(0,0%)	3 (3,3%)
	2	5 (14,7%)	1 (5,3%)	0(0,0%)	0 (0,0%)	0(0,0%)	6 (6,7%)
	3	9 (26,5%)	8 (42,1%)	1(12,5%)	0 (0,0%)	0(0,0%)	18(20,0%)
	4	10(29,4%)	5 (26,3%)	2(25,0%)	12(60,0%)	0(0,0%)	29(32,2%)
	5	8 (23,5%)	4 (21,1%)	5(62,5%)	8 (40,0%)	9(100,0%)	34(37,8%)

The relationship between the administration of adjuvant therapy and the erectile function of patients at the 12th postoperative month is depicted in Table 88 a-b.

Table 88-a.

		IIEF 12M					
		1	2	3	4	5	Total
Adjuvant therapy		**34(100,0%)**	**19(100,0%)**	**8(100,0%)**	**20(100,0%)**	**9(100,0%)**	**90(100,0%)**
	yes	32(94,1%)	16(84,2%)	8(100,0%)	12(60,0%)	0(0,0%)	68(75,6%)
	no	2 (5,9%)	3 (15,8%)	0(0,0%)	8 (40,0%)	9(100,0%)	22(24,4%)

Table 88 – b.

		IIEF 12M					
		1	2	3	4	5	Total
Adjuvant therapy		**34**	**19**	**8**	**20**	**9**	**90**
	yes	32(46%)	16(24%)	8(12%)	12(18%)	0(0,0%)	68(100%)
	no	2 (9%)	3 (14%)	0(0,0%)	8 (36%)	9(41%)	22(100%)

Table 89 expresses the relationship of a number of other pre- and intraoperative indicators and the erectile function of patients at the 12th postoperative month.

Table 89.

		IIEF 12M					
		1	2	3	4	5	Total
Bloodloss (ml)	Count	34	19	8	20	9	90
	Mean	168,529	173,684	137,500	210,000	166,667	175,889
	Standard Deviation	68,363	88,770	91,613	127,321	103,078	93,951
BMI	Count	34	19	8	20	9	90
	Mean	29,656	27,694	27,203	28,398	28,191	28,598
	Standard Deviation	5,639	3,404	3,552	4,069	2,877	4,495
Age	Count	34	19	8	20	9	90
	Mean	63,853	66,421	62,500	63,400	65,000	64,289
	Standard Deviation	6,981	4,868	5,806	5,315	3,674	5,858
Accompanying diseases	Count	34	19	8	20	9	90
	Mean	1,000	1,000	1,250	1,000	,889	1,011
	Standard Deviation	,778	,667	,886	,973	,601	,786

As continent patients after LRP, we defined patients wearing a maximum of one diaper/security pad per 24 hours. Patients were followed up at the first, third, sixth and twelfth postoperative months. The results are reported in Table 90.

Table 90.

Continence	Period post surgery			
	1st month	3rd month	6th month	12th month
No pad/ one safety pad	12 (12%)	50 (50%)	60 (60%)	70 (70%)
Incontinence	88 (88%)	50 (50%)	40 (40%)	30 (30%)

The detailed results regarding the continence of the patients at the 12th postoperative month were: continence patients – 70%; stress incontinence during exercise – 23%; incontinent with diapers – 6%; urethral catheter – 1%. The mean time to continence of the patients was 4.45 ± 3.67 months (range 1 – 18 months).

Table 91 presents the frequency distribution of patients with regard to their continence at the 1st and 12th postoperative months in relation to a number of histological indicators.

Table 91.

		Continence 1st month				Continence 12 month			
		yes		no		yes		no	
Grade Group Biopsy		**11**	**(100,0%) / % of subgroup**	**71**	**(100,0%)**	**59**	**(100,0%)/ % of subgroup**	**23**	**(100,0%)**
	1	1	(9,1%)/6,6%	14	(19,7%)	14	(23,7%)/93%	1	(4,3%)
	2	3	(27,3%)/11%	24	(33,8%)	18	(30,5%)/67%	9	(39,1%)
	3	4	(36,4%)/15%	22	(31,0%)	18	(30,5%)/69%	8	(34,8%)
	4	3	(27,3%)/30%	7	(9,9%)	7	(11,9%)/70%	3	(13,0%)
	5	0	(0,0%)/0%	4	(5,6%)	2	(3,4%)/50%	2	(8,7%)
Grade Group Surgery		**11**	**(100,0%)**	**75**	**(100,0%)**	**61**	**(100,0%)**	**25**	**(100,0%)**
	1	1	(9,1%)/33%	2	(2,7%)	3	(4,9%)/100%	0	(0,0%)
	2	3	(27,3%)/12%	22	(29,3%)	16	(26,2%)/64%	9	(36,0%)
	3	4	(36,4%)/14%	24	(32,0%)	23	(37,7%)/82%	5	(20,0%)
	4	1	(9,1%)/9%	10	(13,3%)	8	(13,1%)/73%	3	(12,0%)
	5	2	(18,2%)/11%	17	(22,7%)	11	(18,0%)/58%	8	(32,0%)
TNM	**Total**	**11**	**(100,0%)**	**75**	**(100,0%)**	**61**	**(100,0%)**	**25**	**(100,0%)**
	pT2	5	(45,5%)/12%	37	(49,3%)	30	(49,2%)/71%	12	(48,0%)
	pT3	6	(54,5%)/14%	37	(49,3%)	30	(49,2%)/70%	13	(52,0%)
	pT4	0	(0,0%)/0%	1	(1,3%)	1	(1,6%)/100%	0	(0,0%)

Table 92 presents an analysis of the relationship between continence at the 1st and 12th postoperative months and the preoperative PSA value, as well as the preoperative PIRADS MRI findings.

Table 92.

		Continence 1 month				Continence 12 months			
		yes		no		yes		no	
PSA groups	**Total**	**11**	**(100,0%)**	**75**	**(100,0%)**	**61**	**(100,0%)**	**25**	**(100,0%)**
	< 10 ng/ml	6	(54,5%)	38	(50,7%)	29	(47,5%)	15	(60,0%)
	> 10 ng/ml	5	(45,5%)	37	(49,3%)	32	(52,5%)	10	(40,0%)
MRI PIRADS	**Total**	**9**	**(100,0%)/ % of subgroup**	**56**	**(100,0%)**	**47**	**(100,0%)/ % of subgroup**	**18**	**(100,0%)**
	2	0	(0,0%)/0%	2	(3,6%)	0	(0,0%)/0%	2	(11,1%)
	3	1	(11,1%)/13%	7	(12,5%)	7	(14,9%)/88%	1	(5,6%)

		Continence 1 month				Continence 12 months			
		yes		no		yes		no	
	4	6	(66,7%)/18%	28	(50,0%)	27	(57,4%)/80%	7	(38,9%)
	5	2	(22,2%)/9,5%	19	(33,9%)	13	(27,7%)/62%	8	(44,4%)

Table 93 depicts the relationship of rates of positive surgical margins and prostatic capsule penetration to patient continence at 1 and 12 months postoperatively.

Table 93.

		Continence 1м				Continence 12м			
		yes		no		yes		no	
R-status (R+)	**Total**	**11**	**(100,0%)/ % of subgroup**	**75**	**(100,0%)**	**61**	**(100,0%)/ % of subgroup**	**25**	**(100,0%)**
	yes	1	(9,1%)/2,5%	39	(52,0%)	25	(41,0%)/63%	15	(60,0%)
	no	10	(90,9%)/22%	36	(48,0%)	36	(59,0%)/78%	10	(40,0%)
Prostate capsule penetration	**Total**	**11**	**(100,0%)**	**75**	**(100,0%)**	**61**	**(100,0%)**	**25**	**(100,0%)**
	yes	2	(18,2%)/8%	23	(30,7%)	18	(29,5%)/72%	7	(28,0%)
	no	9	(81,8%)/15%	52	(69,3%)	43	(70,5%)/70%	18	(72,0%)

The correlation between the preservation of vascular-nerve bundles and the continence of patients after LRP is depicted in Table 94.

Table 94.

		Continence 1м				Continence 12м			
		yes		no		yes		no	
Nerve sparing	**Total**	**11**	**(100,0%)/ % of subgroup**	**75**	**(100,0%)**	**61**	**(100,0%)/% of subgroup**	**25**	**(100,0%)**
	yes	8	(72,7%)/19%	34	(45,3%)	32	(53%)/76%	10	(40,0%)
	no	3	(27,3%)/7%	41	(54,7%)	29	(47%)/65%	15	(60,0%)

Table 95 presents the distribution of patients on antiadjuvant therapy and the relationship of the indicator to postoperative continence at the 1st and 12th months.

Table 95.

		Continence 1м				Continence 12м			
		yes		no		yes		no	
Adjuvant therapy	**Total**	**11**	**(100,0%)/% of subgroup**	**75**	**(100,0%)**	**61**	**(100,0%)/% of subgroup**	**25**	**(100,0%)**
	yes	8	(72,7%)/12%	57	(76,0%)	43	(71%)/66%	22	(88,0%)
	no	3	(27,3%)/14%	18	(24,0%)	18	(29%)/85%	3	(12,0%)

The distribution of patients by blood loss, body mass index, and age with respect to postoperative continence is presented in Table 96.

Table 96.

		Continence 1м		Continence 12м	
		yes	no	yes	no
Bloodloss (ml)	Count	11	75	61	25
	Mean	218,182	172,400	170,164	198,000
	Standard Deviation	132,802	87,439	97,562	85,975
BMI	Count	11	75	61	25
	Mean	29,531	28,618	28,351	29,673
	Standard Deviation	4,240	4,592	4,784	3,786
Age	Count	11	75	61	25
	Mean	60,636	64,893	63,475	66,480
	Standard Deviation	5,697	5,661	5,932	4,993

5.9 Oncological Results

Biochemical recurrence during follow-up of patients was reported in 26% of cases Local recurrence was found in 1 patient. Three patients developed bone metastases.

