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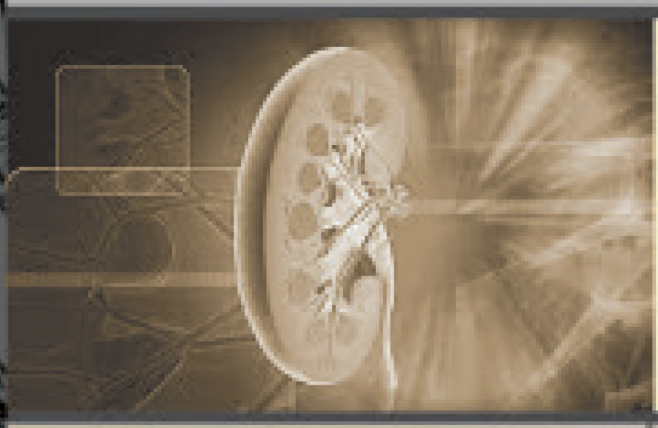

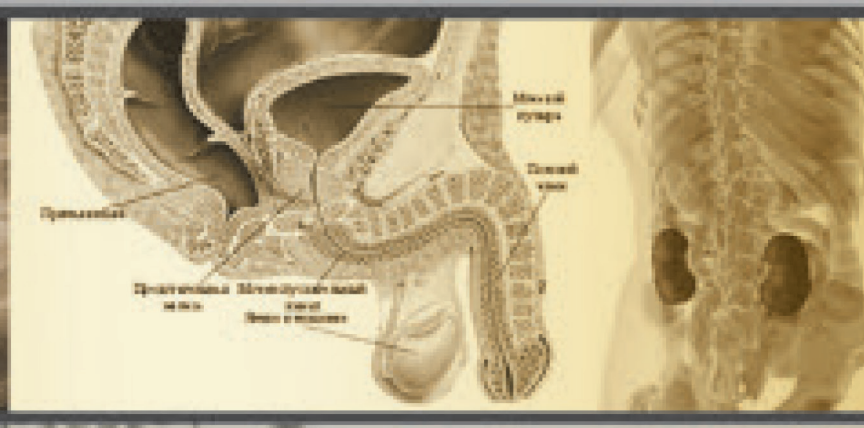

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ORIGINAL RESEARCH
Andrology

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J Urol Surg 2024;11(3):134-139

Can a High Body Shape Index (ABSI) Be a Risk Factor for Peyronie's Disease?

Engin Kölükçü, Kenan Yalçın, Fatih Fırat

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What's known on the subject? and What does the study add?

Peyronie's disease is a wound-healing disorder characterized by penile pain, curvature, and sexual dysfunction. The pathophysiology of Peyronie's disease involves an abnormal healing pattern in response to trauma within the tunica albuginea. Clinical conditions, including hypertension, dyslipidemia, and diabetes mellitus, can increase the incidence of Peyronie's disease by creating a hypoxic microenvironment in erectile tissues. A body shape index (ABSI) is a recent anthropometric measurement of visceral adiposity. This study is the first to define ABSI as a new independent risk factor for Peyronie's disease. We believe that considering ABSI during follow-up and treatment protocols for Peyronie's disease will offer important innovations in andrology practice.

Abstract

Objective: Predisposing factors of Peyronie's disease remain controversial. We know that obesity has extremely negative effects on erectile tissue. Therefore, in our study, we aimed to examine the relationship between Peyronie's disease and the body shape index (ABSI), which is a new parameter for the evaluation of visceral adiposity.

Materials and Methods: In this study, 55 healthy volunteers (group-1) and 50 Peyronie's disease patients (group-2). Age, comorbidities, waist circumference (WC), height, body mass index (BMI), testosterone, fasting glucose, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, International Index of Erectile Function (IIEF), and ABSI scores of all patients were analyzed. In addition, plaque sizes, duration of symptoms, and curvature degrees of patients in group 2 were calculated.