Table 97 reflects the frequency distribution of patients according to the histological result according to the ISUP Grade group of the preoperative biopsy and permanent histological preparation, as well as the pT stage of the disease in relation to the presence of biochemical recurrence of PCa.

Table 97.

		Biochemical recurrence					
		yes		no		Total	
		Count	Column N %/ % of subgroup	Count	Column N %	Count	Column N %
Grade Group Biopsy		**25**	**(100,0%)**	**61**	**(100,0%)**	**86**	**(100,0%)**
	1	3	(12,0%)/ 18%	13	(21,3%)	16	(18,6%)
	2	9	(36,0%)/ 32%	19	(31,1%)	28	(32,6%)
	3	6	(24,0%)/ 21.4%	22	(36,1%)	28	(32,6%)
	4	4	(16,0%)/ 40%	6	(9,8%)	10	(11,6%)
	5	3	(12,0%)/ 75%	1	(1,6%)	4	(4,7%)
Grade Group surgery		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	1	1	(3,8%)/ 33,3%	2	(3,1%)	3	(3,3%)
	2	4	(15,4%)/ 15,3%	22	(33,8%)	26	(28,6%)
	3	8	(30,8%)/ 27,6%	21	(32,3%)	29	(31,9%)
	4	4	(15,4%)/ 33,3%	8	(12,3%)	12	(13,2%)
	5	9	(34,6%)/ 42,8%	12	(18,5%)	21	(23,1%)
TNM		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	pT2	13	(50,0%)/ 28,8%	32	(49,2%)	45	(49,5%)
	pT3	12	(46,2%)/ 26,6%	33	(50,8%)	45	(49,5%)
	pT4	1	(3,8%)/ 100%	0	(0,0%)	1	(1,1%)

The distribution of patients according to preoperative PSA and preoperative MRI findings and the incidence of biochemical recurrence is presented in Table 98.

Table 98.

		Biochemical recurrence					
		yes		no		Total	
		Count	Column N %/ % of subgroup	Count	Column N %	Count	Column N %
PSA groups		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	< 10 ng/	9	(34,6%)/ 19,1%	38	(58,5%)	47	(51,6%)
	> 10 ng/	17	(65,4%)/ 38,6%	27	(41,5%)	44	(48,4%)
MRI PIRADS		**16**	**(100,0%)**	**52**	**(100,0%)**	**68**	**(100,0%)**

2	0	(0,0%)/ 0%	2	(3,8%)	2	(2,9%)
3	2	(12,5%)/ 22,2%	7	(13,5%)	9	(13,2%)
4	9	(56,3%)/ 25%	27	(51,9%)	36	(52,9%)
5	5	(31,3%)/ 23,8%	16	(30,8%)	21	(30,9%)

A correlation index of the above dependencies is presented in table 99.

Table 99

		Biochemical recurrence	Grade Group Biopsy	Grade Group surgery	MRI PIRADS	TNM
Biochemical recurrence	Rank-biserial	1	,173	,199	,052	,027
	Sig. (2-tailed)		,110	,059	,671	,802
	N	91	86	91	68	91

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Biochemical recurrnce	(PSA) ng/ml	Number of histological variants
Biochemical recurrence	Point-biserial	1	,247*	,178
	Sig. (2-tailed)		,018	,092
	N	91	91	91
	N	91	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Table 100 a-c presents the relationship between the rate of biochemical recurrence and established positive surgical margins (R+), as well as penetration of the prostatic capsule by Pca.

Table 100-a.

		Biochemical recurrence					
		yes		**no**		**Total**	
		Count	**Column N %/ % of subgroup**	**Count**	**Column N %**	**Count**	**Column N %**
Pos. surgical margins (R+)		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	yes	10	(38,5%)/ 24,3%	31	(47,7%)	41	(45,1%)
	no	16	(61,5%)/ 32%	34	(52,3%)	50	(54,9%)

Prostate capsule pentration		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	yes	10	(38,5%)/ 38,4%	16	(24,6%)	26	(28,6%)
	no	16	(61,5%)/ 24,6%	49	(75,4%)	65	(71,4%)

Table 100-b. Chi-Square Tests. BCR and positive surgical margins (R+).

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	,639[a]	1	,424	,489	,287	
Continuity Correction[b]	,321	1	,571			
Likelihood Ratio	,644	1	,422	,489	,287	
Fisher's Exact Test				,489	,287	
Linear-by-Linear Association	,632[c]	1	,427	,489	,287	,136
N of Valid Cases	91					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 11,71.

b. Computed only for a 2x2 table

c. The standardized statistic is -,795.

Таблица 100 – с . Chi-Square Tests. BCR and prostate capsule pentration.

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1,745[a]	1	,187	,207	,144	
Continuity Correction[b]	1,132	1	,287			
Likelihood Ratio	1,689	1	,194	,207	,144	
Fisher's Exact Test				,207	,144	
Linear-by-Linear Association	1,725[c]	1	,189	,207	,144	,085
N of Valid Cases	91					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 7,43.

b. Computed only for a 2x2 table

c. The standardized statistic is 1,314.

The relationship between the preservation of vascular-nerve bundles and the frequency of biochemical recurrence is presented in table 101 a-b.

Table 101 - a.

		Biochemical recurrence					
		yes		no		Total	
		Count	Column N %/ % of subgroup	Count	Column N %	Count	Column N %
Nerve sparing		**26**	**(100,0%)**	**65**	**(100,0%)**	**91**	**(100,0%)**
	yes	10	(38,5%)/ 22,2%	35	(53,8%)	45	(49,5%)
	no	16	(61,5%)/ 34,7%	30	(46,2%)	46	(50,5%)

Table 101 - b. Chi-Square BCR and nerve sparing

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1,758[a]	1	,185	,247	,137	
Continuity Correction[b]	1,197	1	,274			
Likelihood Ratio	1,771	1	,183	,247	,137	
Fisher's Exact Test				,247	,137	
Linear-by-Linear Association	1,739[c]	1	,187	,247	,137	,078
N of Valid Cases	91					

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 12,86.

b. Computed only for a 2x2 table

c. The standardized statistic is -1,319.

Table 102 reflects the distribution of patients according to the histological result according to the ISUP grade group of the preoperative biopsy and the permanent histological preparation, as well as the pT stage of PCa according to the frequency of evidence of local recurrence or distant (bone) metastases in the patients.

Table 102.

		Local recurrence/metastasis					
		no		yes		Total	
		Count	%	Count	%/ % of subgroup	Count	%
Grade Group biopsy		**69**	**(100,0%)**	**4**	**(100,0%)**	**73**	**(100,0%)**
	1	14	(20,3%)	1	(25,0%)/ 6,6%	15	(20,5%)
	2	22	(31,9%)	0	(0,0%)/ 0%	22	(30,1%)
	3	24	(34,8%)	1	(25,0%)/ 4%	25	(34,2%)
	4	8	(11,6%)	1	(25,0%)/ 11,1%	9	(12,3%)
	5	1	(1,4%)	1	(25,0%)/ 50%	2	(2,7%)
Grade Group surgery		**71**	**(100,0%)**	**5**	**(100,0%)**	**76**	**(100,0%)**
	1	2	(2,8%)	0	(0,0%)/ 0%	2	(2,6%)
	2	22	(31,0%)	0	(0,0%)/ 0%	22	(28,9%)
	3	22	(31,0%)	2	(40,0%)/ 8,3%	24	(31,6%)
	4	12	(16,9%)	0	(0,0%)/ 0%	12	(15,8%)
	5	13	(18,3%)	3	(60,0%)/ 18,7%	16	(21,1%)
TNM		**71**	**(100,0%)**	**5**	**(100,0%)**	**76**	**(100,0%)**
	pT2	35	(49,3%)	2	(40,0%)/ 4,2%	37	(48,7%)
	pT3	35	(49,3%)	3	(60,0%)/ 7,8%	38	(50,0%)
	pT4	1	(1,4%)	0	(0,0%)/ 0%	1	(1,3%)

Table 103 presents the frequency distribution of patients according to preoperative PSA values and MRI findings and the frequency of local recurrence or distant metastases.

Table 103.

		Local recurrence/ Metastasis					
		no		yes		Total	
		Count	%	Count	%/ % of subgroup	Count	%
PSA groups		**71**	**(100,0%)**	**5**	**(100,0%)**	**76**	**(100,0%)**
	< 10 ng/	40	(56,3%)	1	(20,0%)/ 2,4%	41	(53,9%)
	> 10 ng/	31	(43,7%)	4	(80,0%)/ 11,4%	35	(46,1%)
MRI PIRADS		**52**	**(100,0%)**	**3**	**(100,0%)**	**55**	**(100,0%)**
	2	2	(3,8%)	0	(0,0%)/ 0%	2	(3,6%)
	3	6	(11,5%)	1	(33,3%)/ 14,2%	7	(12,7%)
	4	29	(55,8%)	1	(33,3%)/ 3,3%	30	(54,5%)
	5	15	(28,8%)	1	(33,3%)/ 6,2%	16	(29,1%)
	не	55	(77,5%)	4	(80,0%)/ 6,7%	59	(77,6%)

Correlation index for the above indicators is presented in table 104 and 105.

Table 104.

		Local recurrence/ Metastasis	Grade Group Biopsy	Grade Group surgery	MRI PIRADS	TNM
Local recurrence/ Metastasis	Rank-biserial	1	,182	,221	-,029	,037
	Sig. (2-tailed)		,122	,055	,832	,749
	N	76	73	76	55	76

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 105.

		Local recurrence/ metastasis	(PSA) ng/ml	Histological variants
Local recurrence/ Metastasis	Point-biserial	1	,026	,171
	Sig. (2-tailed)		,823	,140

Table 106 a-b reflects the relationship between the evidence of local recurrence or distant metastases of the disease and the frequency of positive surgical margins or penetration of the prostatic capsule.

Table 106 - a.

		Local recurrence/ metastasis					
		no		yes		Total	
		Count	%	Count	%/ % of subgroup	Count	%
R-status (R+)		**71**	**(100,0%)**	**5**	**(100,0%)**	**76**	**(100,0%)**
	yes	34	(47,9%)	2	(40,0%)/ 5,5%	36	(47,4%)
	no	37	(52,1%)	3	(60,0%)/ 7,5%	40	(52,6%)
Prostate capsule penetration		**71**	**(100,0%)**	**5**	**(100,0%)**	**76**	**(100,0%)**
	yes	19	(26,8%)	3	(60,0%)/ 13,6%	22	(28,9%)
	no	52	(73,2%)	2	(40,0%)/ 3,7%	54	(71,1%)

Table 106 – b. Chi-Square Tests – Local recurrence/Metastasis and prostate capsule penetration.

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2,509[a]	1	,113	,142	,142	
Continuity Correction[b]	1,153	1	,283			
Likelihood Ratio	2,243	1	,134	,313	,142	
Fisher's Exact Test				,142	,142	
Linear-by-Linear Association	2,476[c]	1	,116	,142	,142	,119
N of Valid Cases	76					

a. 2 cells (50,0%) have expected count less than 5. The minimum expected count is 1,45.

b. Computed only for a 2x2 table

c. The standardized statistic is 1,574.

Table 108 reflects the relationship between the average number of histological variations in patients and the incidence of local recurrence or distant metastases of PCa.

Table 108.

		Local recurrence/Metastasis		
		No	**Yes**	**Total**
Histological variants	Count	71	5	76
	Mean	,944	1,600	,987
	Standard Deviation	,924	1,342	,959

Regarding postoperative therapy, the following results were reported. RT was administered in 67% of patients; androgen deprivation therapy was applied in 64% of patients; combined adjuvant therapy was administered in 55% of patients.

Table 109 reflects the frequency distribution of patients according to the application of adjuvant therapy and the histological result according to ISUP Grade group from the preoperative biopsy and permanent histological preparation.

Table 109.

		Adjuvant therapy	
		no	**yes**
Grade Group biopsy		**21 (100,0%)**	**64 (100,0%)/ %of subgroup**
	1	8 (38,1%)	8 (12,5%)/ 50%
	2	8 (38,1%)	19 (29,7%)/ 70%
	3	3 (14,3%)	25 (39,1%)/ 89%
	4	2 (9,5%)	8 (12,5%)/ 80%
	5	0 (0,0%)	4 (6,3%)/ 100%
Grade Group surgery		**22 (100,0%)**	**68 (100,0%)**
	1	2 (9,1%)	1 (1,5%)/ 33%
	2	9 (40,9%)	16 (23,5%)/ 64%
	3	7 (31,8%)	22 (32,4%)/ 24,1%
	4	3 (13,6%)	9 (13,2%)/ 75%
	5	1 (4,5%)	20 (29,4%)/ 95%

Table 110 presents the distribution of patients according to the applied adjuvant therapy and preoperative PSA, as well as the MRI findings according to PIRADS.

Table 110.

		Adjuvant therapy	
		no	**yes**
PSA groups		**22 (100,0%)**	**68 (100,0%)/ % of subgroup**
	< 10 ng/	15 (68,2%)	31 (45,6%)/ 67,4%
	> 10 ng/	7 (31,8%)	37 (54,4%)/ 84%
MRI PIRADS		**17 (100,0%)**	**50 (100,0%)**
	2	0 (0,0%)	2 (4,0%)/ 100%
	3	4 (23,5%)	4 (8,0%)/ 50%
	4	11 (64,7%)	25 (50,0%)/ 69,4%
	5	2 (11,8%)	19 (38,0%)/ 90%

Table 111 presents the relationship between the pT stage of the disease from the permanent histological preparation and the need for postoperative therapy.

Table 111.

		Adjuvant therapy	
		no	**yes**
TNM		**22 (100,0%)**	**68 (100,0%)/% of subgroup**
	pT2	20 (90,9%)	24 (35,3%)/ 54,5%
	pT3	2 (9,1%)	43 (63,2%)/ 95%
	pT4	0 (0,0%)	1 (1,5%)/ 100%

The frequency distribution of patients by number of histological variations versus the need for adjuvant therapy is depicted in Table 112.

Table 112.

		Adjuvant therapy		
		yes	**no**	**Total**
Histological variants	Count	68	22	90
	Mean	1,088	,773	1,011
	Standard Deviation	,958	,813	,930

6. Discussion

PCa is a disease of marked social significance. The number of newly diagnosed cases is growing annually, with 1,276,106 new cases of the disease being diagnosed worldwide in 2018, representing 7.1% of all male cancers [2]. In Bulgaria in 2013, the frequency of PCa was calculated at 79.9/100,000 men. The above-mentioned facts argue the need for the continuous conduct of scientific studies, research and practical activities related to the diagnosis and therapy of the disease.

The incidence of PCa has been found to increase after the age of 50 years, with the average age of diagnosis in Europe being 66 years [32]. According to various scientific data, the lifetime risk of clinically apparent PC is 9.5%, and the risk of death due to PCa is 2.9% [35]. The mean age of the patients in the present sample was 64.7 years (SD – 5.85).

According to worldwide data, a family history is found in about 20% of PCa patients [39]. The association of mutations in HPC1, HPC2/ELAC2 BRCA1, BRCA2 and a number of other genes with an increased predisposition to PC has been widely studied and proven [40] [41] [42]. A number of studies have also investigated the association of the number of CAG repeats in the exon 1 region of the androgen receptor (AR) gene and PC [44]. A meta-analysis by Qingchuan Zhang and colleagues proved the association of polymorphisms in the vitamin D receptor gene (VDR - 3 'UTR VDR (FokI, BsmI, ApaI and TaqI)) and the risk of PCa.

In the present study, consanguinity was found in 15% of patients. The mean age at diagnosis was found to be lower in patients with a family history (60.6 years vs. 63.6 years). Additional analysis demonstrated high values of Gleason's sum from the permanent histological preparation in patients with family history of PCa (the probability of Grade group 4 and 5 from the permanent histological preparation was 22% vs. 13%; 33% vs. 20% - vs. unrelated patients), as well as a higher mean number of histological features associated with poor disease prognosis (0.91 vs. 1.22). Patients with a family history showed a higher risk of biochemical recurrence of the disease compared to patients without a genetic predisposition: 33% versus 29%.

Additional genetic studies were carried out within the framework of scientific project D - 141/23.04 2019 (principal researcher: Dr. G. Ivanov) on the topic: "Monitoring of clinical and histo-pathological parameters, including AR (CAG)n and VDR (AT)n genetic markers in relation to increased predisposition and aggressive clinical course of the disease prostate carcinoma after radical laparoscopic prostatectomy in Bulgarian patients." proving that the presence of a molecular profile with a short number of AR(CAG)n repeats (</=22) and allelic combinations of VDR(AT)n (SL; LL) represent genetic risk factors for predisposition to an aggressive course of prostate cancer, because:

• Patients with AR(CAG)n </= 22 have higher PSA values at diagnosis (35 ng/ml versus 13.5 ng/ml in patients with low genetic risk).

• In patients with AR(CAG)n </= 22, higher values of Gleason score (GS) from biopsy of the prostate gland and Gleason score (GS) from the preparation after radical prostatectomy (mean GS from biopsy 7.33 vs. 6.63; mean GS from permanent preparation 8 vs. 7.57 in patients with low genetic risk).

• In patients with AR(CAG)n </= 22, a higher frequency of histological features in the preparation from radical prostatectomy, determining a poor prognosis of the disease -

Lymphovascular invasion, Angioinvasion, Ductal component and Light cell component was found.

• In patients with AR(CAG)n </= 22, an increased risk of seminal vesicle invasion was found (66% vs. 42% in patients with low genetic risk).

• In patients with SL and LL allelic combinations according to VDR(AT)n, a higher PSA value was found at diagnosis of the disease in contrast to SS allelic combination (6 ng/ml (SS) vs. 21.5 ng/ml (SL) versus 21.67 ng/mL (LL)).

• The Gleason score (GS) of the histological preparation after radical prostatectomy is increased in patients with a VDR(AT)n profile in the high-risk group (mean GS in SS – 7 vs. 7.66 in SL vs. 8 in LL genotype). Allelic combination LL by VDR(AT)n is associated with a significant risk for pathological progression of the disease - mean GS from preoperative biopsy - 7.00; average GS of permanent preparation - 8.00.

• The risk genotype combinations SL and LL according to VDR(AT)n are characterized by a higher frequency of histological features in the preparation from radical prostatectomy, which are associated with a poor prognosis of the disease - perineural invasion, angioinvasion, cribriform component and clear cell component.

• In patients with the LL genotype according to VDR(AT)n, an increased risk of invasion of the disease in the seminal vesicles was found compared to patients with the SL genotype according to VDR(AT)n – 66.6% versus 33.3%.

A 2013 meta-analysis demonstrated the association of increased body mass index (BMI) with the risk of PCa development, aggressive course of the disease, biochemical recurrence, and worsened functional outcomes after surgical treatment [59].

In the present series of patients, the mean BMI was 28.464 ± 4.387. 51% of patients were preobese (BMI between 25.00 – 29.99), followed by patients with obesity grade I (22%). Analysis of the data from the present work found no correlation between BMI and intraoperative blood loss or the need for hemotransfusion. A pronounced statistical relationship between the average operating time and the increase in BMI was proven: the longest average operating time took place in patients with obesity of the third degree - 230,000 ± 56,569, while the shortest operating time was in patients of normal weight - 176,25 ± 27,042. In the patients in the present sample, increasing BMI had no effect on the incidence of early and late postoperative complications. We also found no significant relationship between the increase in BMI and the patients' erectile function at 6 and 12 months postoperatively. In the present study, it proved to be a risk factor for incontinence at 12th postoperative month: BMI 29.67 vs. 28.35 in incontinent vs. continent patients.

After the discovery of PSA in 1979 by Wang et al., this marker became a cornerstone of PC screening. According to an analysis by the American Cancer Society, using an upper limit of 4 ng/ml, the sensitivity of the indicator in diagnosing any PC is 21% and significantly higher for PC with high grading (GS above 8) – 51%; average positive predictive value – 30% [73].