Results: The mean ages of group 1 and group 2 were 57.02±8.34 years and 56.02±10.65 years, respectively ($p>0.05$). Fasting glucose, WC, BMI, and ABSI values were significantly higher in group 2 ($p=0.031$, $p<0.001$, $p=0.026$ and $p<0.001$). LDL and HDLvalues were similar between both groups ($p>0.05$). The IIEF score was observed to be lower in group 2 ($p<0.001$). In terms of ABSI values, the discrimination power of Peyronie's disease was strong. The cut-off value for the ABSI score was 0.08. For this cut-off point, classification success was determined as 88.0% sensitivity and 80.0% selectivity.

Conclusion: ABSI can be a reliable independent risk factor for Peyronie's disease and a predictor of visceral adiposity.

Keywords: Peyronie's disease, a body shape index, men, visceral adiposity

Introduction

Peyronie's disease is a wound-healing disorder characterized by penile pain, curvature, and sexual dysfunction. The pathophysiology of Peyronie's disease involves an abnormal healing pattern in response to trauma within the tunica albuginea (1). Although the etiology has not yet been fully elucidated, numerous studies have linked Peyronie's disease with clinical conditions such as advanced age, diabetes mellitus, obesity, and dyslipidemia, which create a hypoxic microenvironment in erectile tissues (2). In their study evaluating Peyronie's disease in patients aged 40 years, Tefekli et al. (3) reported that more than half of the cases had at least one of the risk factors for vascular disease.

Today, there is a significant increase in the prevalence of obesity and obesity-related health problems directly related to changing

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lifestyles. Obesity leads to endothelial dysfunction by increasing susceptibility to hypertension and metabolic syndrome (4). On the other hand, it can also cause changes in the hormone profile. This condition negatively affects male sexual function (4,5). Visceral fat accumulation significantly increases the risk of metabolic and cardiovascular diseases. Therefore, body fat distribution rather than total adipose tissue content is critical for metabolic abnormalities. The most basic approach to assess fat distribution is the use of detailed diagnostic tools, such as computed tomography or magnetic resonance imaging. However, these diagnostic tools are expensive and are limitedly used in daily practice (6,7). This has recently encouraged health professionals to search for new anthropometric indices using traditional measurements. A body shape index (ABSI) is most important of these indices. The value is calculated using allometric regression of waist circumference (WC), weight, and height. Previous clinical studies have documented a significant relationship between ABSI, metabolic disorders, and cardiovascular pathologies (8,9). On the other hand, in another study we conducted in the past, we observed that the visceral adiposity index, which is a marker of adipose tissue dysfunction, is closely related to Peyronie's disease (10).

This retrospective study aimed to evaluate the relationship between Peyronie's disease and ABSI. To the best of our knowledge, this is the first study in English literature where ABSI was analyzed in Peyronie's disease patients.

Materials and Methods

Patients

The data of patients who applied to our clinics between January 2020 and February 2024 were retrospectively analyzed. Patients who applied for routine care and did not have neuropathology were categorized into group 1. Peyronie's disease patients were defined as group 2. Demographic data, comorbidities, clinical complaints, duration of symptoms, physical examination findings, trauma, pelvic radiotherapy, and surgical histories of the patients were analyzed in detail. The diagnosis of Peyronie's disease was established based on characteristic symptoms and the presence of palpable penile plaque on physical examination.

Plaque size was determined via physical examination. The penile plaque was marked with a marker pen, and its dimensions were measured using a meter. The curvature degree was calculated by reviewing images obtained after intracavernosal injection (11,12). On the other hand, the weight, height, and WC of the patients were also measured. The erectile function of the patients was calculated using the International Index of Erectile Function (4). Blood was collected from all patients between 08.30 and 10.00 after overnight fasting. In our blood analysis, total testosterone, fasting blood glucose, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol levels were analyzed.

Our analyses were performed in accordance with the Declaration of Helsinki Principles and with the approval of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee approved this study (decision no: 24-KAEK-138, date: 18.04.2024).

Measurement of BMI, WC, and ABSI

WC was calculated by measuring the circumference of the circle passing through the midpoint of the lines perpendicular to the 10^{th} rib on both sides and the spina iliaca anterior superior. BMI was calculated as weight/height^2 (kg/m^2). ABSI was calculated as WC divided by $BMI^{2/3}$ x $height^{1/2}$ (13).

Exclusion Criteria

Patients with a history of trauma, radiotherapy, malignancy, or pelvic surgery were excluded.

Statistical Analysis

A descriptive statistical work-up was conducted for the study to provide insight into the general characteristics. Data for continuous variables are presented as the arithmetic mean and standard deviation. Levene's test was used to determine whether continuous variables matched with normal distribution or not. Regarding inter-group comparisons of variables indicated with measurements, a t-test was used for independent samples to study inter-group differences. Receiver operating characteristics (ROC) curve analysis was applied to determine the cut-off values of the variables, and the area under the ROC curve (AUC) was also evaluated. Also, correlation and regression analysis were performed to examine the relationships between continuous variables. A p-value 0.05 was considered statistically significant. Calculations were made with available statistical software (IBM SPSS 26, SPSS Inc., an IBM Co., Somers, NY).

Results

The data from a total of 105 male patients were analyzed. Group 1 was the control group, and there were 55 patients. In group 2, 50 patients were diagnosed with Peyronie's disease. Mean age was 57.02±8.34 years and 56.02±10.65 years in groups 1 and 2, respectively. There were no significant differences between the groups in terms of age distribution (p>0.05). The mean symptom duration in group 2 was 19.88±4.58 months. The mean plaque size and penile curvature degree of patients in this group were 16.4±4.87 mm and 48.14±10.15°, respectively. It was determined that diabetes mellitus, hypertension, hyperlipidemia, and smoking were higher in this group than in group 1 (p=0.044, p=0.043, p=0.008, and p=0.019, respectively). On the other hand, no difference was found between groups 1 and 2 in terms of coronary artery disease (p>0.05) (Table 1).

WC and BMI measurements were higher in group 2 than in group 1 (p<0.001 and p=0.026). When blood biochemical analyses were examined, mean fasting glucose, HDL cholesterol, and LDL cholesterol levels in group 2 were 123.69±68.84 mg/dL, 44.14±9.81 mg/dL and 149.08±135.72 mg/dL. Glucose values were found to be significantly higher than in group 1 (p=0.031). HDL-C and LDL-C values were similar between groups 1 and 2 (p>0.05). On the other hand, total testosterone levels were significantly lower in group 2 than in group 1 (p<0.001). The mean ABSI values in groups 1 and 2 were recorded as 0.08±0.01 and 0.09±0.01, respectively. These values were significantly higher in group 2 (p<0.001). Although erectile dysfunction was observed in only 19 (34.54%) patients in group 1, it was detected in 27 (54%) patients in group 2. In this context, the IEFF score of group 2 was significantly lower than that of group 1 (p<0.001) (Table 2).

ROC analysis was performed to determine the success of ABSI scores in the prediction of Peyronie's disease and AUC values, accuracy, sensitivity, selectivity, positive-negative predictive values, and likelihood ratio (+) values together with the 95% confidence intervals calculated as a result of the ROC analysis are shown in Table 3. The ROC curve is shown in Figure 1. As a result of the ROC analysis, the ABSI score was found to be statistically significant between groups 1 and 2 [AUC=0.890 (0.819-0.946); p<0.001]. In terms of ABSI values, the discrimination power of Peyronie's disease was strong. The cut-off value for the ABSI score was 0.08. For this cut-off point, classification success was determined as 88.0% sensitivity and 80.0% selectivity.