In the present patient sample, the mean PSA value at diagnosis was 14.81 ng/ml ± 11.89. We found a statistically significant difference in mean PSA values between the three groups by pT (H=7.786, df=2, Sig.=0.020) – 9.6 ng/ml at T2 vs. 13.57 ng/ml at T3 vs. 40 ng/ml at T4. A statistically significant difference in mean PSA values was demonstrated between subjects with

and without capsule penetration (16.2 ng/ml vs. 9.75 ng/ml; Sig.=0.007), as well as in subjects with and without biochemical recurrence (17.5 ng/ml vs. 9.60 ng/ml; Sig.=0.018).

Since its introduction in 1982, MRI has offered increasingly reliable visualization of potentially significant cancerous lesions of the prostate. The importance of MRI as a diagnostic modality in PC has significantly increased since the introduction of mNRI, in which, according to various data, up to 88% specificity and 74% sensitivity have been achieved in the visualization of PC [89].

The results of the present work show that a statistically significant correlation is established between the MRI finding and the Grade Group of the preoperative biopsy (R=0.262; Sig.=0.027). In a sub-analysis by groups, no statistically significant difference was found in the number of persons ($\chi 2$=10.732, df=12, Sig.=0.552). Notably, 100% of patients with an ISUP Grade Group 5 biopsy result displayed a PIRADS v2 type 5 lesion. We found no correlation between MRI findings and intraoperative blood loss (R=0.12; p=0.922). Regarding the need for intraoperative hemotransfusion, it is proven that as the type of lesion increases, so does the frequency of hemotransfusion, with 40% of patients transfused during LRP falling into the PIRADS 4 group, and the remaining 60% of those transfused into the PIRADS 5 group. The correlation did not reach statistical significance (p=0.124). In the current sample, it was also found that 66.7% of patients with an intraoperative complication during LRP had a type 4 lesion, and the remaining 33.3% had a PIRADS type 5 lesion (p=0.331). We established an inversely proportional relationship between PIRADS findings and operative time: PIRADS 3 - 193,500 ± 34,964 minutes, and the shortest - patients with PIRADS 5 type lesion - 170,455 ± 29,192 minutes (p=0.128). Regarding the pT stage of the disease, PIRADS 3 found that 70% of patients were pT2, PIRADS 4 56.4% of patients were pT2 and 43.6% were pT3, and PIRADS 5 36.4 % were with pT2 versus 63.6% with pT3 (p=0.070). We demonstrated an increase in the frequency of positive surgical margins with increasing PIRADS findings: 20% in PIRADS 3 versus 41% in PIRADS 4 versus 54.5% in PIRADS 5 (p=0.429). No significant correlation was found between the increase in the PIRADS finding and the frequency of biochemical, local recurrence and distant metastases of the disease (p=0.671; p=0.832). These results confirm the increasing role of MRI in the diagnosis and risk stratification of PC.

With regard to the histological indicators of PCa in the world literature and, accordingly, in the present work, the following dependencies are demonstrated:

Analyzes of large LRP series by J. Rassweiler, M. Schulze, D. Teber, O. Seemann, T. Frede, B. Guillonneau, and P. Bove regarding pTNM in the world literature estimated the probability of positive resection lines at an average of 4 % at stage pT1 – pT2a/b; 18% at stage pT2c; 33-39% in pT3a; up to 81% in pT3b-c. The incidence of biochemical recurrence was 8.6% (4 to 15.3%) for pT2 and 17.5% (15 to 20.6%) for pT3 at five-year follow-up, respectively. The disease-free survival rate reached 92% for pT2a/bN0; 88% for pT2cN0; 77% for pT3aN0; 44% for pT3bN0 and 50% for pT1-3N1 [112] [113] [114].

In their 2012 analysis, Busch et al demonstrated a correlation of pathologic tumor stage, postoperative Gleason score, and surgical margin status as significant predictors of biochemical disease recurrence ($P < 0.001$) [115]. In the series of patients in this study, biochemical recurrence-free survival at 5, 8, and 10 years was 83.9%, 78.6%, and 75.6%, respectively.

In 2020, Georgieva R, Slavov CH and colleagues published an analysis based on 121 radical prostatectomies on the correlation between preoperative GS and the result of permanent histological preparation [207]. The authors found concordance between histological results in 59.2%; pathological progression of the disease (upgrading) was demonstrated in 30.1%, and downgrading in 10.7%.

In the present series of patients, the distribution of patients by ISUP Grade group from the biopsy was: GG 1 – 16%; GG2 – 33%; GG 3 – 29%; GG4 – 11%; GG5 – 4%. A statistically significant relationship was demonstrated between the PIRADS MRI finding and the prostate gland biopsy result according to ISUP Grade groups (r=0.262; p=0.027). A statistically significant correlation was found between the ISUP Grade Group prostate biopsy result and the T stage of the disease after LRP (r=0.252; p=0.015). We demonstrated a statistically significant correlation between the ISUP Grade Group prostate biopsy score and the number of histological variations in the permanent histological preparation (r=0.252; p=0.015). A statistically significant correlation was demonstrated between the result of the prostate gland biopsy according to ISUP Grade biopsy groups and the probability of the occurrence of histological progression of the disease (r = -0.280; p = 0.007), as well as the establishment of penetration of the prostatic capsule by PC (r=0.387; p=0.000).

In the patients from the current sample, the following distribution of patients according to the ISUP Grade group of the permanent histological preparation was established: GG 1 – 4%; GG2 – 31%; GG3 – 30%; GG4 = 13%; GG5 – 22%. Histological (pathological) progression of PC was demonstrated in 47% of patients.

The distribution of patients by pT stage in the present study was as follows: pT2a – 9%; pT2b – 10%; pT2c – 38%; pT3a – 19%; pT3b – 23%; pT4 – 1%.

Histological features such as cribriform component (n=16), ductal component (n=12), mucinous component (n=3) and perineural invasion (n=67) were found in 68% of patients.

When examining the data, it was found that as the score increased by ISUP Grade groups, the frequency of pT3 stage of the disease grew: 0% of cases with GG1, 32.3% of cases with GG2, 46.7% of cases with GG3, 61.5% of cases with GG4 and 72.7% percent of cases with GG5. The only patient with pT4 stage falls into GG4 according to ISUP. A statistically significant relationship was demonstrated between an increase in GG from a durable preparation and the pT stage of the disease (r=0.368; Sig = 0.00). In the current study, it was demonstrated that with increasing ISUP Grade Group from the permanent preparation, histological progression occurred in 48.1% of GG3 patients, 53.8% of GG4 patients, and 81% of GG5 patients. An increasing probability of presence of prostatic capsule penetration was reported with increasing ISUP Grade group. The data show that the percentage of positive surgical margins was highest in patients with Grade Group 5 – 59.1% of patients in the group. The second most frequent R+ status of the disease are patients with Grade group 3 – 53.3%. Positive surgical margins were not documented in any Grade Group 1 patient. There was a marked tendency for biochemical recurrence to increase with increasing ISUP Grade Group – 15.4% of GG2 patients, 27.6% of GG3 patients, 33.3% of GG4 patients and 42.9% of GG5 patients. It was found that the main number of patients with clinical recurrence of PCa (3 of 5 cases) were patients with GG5 (18.8% of patients in the ISUP group.

In the present study, the following correlations were found with respect to pT stage of disease: an increase in the incidence of pathologic disease progression with increasing pT stage (43.8% in pT2 vs. 50% in pT3 vs. 100% in pT4); an increase in the frequency of positive surgical margins with increasing pT stage (25.5% with pT2 vs. 66.7% with pT3 vs. 100% (n=1) with pT4); the increase in the pT stage of the disease and the frequency of penetration of the prostatic capsule: 5.9% in pT2 vs. 45.8% in pT3 vs. 100% (n=1) in pT4); an increase in the mean number of histological variations of patients with pT3 versus pT2 (1.29 vs. 0.7).

Multiple studies have compared the operative, oncologic, and functional outcomes of open, laparoscopic, and robotic-assisted radical prostatectomy.

A meta-analysis of 19 studies published by Parsons et al reported less blood loss and a 77% lower rate of hemotransfusion for LRP and RALP (SMD -1.74, 95% confidence interval [CI] -1.74 to -1.49, P<0.001); (RR 0.23, 95% CI 0.11 to 0.49, P < 0.001) [118]. The percentage of positive surgical margins was comparable for the three groups. (RR 0.88, 95% CI 0.74 to 1.06, P = 0.17).

A comparative analysis by Frota et al demonstrated the superiority of RALP in terms of postoperative continence (at 0-1 pad per day): between 90% to 92% after open prostatectomy, 82% to 96% after LRP, and 95% to 96% after RALP [119]. With similar oncological results, an advantage of LRP and RALP was demonstrated in terms of blood loss, frequency of hemotransfusion, hospital stay.

Coelho et al pooled data from a total of 58 studies and reported the following results comparing the open technique versus LRP versus RALP: rate of hemotransfusion: 20.1% vs. 3.5% vs. 1.4%; rate of postoperative complications: 10.3% vs. 10.9% vs. 10.3%; positive surgical margins: 24% vs. 21.3% vs. 13.6%; 12-month continence: 79% vs. 84.8% vs. 92%; potency at 12 months (with neurovascular preservation): 43-60% vs. 31-54% vs. 59-93% [120].

In a study by Georgiev, M and a team from the Department of Urology at the Sofia University, the effectiveness and safety of LRP and RALP were also compared [123]. The comparative analysis demonstrated an advantage regarding the recovery of micturition control in the early period (up to the third postoperative month) in RALP. Robotic prostatectomy has also been shown to have a lower rate of positive surgical margins and less blood loss. No significant difference was demonstrated in terms of operative time, time to decatheterization, hospital stay, frequency of complications.