Table 1. Distribution of study population by comorbidity

Comorbidity	Group		p-values
	Group 1 (n=55)	Group 2 (n=50)	
Diabetes mellitus	6 (10.9%)	14 (28%)	**0.044***
Hypertension	5 (9.1%)	12 (24%)	**0.043***
Hyperlipidemia	8 (14.5%)	20 (40%)	**0.008***
Coronary artery disease	4 (7.3%)	11 (22%)	0.067
Smoking	12 (21.8%)	23 (46%)	**0.019***

Chi-square test, *: Bold values indicate statistically significant (p<0.05)

Table 2. General characteristics of groups 1 and 2

	Groups		p-values
	Groups 1 (n=55)	Groups 2 (n=50)	
Age (years)	57.02±8.34	56.02±10.65	0.597
Height (cm)	173.22±5.03	170.50±7.08	0.225
BMI (kg/m²)	27.38±2.83	28.94±4.17	**0.026***
WC (cm)	91.98±5.14	105.82±10.90	**<0.001***
ABSI	0.08±0.01	0.09±0.01	**<0.001***
Glucose (mg/dL)	99.15±39.01	123.69±68.84	**0.031***
HDL cholesterol	45.15±9.88	44.14±9.81	0.600
LDL cholesterol	110.89±49.71	149.08±135.72	0.054
Testosterone (ng/dL)	462.49±110.42	346.33±159.29	**<0.001***
IIEF	23.64±3.60	19.02±3.35	**<0.001***

Student's t-test with mean ± standard deviation
*: Bold values indicate statistically significant (p<0.05).
BMI: Body mass index, WC: Waist circumference, ABSI: A body shape index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, IIEF: International Index of Erectile Function

Discussion

The history of Peyronie's disease dates back to the early 7th century. Despite having an extensive clinical history, there are many uncertainties regarding the etiopathogenesis and treatment approaches of Peyronie's disease. It is estimated that the prevalence of all cases of Peyronie's disease in the world varies between 0.3% and 13.1% (14). On the other hand, the easy availability of treatment options for erectile dysfunction in the modern century has led to a significant increase in the frequency of Peyronie's disease evaluation by healthcare professionals (10). In a recent study in Turkiye, which is also the

Table 3. ROC curve analysis of the ABSI score in disease prediction

	ABSI score
Area under curve	0.895 (0.819-0.946)
Sig. p (area=0.5)	<0.001*
Cut-off	>0.08
Sensitivity (95% CI)	88.0 (75.7-95.5)
Specificity (95% CI)	80.0 (67.0-89.6)

ROC: Receiver operating characteristics, ABSI: A body shape index CI: Confidence interval

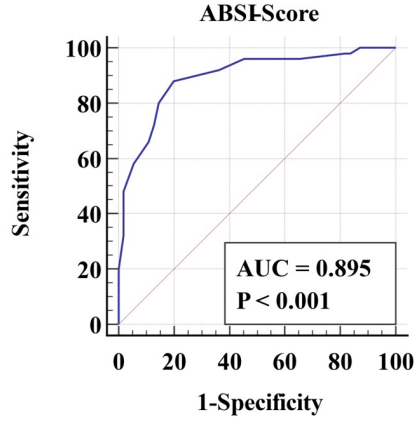

Figure 1. ROC curves for the ABSI score in disease prediction

ABSI: A body shape index, AUC: Area under curve, ROC: Receiver operating characteristics

geographical region of our study, Kadioglu et al. (15) reported the prevalence of Peyronie's disease to be 5.3%. The same study documented that this pathology was associated with a higher incidence of diabetes, hypertension, heart disease, smoking, age, and poor sexual intercourse experience (15). On the other hand, in our study, a close relationship was found between Peyronie's disease and comorbidity. In the physiopathology of Peyronie's disease, which is mainly emphasized, there is tissue damage caused by penile micro-traumas with a cumulative effect in later periods. For this reason, many authors have reported that factors that negatively affect wound healing can also negatively affect the course of Peyronie's disease (10,16).

The adipose tissue is a connective tissue composed mostly of adipocytes. Adipose tissue is divided into two components: Subcutaneous and visceral. Visceral adipose tissue is the most pathogenic component (17). Therefore, the function of adipose tissue is very important for a healthy life. The term adipose tissue dysfunction refers to a condition in which adiponectin production decreases to very low levels, whereas proatherogenic, proinflammatory, and prediabetic adipocytokine are excessively secreted (18). Adiposity is characterized by adipocyte deposition and hypertrophy of visceral adipose tissue (19). It is accepted that adipose tissue dysfunction is a key process in the pathophysiology of obesity-related disorders by negatively affecting oxygenation (20). Previous studies have observed that adipose tissue dysfunction is closely related to high rates of diabetes mellitus, insulin resistance, dementia, stroke, coronary artery disease, hypertension, obstructive sleep apnea, hormonal imbalance, non-alcoholic fatty liver, and many types of cancer in obese patients (21,22).

ABSI is a recent anthropometric measurement indicating visceral adiposity rather than peripheral fat (8,13). It is a useful index for cardiometabolic risk assessment independent of WC and BMI, which was developed by Krakauer and Krakauer (7) in 2012 (7,23). On the other hand, ABSI has been reported to be positively correlated with visceral adiposity estimated by ultrasonic and bioelectrical impedance analysis in clinical analyses. However, Lin and Lin (23) observed that ABSI was more closely associated with impotence than other obesity indices (23). In a study of 607 patients, Bouchi et al. (8) reported that ABSI was an important indicator of arterial stiffening in patients with type 2 diabetes. Haghighatdoost et al. (13) reported that ABSI was a poor predictor of metabolic syndrome and cardiovascular disease. On the other hand, recent studies have also shown that ABSI is a strong predictor of all-cause mortality (24,25). Our study analyzed several factors suspected of the etiopathogenesis of Peyronie's disease in detail and examined the relationship between ABSI and Peyronie's disease. The findings suggest that the ABSI is a risk factor of Peyronie's disease as a predictor of visceral adipose dysfunction.

Testosterone is an endogenous anabolic hormone that plays an important role in wound healing (26,27). It has been observed that previous studies have dealt with Peyronie's disease and testosterone levels in detail. In a series of 121 cases, Moreno and Morgentaler (28) reported that low testosterone levels were correlated with Peyronie's disease. In the same study, it was also reported that there is a relationship between low testosterone levels and the severity of curvature. In a study including 106 patients with Peyronie's disease by Nam et al. (29), they reported that low testosterone levels were associated with erectile dysfunction, plaque size, and penile deformity. Similarly, in the studies of Cavallini et al. (27), it was found that the levels of testosterone were lower in patients with Peyronie's disease compared with the control group. Differently, in the study of Kirby et al. (30), low testosterone levels were not associated with the severity of Peyronie's disease. Similarly, in the study of El-Sakka (31), there was no relationship found between hormonal abnormalities and Peyronie's disease. Obesity and hypotestosteronemia are closely related. In previous studies, it has been noted that depending on the level of obesity, there is a decrease in the level of sex hormone-binding globulin associated with insulin resistance and a suppression in the hypothalamic-pituitary-testicular axis, followed by a decrease in testosterone levels (5,32). Wang et al. (32) reported that obesity and hypogonadism were closely related in males in their study. In our study, we found that there was a decrease in testosterone levels in patients with Peyronie's disease compared with the control group. This trend was directly related to ABSI levels.

Other factors that negatively affect wound healing include comorbid conditions such as diabetes mellitus, dyslipidemia, and hypertension. It is observed that in many clinical studies conducted in the past, the relationship between comorbidity and Peyronie's disease was analyzed in detail, and quite different results were documented. Diabetes mellitus activates transforming growth factor (TGF)-beta 1. Increasing glucose and TGF-beta 1 level upregulated plasminogen activator inhibitors. Thus, although matrix metalloproteinases are inhibited, the tissue inhibitory activity of metalloproteinases is high (33). This condition causes abnormalities in the extracellular matrix composition, such as collagen accumulation, scar formation, and fibrosis, in patients with diabetes mellitus (33,34). In a very large series of 1208 cases by Kadioglu et al. (15), it was reported that 17.5% of Peyronie's disease patients were diagnosed with diabetes mellitus, and this rate was higher than that of the control group. In a similar study, Tefekli et al. (34) reported that patients with Peyronie's disease and diabetes mellitus had much more severe penile deformity. In this study, diabetes mellitus was observed in 19.1% of patients with Peyronie's disease, a significantly higher rate than in the control group.