The importance of preserving the neurovascular bundle in prostatectomy has been the subject of numerous studies since the late 1980s. In 2009, Stolzenburg et al published results from 2400 consecutive LRPs. In the series, neurovascular preservation was performed in 956 patients (in 672 bilaterally; in 284 unilaterally) [127]. Results indicated that performing bilateral neurovascular bundle preservation (especially in patients younger than 55 years) resulted in potency rates of 32.4%, 75.3%, and 84.9% at 3, 6, and 12 months after the operation. A 2015 meta-analysis by Reeves et al examined the role of nerve bundle preservation on postoperative continence after LRP [128]. A total of 13,749 patients were included in the study. The results indicate that the preservation of vascular-nerve bundles (especially with bilateral preservation) leads to a significant increase in urinary continence levels in the period up to 6 months postoperatively. In a period after 6 months, the levels of continence equalized for both groups.

The so-called posterior reconstruction (or Rocco stitch) is widely used in LRP in order to achieve better and earlier postoperative continence. A 2012 meta-analysis summarized the results of 11 studies on the topic [133]. The data indicated that posterior reconstruction significantly improved early continence up to 90 days after catheter removal ($p = 0.004$), while continence after Day 90 is not significantly affected. No statistically significant effect was reported in terms of positive surgical margins or incidence of complications such as acute urinary retention or bladder neck sclerosis. In 2016, Grasso, A. and colleagues published a meta-analysis of 21 studies related to posterior reconstruction in radical prostatectomy [208]. Analysis of the data yielded similar results, with the authors reporting that the technique increased continence rates at 7, 30, and 90 postoperative days, but not at 180 postoperative days. Performing a posterior reconstruction also significantly lowers the risk of urinary leakage from the anastomosis without increasing the incidence of positive surgical margins, urinary retention, and bladder neck sclerosis.

The role of LRP in locally advanced PC has been studied by a number of authors. Gözen et al published a study of 2375 patients after LRP, in which the patients were divided into three groups: group 1 - stage cT1 PC (417 patients); group 2 – PC in stage cT2 (1842 patients); group 3 – PC in stage cT3 (492 patients) [148]. Patients in group 3 demonstrated the highest incidence of extracapsular invasion, seminal vesicle invasion, positive surgical margins, and administration of adjuvant therapy. The results in the three groups regarding urinary continence were similar in the three groups. The lowest degree of erectile dysfunction was demonstrated in patients in group 1. Cancer-specific survival (CSS) was highest in group 1, while overall survival (OS) and complication rates were without statistically significant difference for the three groups.

The results of a series of 40 patients after LRP were published by Zh. Chitalov and colleagues in 2019 [214]. The authors reported a mean operative time of 190 minutes, positive surgical margins in 13% of patients, postoperative hemotransfusion in 17% of patients. Rectal trauma was demonstrated in three patients, one requiring a colostomy. A 52.5% patient continence rate at the second postoperative month was reported.

The mean operative time for the patients in the present series was 183.2 ± 41 minutes. Average blood loss is 174 ml (50 - 550 ml). Intraoperative hemotransfusion of 1 bag of Er-mass was performed in 11% of patients.

We recorded the longest average operative time in patients with third degree obesity - $230{,}000 \pm 56{,}569$, while the shortest operative time in patients with normal weight - $176{,}25 \pm 27{,}042$. We found that in patients with a PSA value above 10 ng/ml, LRP lasted an average of 5 minutes longer: $185{,}900 \pm 43{,}162$ versus $180{,}600 \pm 40{,}891$ minutes. No correlation was found between histological results according to ISUP Grade groups, pT stage of the disease and operative time. We reported a significant relationship between the increasing volume of the gland and the longer operative time, as for glands under 49 cubic centimeters the average operative time was 173.97 ± 45.21 minutes, while when performing LRP on prostate glands with a volume of more than 100 cubic centimeters the average operative time was 197.14 ± 34.53.

No correlation was found between intraoperative blood loss and BMI ($r=0.87$; $Sig = 0.389$) and the presence of comorbidities in patients ($r=0.113$; $Sig = 0.261$). The data from the analysis proved the existence of a statistically significant relationship between the presence of past diseases and greater blood loss in LRP: mean blood loss 184.375 ± 99.01 vs. 165.965 ± 89.40

ml. The results indicate higher values of blood loss in patients with PSA below 10 ng/ml – 187.6 ml versus 162 ml for preoperative PSA above 10 ng/ml. A statistically significant correlation was found between blood loss (ml) and pT stage (r=0.228, N=100, p=0.017). Mean blood loss pT2 vs pT3 vs pT4 - 154,510 ± 108,154 vs 194,792 ± 72,376 vs 250,000 mL. In a comparative analysis of the intraoperative blood loss data and the preoperative histological result of the patients according to ISUP Grade groups, it was found that the greatest blood loss was in the patients with Grade group 4 - 227,273 ± 84,746 ml. Second, in patients with Grade group 5, a blood loss of 187,500 ± 25,000 ml was documented. Regarding GG from the permanent histological preparation, it was found that the greatest blood loss was reported in patients with Grade group 4 - 200,000 ± 95,743 ml. We found an inverse relationship between prostate gland volume and intraoperative blood loss: the highest average blood loss was reported in patients with a prostate gland below 49 cubic centimeters - 182.286 ± 97.626 milliliters; in patients with a prostate gland volume between 50 and 99 cubic centimeters, the mean blood loss was 177,272 ± 94,448 milliliters, and in patients with a prostate gland volume greater than 100 cubic centimeters, the mean blood loss was 137,500 ± 47,871. A greater mean blood loss was demonstrated in the patients in whom preservation of the vascular-nerve bundle was performed - 178,571 ± 110,867 ml. against 171.176 ± 75.568 ml – without reaching statistical significance.

Establishes a relationship between the presence of comorbidities and the inevitability of blood transfusion, as 81.8% of patients who received hemotransfusion during LRP had at least one comorbidity, but statistical significance was not reached (Sig=0.22) . The relative frequency of intraoperative hemotransfusion in patients with comorbidities was 12% versus 8% in patients without comorbidities. A significant relationship between the presence of past diseases and the inevitability of blood transfusion was demonstrated, with 63.6% of patients receiving hemotransfusion during LRP having at least one past surgically treated disease. The relative frequency of intraoperative hemotransfusion in patients with past surgical diseases was 14.5% versus 9.62% in patients without them. No correlation was found between the frequency of intraoperative hemotransfusion and ISUP Grade group from biopsy and permanent histological preparation (r= -0.19; p = 0.856 and r= -0.106; p=0.295, respectively). The main percentage of patients with a blood transfusion were in ISUP Grade group 2 of the preoperative biopsy - 55.6%, followed by patients with ISUP Grade group 3 - 22.2%. The distribution by ISUP Grade groups of the permanent histological preparation is similar, with 45.5% of patients in need of intraoperative hemotransfusion being in ISUP Grade group 2, and in second place are patients with ISUP Grade group 3 and 5 - 18.2 % respectively for each group. No statistically significant relationship was found between the pT stage of the disease and intraoperative transfusion (r=-0.92; p =0.361). 63.6% of transfused patients diagnosed with pT2 disease, and 36.4% of patients with pT3. The relative frequency of intraoperative hemotransfusion in pT2 – 13.7% vs. 8.3% in pT3 vs. 0% in pT4. In 63.6% of cases with blood transfusion, PSA was below 10 ng/ml, and no statistically significant correlation was reached (r= -0.146; p = 0.147). It was proven that nerve sparing was performed in 72.7% of the patients who were hemotransfused. The relative frequency of intraoperative hemotransfusion in patients with nerve sparing was 16.3% versus 5.8% in patients without nerve sparing. However, the dependence did not reach statistical significance (p=0.118).

Positive surgical margins in the present sample were found in 45% (n=45) of patients. The main locus was the apex of the prostate (n=37), followed by the base of the gland (n=13). Penetration of the prostatic capsule was found in 26% of patients.

The frequency of various intra- and postoperative complications in LRP is considered in numerous studies in the world literature.

According to the results of various studies in patients after open, LRP or RALP, the frequency of occurrence of sclerosis of the bullous neck varies between 0.2% and 4.5% (average about 2%) [162] [163] [164].

In studies by Naselli et al, Liss et al, Briganti et al, Yuh et al, et al. when conducting LRP and RALP with lymphatic dissection, reported a frequency of occurrence of lymphocele about 5% (2.2% - 12.6%) [169] [170] [171] [172]. A prospective randomized trial by Grande et al found no statistically significant difference comparing surgical techniques of clipping versus bipolar lymphatic vessel coagulation on the incidence of lymphocele formation [175]. Stolzenburg et al demonstrated that peritoneal fenestration during extraperitoneal LRP significantly reduced the incidence of postoperative lymphocele from 32% to 6% [176]. In 2011, Waldert et al. proved that the application of hemostatic agents (Floseal) in the area of performed lymphatic dissection in LRP or RALP reduced the frequency of lymphocele formation from 14.5% to 3.1% [177].

In a multi-institutional study, Secin et al investigated the incidence of DVT and BTE in prostate cancer patients undergoing LRP [179]. Symptomatic thromboembolism developed in 31 (0.5%) of 5951 patients (95% confidence interval [CI], 0.4%, 0.7%). In 22 (71%) of the above patients only DVT was demonstrated, in 4 BTE was found without DVT, and in 5 both DVT and BTE were found. As a result of BTE, exitus lethal occurred in two of the patients. The analysis shows that the main risk factors for the occurrence of the mentioned complications are: history of previous thromboembolism (OR = 13.5; 95% CI, 1.4, 61.3), smoking (OR = 2.8; 95% CI, 1.0, 7.3), larger prostate volume (OR = 1.18; 95% CI, 1.09 , 1.28), need for patient revision (OR = 20.6; 95% CI, 6.6, 54.0), longer operative time (OR = 1.05; 95% CI, 1.02, 1.09). On the other hand, non-adjuvant therapy, body mass index, surgical approach, pathological stage, perioperative transfusion and heparin administration did not have a significant correlation with the occurrence of thromboembolism. In other series of patients after LRP, a similar frequency of thromboembolism was found: Stolzenburg et al – 0.6%; Lein et al. – 0.8% [180] [181].

A number of studies have looked at the incidence of hemorrhagic complications after LRP. In their series of patients, Rassweiler, Türk, Guillonneau, Hoznek reported damage to the epigastric vessels in 0.27% and damage to the external iliac vessels in 0-0.8% of cases [109]. In 2.8% of cases, hemorrhagic complications are proven in the early postoperative period. Hemotransfusion was performed in 1.6 – 4.1% of patients.

Ureteral damage in LRP Türk, Guillonneau, Hoznek reported in 0.36% (0 – 0.7%) of cases in their large patient samples [109]. Teber, Rassweiler et al published the experience of the Heilbronn center with ureteral lesions in LRP [183]. The frequency of ureteral lesion was 0.13% in 2164 LRP performed. The authors report two cases of complete transection of the ureter.

In large series of LRP by Rassweiler, Türk, Guillonneau, Hoznek, neurological damage was reported in less than 1% of cases [109]. Lein et al published results of over 1000 LRPs performed, with a neurological lesion found in 1.8% of cases [171].

In large series of LRP by Rassweiler, Türk, Guillonneau, Hoznek, intestinal damage was reported in 1% of cases (0.8-1.9%) [109]. In another large series of PC patients who underwent

LRP, published by Lein et al., a similar incidence of the described complication was found – 0.9% of cases, postoperative ileus/subileus in 2.5% of cases [171].

Regarding lesions of the rectum, Rassweiler, Türk, Guillonneau, Hoznek reported intestinal damage in 1.5% of cases (1-2.4%) [109]. Lein and colleagues found a similar frequency of the described complication – 3.3% of cases in their series of patients after LRP [171]. In 2017, in the series Dimitrov Pl. and a team of the Department of Urology at the Sofia University reported an incidence of rectal damage of 1.6% in 118 cases of LRP [185].

Intraoperative complications in the present series of patients were reported in 6% of the patients – respectively: lesion of the peritoneum (n=2); need for extended cystoplasty (n=1); conversion due to intractable adhesions (n=1); bleeding and difficult course of surgery due to pronounced intravesical partition (n=1); marked adhesions to inguinal hernioplasty cloth (n=1). We found no statistically significant correlation between the occurrence of intraoperative complications and anesthetic risk (p=0.90); the presence of accompanying diseases (p=0.311); the age of the patients (p=0.740). The incidence of intraoperative complications was 8% in patients with comorbidities versus 0% in patients without comorbidities. The incidence of intraoperative complications was 6.2% in patients with past surgical diseases versus 5.7% in patients without them. The percentage of intraoperative complications was the highest in patients aged between 60 and 70 years - 8.3%. It was found that in 66.7% of patients with an intraoperative complication, the preoperative PSA value was above 10 ng/ml (p =0.928). The incidence of intraoperative complications was 4% in patients with PSA below 10 ng/ml versus 8% in patients with preoperative PSA above 10 ng/ml. Regarding MRI, it is proven that 66.7% of patients with a complication during LRP had a type 4 lesion, and the remaining 33.3% had a PIRADS type 5 lesion, suggesting a statistical relationship between the two parameters, without this being unequivocally proven (p=0.331). No correlation was found between the histological result according to ISUP Grade Group from the preoperative biopsy and the permanent histological preparation and the indicators of intraoperative complications (p= 0.162; p=0.910). We found that 66.67% of the patients with a complication during LRP had a pT3 disease stage against 33.3% of the remaining patients with a complication, in which pT2 disease was proven (p=0.584); relative frequencies of complications for pT2 and pT3, respectively – 3.9% and 8.3% in the subgroups. An intraoperative complication was not documented in the only patient with stage pT4 disease Our data analysis indicated that there was no statistically significant relationship between the performance of Nerve sparing and the occurrence of intraoperative complications (Pearson Chi-Square = 1.150; p=0.390). The incidence of intraoperative complications was 6.1% in patients with nerve sparing versus 5.8% in patients without nerve sparing.

Early postoperative complications were found in 12% of patients in the present sample. The most frequent early postoperative complication in our sample was the evidence of uroinfection – in 7 of the patients. Second in frequency was bleeding with the need for transfusion (2 cases), followed by the other complications that occurred in one patient each – leakage of urine from the anastomosis, hematuria, hematoma of the scrotum. Hemotransfusion was performed in two patients (2%) in a volume of 2 bags of erythrocyte mass and 1 bag of erythrocyte mass, respectively. The mean preoperative hemoglobin was 151 ± 12.9 g/L, and the mean postoperative hemoglobin was 131.2 ± 12.74 g/L. A mean drop in hemoglobin of 19.8 ± 9.71 g/l was reported in patients after LRP. The data of the analysis did not allow us to prove a correlation between the occurrence of early postoperative complications and the anesthetic risk,

the patient's age (p=0.119) and the presence of accompanying diseases (p=0.761). 66.7% of early complication cases occurred in patients with a preoperative PSA value below 10 ng/ml (p=0.119). However, the following dependence was established: significantly higher frequency of complications in patients over 70 years of age – 20%. We found no correlation between an increase in Grade group from the preoperative or permanent histology and the occurrence of early complications (p=0.636; p=0.832). However, it was found that the risk of early complications was highest in patients with GG5 from the preoperative biopsy - 25% and GG4 from the permanent preparation - 23%. The same applies to the pT stage of the disease (p=0.241). The incidence of early complications was 15% in pT2 vs 8.3% in pT3 vs 0% in pT4 (N=1). Although 66.7% (n = 8) of early postoperative complications occurred in patients in whom nerve sparing was performed, a statistically significant relationship between the two parameters was not demonstrated (Pearson Chi-Square - 1.703; p = 0.230). The incidence of early postoperative complications was 16% in patients with Nerve sparing versus 7.8% in patients with non-SNS sparing LRP.

In their 2018 study related to late complications after prostatectomy, Siromakhov Zh, Neykov Kr. and colleagues found that the median time to onset of hematuria due to radiation cystitis was 1.3 years after RT for prostate cancer [209]. In the series of patients from 2015-2018 (44 patients), electrocoagulation of the bladder was performed in 18 patients, intravesical therapy with hyaluronic acid solution was performed in 7 patients, ligation of a. iliac interna.

The incidence of late postoperative complications was 39% in the present sample. Radiation cystitis or proctitis with a pronounced clinical manifestation was reported in a total of 10% of patients. Sclerosis of the bladder neck was found in 3% (n = 3) of patients, and urethral stricture in 1% (n = 1). Chronic uroinfection was demonstrated in 5% of patients (n = 5). Unilateral or bilateral hydronephrosis was found in 3% of patients (n = 3), and in two of the three cases the condition developed after the administration of radiotherapy. 4% of the patients reported adverse reactions to applied antiandrogen therapy – depressive symptoms, hot flashes, intolerance to the applied LHRH-agonist. Exitus lethal was registered in three patients (3%), occurring at the 7th, 14th and 17th postoperative months, respectively. We did not demonstrate a statistically significant relationship between the occurrence of late postoperative complications and the ISUP Grade Group histological result of the preoperative biopsy and permanent histological preparation. The highest rate of late complications occurs in patients with GG3 from the preoperative biopsy – 51% and GG1 from the permanent preparation. The rate of late postoperative complications was shown to increase with increasing pT stage of the disease (34.04% in pT2, 42.5% in pT3; 100% in pT4). It was shown that 56% of patients with a late complication had a preoperative PSA above 10 ng/ml; frequency of late complications in preoperative PSA above 10 ng/ml - 43% versus 34% in patients with PSA below 10 ng/ml. A total of 95.5% of cases with postoperative complications occurred in patients with a PIRADS 4 and 5 finding on the preoperative MRI. The incidence of late complications was 36% in PIRADS 4 patients and 31% in PIRADS 5 patients. No correlation was found between the occurrence of late postoperative complications and the conduct of nerve sparing - frequency of late complications in patients with nerve sparing – 34% versus 42% in patients without SNS preservation. We found a weak association between the presence of positive surgical margins (40% for R+ vs. 37% for no positive margins) or prostatic capsule penetration (46% for capsule penetration vs. 36% for no penetration) and an increased incidence of late postoperative complications. A pronounced correlation was found between the administration of adjuvant postoperative therapy and the occurrence of late complications (87.9% of cases were observed

in patients with adjuvant therapy). We demonstrated a frequency of late complications in patients with adjuvant therapy – 43% versus 18% in patients without it.

Functional outcomes after LRP mainly include assessment of patients' continence and erectile function. In an early series of patients after LRP, the following results were found regarding continence [109]: The Montsouris group reported in a series of 255 patients with a 12-month follow-up after LRP that 209 patients (82.3%) were pad-free, 31 (12%) required one pad per day and 15 patients (5.9%) had urinary incontinence requiring more than two pads per day; Stolzenburg et al. reported that among 500 patients who had a 6-month follow-up, 419 patients (83.8%) were pad-free, 52 (10.4%) required one to two pads per day, and 29 patients (5.8%) had urinary incontinence requiring more than two pads per day. Rassweiler et al. reported that at 12-month follow-up the continence rate was 91%. Galli et al. also found that the rate of long-term continence after LRP was 91.7% at the 12th postoperative month. In a study by Georgiev M, Yanev K, Ivanov G and a team of the Department of Urology at the Sofia University, continence was compared in 558 patients after LRP and RALP [192]. The following level of continence was reported in the RALP group compared to the LRP: at the 24th hour – 35 versus 22%; on the 1st month – 57 versus 34%; in the third month – 77 versus 59%.

In a study by Asimakopoulos A. and associates, the effect of RALP and LRP on the erectile function of a patient was compared [210]. Evaluation of the ability to have sexual intercourse at the 12th postoperative month (with or without phosphodiesterase type 5 inhibitors) showed a clear and significant advantage of RALP over LRP (77% vs. 32%, $P < 0.0001$). Time to intercourse was also statistically significantly shorter with RALP. Rates of return to baseline International Index of Erectile Function (IIEF-6) EF domain assessment questionnaires (questions 1–5 and 15) (58% vs 25%) and to IIEF-6 > 17 (63% vs 38%) also reported an advantage for RALP over LRP ($P = 0.0002$ and $P = 0.008$, respectively). Erectile function at the first, third, sixth and twelfth months after RALP and LRP was also compared by Porpiglia and colleagues [211]. At the twelfth postoperative month, the authors report 80% restored erectile function in RALP versus 54.2% in LRP.