Hypertension and dyslipidemia are other risk factors that negatively affect the oxygen level in the penile microenvironment (15). It has been observed that many clinical studies conducted in the past have investigated the relationship between Peyronie's disease and hypertension and dyslipidemia. In a study by Bjekic et al. (35) in which they evaluated a total of 328 cases diagnosed with 82 cases of Peyronie's disease, they reported that comorbidities such as diabetes mellitus, hypertension, and hyperlipidemia were more common in this group. In another study, Pavone et al. (36) reported that 44% of patients with Peyronie's disease were diagnosed with hypertension, a rate that was considerably higher than that in the control group. In our study, we found that the incidence of hypertension and hyperlipidemia was higher in patients with Peyronie's disease than in the control group. In a series of 307 cases by Kadioglu et al. (11) reported that 67.5% of patients with Peyronie's disease had at least one risk factor; however, diabetes mellitus and hypercholesterolemia were the most common comorbidities. These systemic conditions have repercussions in the penile microenvironment, such as chronic inflammation, increased levels of reactive oxygen species, disruption of intercellular connections, and endothelial dysfunction (37). In this context, the physiopathology of Peyronie's disease has been analyzed from a broad perspective in our study by analyzing ABSI, which is closely related to a wide range of pathologies, such as hypertension, insulin resistance, pre-diabetes, diabetes mellitus, dyslipidemia, and hormonal disorders. Our study documented the relationship between ABSI and Peyronie's disease for the first time in the literature.

Study Limitations

The main limitation of our study is that it was conducted retrospectively with a limited number of patients. On the other hand, due to the inadequacy of our technical conditions, the fact that a detailed biochemical analysis could not be performed, the plaque size and penile arterial and venous system blood flow could not be documented with Doppler ultrasonography were other limitations of our study.

Conclusion

In this retrospective study, ABSI was found to be higher in patients with Peyronie's disease than in controls. In line with our results, we believe that it is extremely important to consider high ABSI as a risk factor for Peyronie's disease. Our study should be supported by prospective, randomized, and large series studies.

Ethics

Ethics Committee Approval: Our analyses were performed in accordance with the Declaration of Helsinki Principles and with the approval of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee approved this study (decision no: 24-KAEK-138, date: 18.04.2024).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: E.K., K.Y., F.F., Concept: E.K., F.F., Design: E.K., K.Y., Data Collection or Processing: E.K., K.Y., F.F., Analysis or Interpretation: E.K., K.Y., Literature Search: E.K., K.Y., F.F., Writing: E.K., K.Y., F.F.

Conflict of Interest: No conflict of interest was declared by the authors.

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An Observational Study on the Effect of Sextant TRUS-Guided Biopsy on Erectile Function

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What's known on the subject? and What does the study add?

The literature on erectile dysfunction after prostate biopsy is variable. In some studies, erectile dysfunction was observed after the biopsy, but this effect resolved after 3 or 6 months. In our study, there was no difference in IIEF scores before and after the biopsy; only patients with prostate cancer had significantly higher erectile dysfunction.

Abstract

Objective: Many complications after prostate biopsy (PB) have been reported. One of the possible complication after PB is erectile dysfunction (ED). In this study, we showed the early (1 month after PB) effect of PB on erectile function.