The following functional outcomes were reported in the present study: Regarding erectile function at 6th postoperative month, the following distribution of patients was reported: No ED – 1%; mild ED – 13%; Mild to moderate ED – 6%; Moderate ED – 13%; Severe ED – 57%; N/A – 10%. We found a mean decline in patients by group of erectile function preoperatively at the 6th postoperative month of 2.18 points. No correlation of EF at 6 months postoperatively with ISUP Grade group from the permanent histological preparation was established. 100% of IIEF group 5 patients and 50% of IIEF group 4 patients at month 6 were GG 1 on preoperative biopsy, suggesting an association between early EF recovery and preoperative GS. A correlation between the lower values of the pT stage of the disease and better erectile function of the patients at the 6th postoperative month was proven: pT2 disease was found in 100% of IIEF group 5 patients and 92.3% of IIEF patients group 4. pT3 is found in 50% of patients with IIEF group 3, 53.8% of patients with IIEF group 2 and 59.6% of patients with IIEF group 1. The only patient with pT4 falls into group IIEF 1 - that is, severe erectile dysfunction. A marked correlation was found between PSA values below 10 ng/ml preoperatively and the recovery of erectile function at the 6th postoperative month (with PSA below 10 ng/ml were 100% of patients with IIEF group 5, 61.5% of patients with IIEF group 4 and 100% of patients with IIEF group 3; with PSA above 10 ng/ml are 61.4% of patients with IIEF group 1 – that is, severe erectile dysfunction at the 6th postoperative month). We did not prove a significant relationship

between the erectile function of patients at the 6th postoperative month and: MRI-PIRADS, intraoperative blood loss, body mass index, average age of patients, number of accompanying diseases, positive surgical margins. A significant relationship was found between the preoperative IIEF value by group and the 6th postoperative month value. A pronounced relationship between the preservation of the vascular-nerve bundles and the restoration of the erectile function of the patients on the 6th postoperative month was proved, as 100% of the patients with IIEF group 4 and 5 (that is, preserved erectile function) underwent nerve sparing. In group IIEF 1 fall 91% of patients without nerve sparing versus 34% of patients with nerve sparing. In group IIEF 4 – 0% versus 29%; IIEF 5 – 0% vs. 2%. The probability of a patient falling into group IIEF 4 or 5 at the 6th month after performing Nerve sparing is 31% versus 0% in patients without nerve sparing. There is a pronounced inversely proportional relationship between the administration of adjuvant therapy and the erectile function of patients at the 6th postoperative month. 100% of patients with IIEF group 4 and 5 (preserved EF) did not receive adjuvant therapy. 93% of patients with IIEF group 1 (severe erectile dysfunction) underwent adjuvant therapy. 77% of patients with adjuvant therapy versus 18.3% of patients without adjuvant therapy fell into the IIEF 1 group at month 6. In group IIEF 4 – 0% versus 59%; IIEF 5 – 0% vs 4.5%.

At the 12th postoperative month, the following were reported: No ED – 9%; mild ED – 20%; Mild to moderate ED – 8%; Moderate ED – 19%; Severe ED – 34%; N/A – 10%. The average decline of patients by group of erectile function preoperatively at the 12th postoperative month was 1.48 points. The correlations found for EF at month 12 were similar to those at month 6 postoperatively. It establishes a relationship between the ISUP Grade group of the patients preoperatively and the erectile function at the 12th postoperative month - 77% of the patients with IIEF 5 and 78% of the patients with IIEF 4 have, respectively, ISUP GG 1 or GG2 from the preoperative biopsy. The same dependence is established to a lesser degree in relation to ISUP Grade group from the permanent preparation – 44.4% of IIEF 5 patients and 65% of IIEF 4 patients have ISUP GG 1 or GG2 respectively from the permanent histological preparation. A correlation was established between the lower values of the pT stage of the disease and better erectile function of the patients at the 12th postoperative month: pT2 disease was found in 88.9% of IIEF group 5 patients and 55% of IIEF patients group 4. pT3 was detected in 57.9% of patients with IIEF group 2 and 64.7% of patients with IIEF group 1. The only patient with pT4 falls into group IIEF 2 – that is, moderate to severe erectile dysfunction. A correlation was demonstrated between PSA values below 10 ng/ml preoperatively and the recovery of erectile function at the 12th postoperative month (66.7% of patients with IIEF group 5 had PSA below 10 ng/ml, 75% of patients with IIEF group 4 and 62.5% of patients with IIEF group 3; with PSA above 10 ng/ml are 58.8% of patients with IIEF group 1 – that is, severe erectile dysfunction at the 12th postoperative month). A significant inverse correlation was found between the frequency of positive surgical margins and erectile function at the 12th postoperative month. 88.9% of patients with IIEF group 5 had no data on positive surgical margins, 75% of patients with IIEF group 4. 58.8% of patients with severe erectile dysfunction (IIEF group 1) had data on positive surgical margins. A pronounced relationship between the preservation of the vascular-nerve bundles and the recovery of the patients' erectile function at the 12th postoperative month was proven, as nerve sparing was performed in 100% of the patients with IIEF group 4 and 5 (that is, preserved erectile function). In group IIEF 1 fall 58% of patients without nerve sparing versus 15% of patients with nerve sparing. In group IIEF 4 – 0% versus 45%; IIEF 5 – 0% vs. 20%. A significant relationship was confirmed between the

preoperative IIEF value by group and the 12th postoperative month value. A pronounced inversely proportional relationship was established between the administration of adjuvant therapy and the erectile function of the patients at the 12th postoperative month. 100% of patients with IIEF group 5 (preserved EF) did not receive adjuvant therapy. 94.1% of patients with IIEF group 1 (severe erectile dysfunction) underwent adjuvant therapy. In group IIEF 1 fall 46% of patients with adjuvant therapy against 9% of patients in whom such was not conducted. In group IIEF 4 – 18% versus 36%; IIEF 5 – 0% vs 41%.

Results regarding patient continence in the current series of patients were as follows: incontinence at month 1 – 88%; in the third month – 50%; on the 6th month – 40%; on the 12th postoperative month – 30%. The mean time to continence in patients was 4.45 ± 3.67 months (range 1–18 months). No significant relationship was demonstrated between the histological result according to the ISUP Grade group of the preoperative biopsy of the prostate and the permanent histological preparation, as well as the pT stage and the continence of the patients at the 1st and 12th postoperative months. However, at the 12th postoperative month, the highest percentage of continence was found in patients with GG1 – 93%, and the lowest – in patients with GG5 – 50%. On the 1st postoperative month, the highest percentage of continence was found in patients with GG1 from the permanent histological preparation - 33%, and the lowest - in patients with GG4 - 9%. At month 12, the same ratio was maintained, with 100% of GG1 patients versus 58% of GG5 patients being continent. A significant inverse relationship was found between the frequency of positive surgical margins and the continence of patients at 1 and 12 postoperative months as: 90.9% of continous patients at 1 postoperative month and 59% of continous patients at 12 The postoperative month has no data on positive margins. A detailed examination of subgroups found that 2.5% of patients with positive surgical margins were continent at 1 postoperative month versus 22% of patients without R+ status. At 12 months postoperatively, the correlation was weaker, with 63% of patients with positive surgical margins being continent versus 78% of patients without R+ status. A significant inverse relationship was also found between the rate of penetration of the prostatic capsule and the continence of the patients at the 1st and 12th postoperative months as: 81.8% of the continence patients at the 1st postoperative month and 70.5% of the continent patients at the 12th postoperative month had no evidence of prostatic capsule penetration. Detailed subgroup analysis found that 8% of patients with prostatic capsule penetration were continent at 1 postoperative month versus 15% of patients without penetration. At the 12th postoperative month, the correlation was not demonstrated, with 72% of patients with capsular penetration versus 70% of patients without penetration being continent. No statistically significant relationship was demonstrated between preoperative PSA values and MRI findings and patient continence at 1 and 12 postoperative months. We demonstrated a significant relationship between the preservation of the vascular-nerve bundles and the restoration of continence in the patients, as in 72.7% of the continent patients at the 1st postoperative month and 52.5% of the continent patients at the 12th postoperative month was carried out nerve sparing. When examining subgroups in detail, it was found that 19% of patients with nerve sparing were continent on the 1st postoperative month versus 7% of patients without nerve bundle preservation. At the 12th postoperative month, 76% of the patients with nerve sparing borders were continent against 65% of the patients without SNS preservation. 88% of incontinent patients at the 12th postoperative month received postoperative therapy. At the 12th postoperative month, 66% of patients with adjuvant therapy were continent versus 85% of patients without additional treatment, suggesting a correlation between the two indicators. Greater mean blood loss (198 vs. 170 mL), higher body mass index

(29.67 vs. 28.35), and higher mean age (66.4 vs. 63.4) were demonstrated in incontinent vs. continent patients on the 12th postoperative month.

Hruza and colleagues published in 2013 their oncological results after LRP [212]. Estimated biochemical recurrence-free survival (BCRFS) rates 10 years after LRP were 80.2% in pT2 patients, 47.4% in pT3a patients, and 49.8% in pT3b/4 patients, confirming -good prognosis in patients with organ-limited disease ($P < 0.001$). In multivariate Cox regression analysis, only Gleason score and T stage of disease significantly affected BCRFS. 10-year clinical progression-free survival was 97.2% (pT2), 84.4% (pT3a) and 78.1% (pT3b/4), and prostate cancer-specific survival estimates were 100% (pT2), 97.3% (pT3a) and 90.6% (pT3b/4). A meta-analysis by Cao L et al compared oncologic and functional outcomes in open radical prostatectomy, LRP, and RALP [213]. The analysis includes a total of 11 studies. According to the results, the overall rate of positive surgical margins in RALP and LRP was 22.3% compared to 28.6% in open surgery. When the rate of positive surgical margins was analyzed by subgroups by T-stage, the results were as follows for LRP/RALP vs. open prostatectomy: 14.7% vs. 18.8% for ≤pT2 tumors 41.4% vs. 50.1% for ≥ pT3 tumors. Biochemical recurrence rates were 3.1% (57 of 1853 cases), 7.4% (204 of 2766 cases), and 11.3% (320 of 2835 cases) at 3, 12, and 24 months after RALP/LRP, respectively. Similarly, biochemical recurrence rates were 5.3% (44 of 830 cases), 12.2% (239 of 1955 cases), and 16.2% (327 of 2020 cases) at 3, 12, and 24 months, respectively, after open radical prostatectomy.

In the present sample of patients, biochemical recurrence was found in 26% of patients. Local recurrence of PK was demonstrated in 1 patient. Bone metastases developed in three patients.

In the present study, we found no correlation between the incidence of BCR and ISUP Grade group from the preoperative biopsy and permanent histological preparation (respectively: $r=0.173$; $p=0.110$ and $r=0.199$; $p=0.59$). However, of the patients with BCR, the share of patients with ISUP Grade Group 5 of the permanent histological preparation was the highest – 34.6%. In addition, the percentage of patients with BCR was highest in the GG5 groups from preoperative histology – 75% and from permanent histological preparation – 42.8%. No significant correlation between pT stage and the frequency of BCR - (50% vs. 46.2% of cases for pT2 and pT3, respectively) ($r=0.27$; $p=0.802$) was proved. No statistically significant correlation was found between the rate of biochemical recurrence in patients and the rate of positive surgical margins (32% BCR in negative surgical margins vs. 24% in positive surgical margins; Pearson Chi-Square 0.639; $p=0.489$ and the rate of penetration of the prostatic capsule in the present sample (38% BCR with capsule penetration vs. 24.6% with no penetration; (Pearson Chi-Square 1.745; $p=0.187$). Preoperative PSA above 10 ng/ml proved to be an independent predictor of BCR rate ($r=0.247$; $p=0.018$). Preservation of the vascular-nerve bundles does not correlate with an increased frequency of biochemical recurrence (38% BCR with nerve sparing versus 34% BCR in patients without nerve sparing - Pearson Chi-Square - 1.758; $p=0.247$).

When analyzing the data against evidence of local recurrence or distant metastases, the following relationships were found: no statistical significance was found between the Grade group of the preoperative biopsy ($r = 0.182$; $p = 0.122$) and the permanent histological preparation ($r = 0.221$; $p = 0, 55$) and the incidence of local recurrence or distant metastases in the present sample. However, it is striking that the incidence of local recurrence or distant metastases was highest in patients with GG5 from the preoperative biopsy (50%) and in patients

with GG5 from the permanent histology preparation (18.7%). A dependence was established between an increase in the pT stage and the occurrence of local recurrence or distant metastases, with 60% of cases occurring in patients with pT3 disease. The rate of evidence of local recurrence or distant metastases in patients with pT3 disease was 7.8% versus 4.2% in pT2 ($r = 0.37$; $p = 0.749$). No statistically significant relationship was found between the frequency of positive surgical margins and the occurrence of local recurrence or distant metastases (7.5% in patients with R+ disease versus 5.5% in patients without positive surgical margins). Local recurrence or distant metastases were demonstrated in 13.6% of patients with prostatic capsule penetration versus 3.7% of patients without such a finding ((Pearson Chi-Square = 2.509; $p = 0.142$). The preoperative PSA value was shown to be an independent predictor of the occurrence of local disease recurrence or metastasis ($r = 0.26$; $p = 0.823$). The rate of evidence of local recurrence or distant metastases was 2.4% in patients with PSA below 10 ng/ml versus 11.4% in patients with PSA above 10 ng/ml. No correlation was demonstrated between the preservation of vascular bundles and the occurrence of local recurrence or distant metastases (Pearson Chi-Square = 1.927; $p = 0.358$). Local recurrence or distant metastases were proven in 2.6% of patients with nerve sparing versus 10.5% in patients without nerve sparing. A correlation was found between the mean number of histological variations and the frequency of occurrence of local recurrence or distant metastases, and in cases of recurrence/metastases the mean number of variations was 1.6 versus 0.94 in patients without a finding.

Regarding postoperative therapy in the present sample, the following results were reported: RT was applied in 67% of patients; androgen deprivation therapy was applied in 64% of patients; combined adjuvant therapy was administered in 55% of patients. The administration of adjuvant therapy correlates with an increase in the ISUP Grade group score of preoperative biopsy and permanent histological preparation. Adjuvant therapy was administered in 100% of GG5 patients and 80% of GG4 patients from the preoperative biopsy, as well as in 95.2% of GG5 patients and 75% of GG4 patients from the permanent histological preparation. 54.4% of patients who underwent adjuvant therapy had a preoperative PSA value above 10 ng/ml. In patients with PSA below 10 ng/ml, adjuvant therapy was applied in 67.4%. In patients with PSA above 10 ng/ml preoperatively, adjuvant therapy was administered in 84% of cases. In addition, it was shown that patients who received adjuvant therapy demonstrated a higher mean number of histological variations of the disease: 1.08 versus 0.77 histological features.

According to the presented data of the present study and after carrying out a comparison with the results of studies from the world literature, it can be concluded that LRP is an oncologically effective treatment of Pca. The percentage of intraoperative, early and late complications, oncological and functional results achieved in the series of reported patients are comparable to those reported by leading international and Bulgarian authors in the field.

7. Conclusions

1. Higher preoperative PSA values correlate with: higher pT stage of the disease from the permanent histological preparation, increased risk of penetration of the prostate capsule by the neoplastic process, increased risk of biochemical recurrence.

2. A family history of PC correlates with a lower mean age at PC diagnosis as well as a higher risk of biochemical recurrence. The probability of proving ISUP GG5 disease by preoperative biopsy, as well as the probability of proving ISUP GG4 and GG5 disease by permanent histology, was significantly higher in patients with a family history of PCa.

3. A correlation was proven between the histological result according to ISUP Grade group from the preoperative biopsy and: the MRI findings according to PIRADS; pT stage of PCa; the demonstration of histological features in the permanent postoperative preparation; higher penetration rate of the prostate capsule in the permanent histological preparation.

4. The presence of genetic aberrations in the genes for the androgen receptor and the vitamin D receptor - molecular profile AR(CAG)n (</=22) and allelic combinations according to VDR(AT)n (SL; LL) - are risk factors for aggressive course of PC - increased Gleason score from biopsy and permanent preparation, higher preoperative PSA values, increased frequency of pathological progression of PC, increased frequency of histological features and variations of PC, increased frequency of seminal vesicle involvement by PCa.

5. The following were proven as independent risk factors for increased intraoperative blood loss: the presence of previous operative interventions, histological result ISUP Grade group 4 and 5 of the preoperative biopsy, increase in the pT stage from the permanent histological preparation, preservation of vascular-nerve bundles.

6. Independent risk factors for the need for intraoperative hemotransfusion are: history of previous surgical interventions, values 4 and 5 according to PIRADS from MRI, preservation of vascular-nerve bundles.

7. A relationship was established between the frequency of occurrence of intraoperative complications and: the presence of accompanying diseases in the patients, preoperative PSA values above 10 ng/ml; values 4 and 5 according to PIRADS from the preoperative MRI, increase in pT stage of PCa.

8. A significant relationship between longer operative time and: patients' body mass index, preoperative PSA value above 10 ng/ml, increasing volume of the prostate gland was proven.

9. Higher values according to the ISUP Grade group of the permanent histological preparation correlate with: an increase in the pT stage of the disease, an increased risk of pathological progression of the disease, an increased risk of penetration of the prostate capsule, an increased risk of biochemical recurrence, an increased risk of local recurrence or metastases, increased risk of positive surgical margins.

10. As possible predictors for the occurrence of early postoperative complications, the following were proven: age of the patients over 70 years old, PIRADS type 4 and 5 MRI findings, preservation of vascular-nerve bundles.

11. An increase in pT stage correlates with: an increase in the frequency of pathological progression of the disease, an increase in the frequency of positive surgical margins and penetration of the prostatic capsule.

12. The frequency of late postoperative complications increases with: an increase in the pT stage of the disease, the value of PSA, the MRI finding according to PIRADS, the presence of positive surgical margins and penetration of the prostate capsule, the frequency of adjuvant therapy.

13. Recovery of erectile function of patients at the 6th and 12th postoperative month correlates with: GG1 and GG2 from the preoperative biopsy, higher values of the preoperative IIEF, lower values of the pT stage of the disease, preoperative PSA values below 10 ng/ml, conducting

preservation of vascular-nerve bundles. The administration of adjuvant therapy demonstrated a marked dependence with worsening erectile function at the 6th and 12th postoperative months.

14. A higher rate of patient continence at the 1st and 12th postoperative months correlates with the preservation of vascular-nerve bundles. Greater mean blood loss, higher body mass index, and higher mean age were found in incontinent versus continent patients at 12th postoperative month.

8. Contributions

1. A comprehensive review of the available world literature regarding the disease prostate carcinoma, its diagnosis and therapy was carried out.

2. A description of the methodology for performing laparoscopic radical prostatectomy with specific steps and details is presented. Detailed photographic material is included.

3. Results of an innovative pilot genetic study are presented, demonstrating the association between androgen receptor and vitamin D receptor gene polymorphisms and the course of PC. In the future, the data can be applied in urological practice in order to refine the prognosis of the disease and make optimal therapeutic decisions for patients.

4. An analysis of the data on the course of the disease of one hundred patients, who were followed for a minimum of 24 months, was performed. Correlations between various preoperative, intraoperative, postoperative, functional, and oncologic outcomes are presented. The presented data can be useful to the practicing urologist in the treatment-diagnostic plan of patients with carcinoma of the prostate gland.

5. The results of the present work are compared with the data of articles and studies with a large cohort of patients published in world-renowned publications. The comparison proves the applicability, effectiveness and safety of laparoscopic radical prostatectomy in Bulgaria.

Описание на публикации, приложени с цел защита на дисертация:

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