Materials and Methods: A total of 207 men who underwent PB between April 2021 and October 2021 were evaluated. Before and 1 month after PB, all patients were evaluated with the IIEF-5 (5-item version of the International Index of Erectile Function) prospectively. Patient data such as age, body mass index, prostate-specific antigen levels, prostate volume, periprostatic local anesthesia, pathological results, and post-biopsy complications were noted.

Results: The mean IIEF-5 score was 13.3 (5-25) before PB. One month after the biopsy it was 13.5 (5-25). There were no differences between the before and after PB IIEF scores. The only significant change was observed in the prostate cancer (PCa) group.

Conclusion: In past studies, it has been shown that ED after prostate biopsy is mostly seen at the first month and improves after that. In our study, PB did not affect erectile function. Only the PCa-diagnosed group showed a significant decrease in erectile function, and this effect was not attributed to prostate biopsy.

Keywords: Sextant prostate biopsy, erectile dysfunction, prostate cancer

Introduction

Transrectal ultrasound-guided sextant prostate needle biopsy (PB) is still the most commonly used procedure for the diagnosis of prostate cancer (PCa) (1). Frequent complications following this procedure include hematuria, rectal bleeding, hematospermia, urinary tract infection and rectal discomfort. More severe complications, such as urinary retention, serious infection, and sepsis, are comparatively rare (2).

Various studies have suggested that PB is associated with erectile dysfunction (ED). These effects have been associated with several factors such as anxiety related to the biopsy (3), periprostatic nerve block (PNB), neurovascular bundle injury (4,5), the number of biopsy cores taken (6), and the type of the biopsy (either transperineal or transrectal). By contrast, some studies did not find a relationship between PB and ED (7). In addition, the diagnosis of PCa may cause ED because of psychological stress, anxiety, and depression (8).

The literature on ED after prostate biopsy is variable. In some studies, a significant decrease was observed in IIEF scores 1 month after biopsy, but this effect resolved with non-significant differences at 3 and 6 months after PB (9). Therefore, there is a need to better understand the association between PB and ED.

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Our study investigated the incidence of early (1 month after PB) ED after PB and possible contributing factors.

Materails and Methods

A total of 207 men who underwent PB between April 2021 and October 2021 were prospectively evaluated. Patients with prior prostate biopsy history, different pathologies of the specimen [Prostatic intraepithelial neoplasia (PIN), urothelial cancer and Atypical small acinar proliferation suspicious (ASAP)], and ED treatment history were excluded from the study. Elevated prostate-specific antigen (PSA) levels (>2.5 ng/mL) and/or abnormal digital rectal examination (DRE) (nodule, stiffness) were indications for PB. Written informed consent was obtained from all patients. The research was approved by the Ethics Committee of Hitit University Faculty of Medicine (protocol number: 447-07/04/2021, date: 29.03.2021).

Second-generation cefalosporin sefpodoksim proksetil 200 mg and ornidazole 500 mg (twice a day) were started 2 days before the procedure. Ten milliliters of 2% lidocaine was instilled into the rectum 15 minutes before the procedure to obtain local anesthesia. We used a disposable biopsy device and a disposable 18-gauge 20 cm biopsy needle, which were all compatible with transrectal ultrasound (Geotek healthcare products TRUS Biopsy Kit-CE1984). We performed 12 core-sextant biopsy with additional cores from the suspected areas. Before the biopsy, PNB made to 134 patients with 2% prilocaine-HCl 5 cc on each side of the prostate by 18-gauge Chiba needle. Prostate volume was calculated using the ellipsoid formula (volume = height × length × width × 0.53).

Before PB and 1 month after PB, all patients were evaluated with the IIEF-5 (5-item version of the International Index of Erectile Function) prospectively. The IIEF-5 questionnaire is a shortened version of the IIEF-15, which is the final item of sexual intercourse satisfaction. In this study, we used the Turkish version of the IIEF-5 validated by Turunc et al. (10) in 2007. We categorized the severity of ED into five groups according to IIEF-5 scores; severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25). These 207 patients were divided into three groups according to the change in their total IIEF scores after one month. These groups determined with increase, decrease and no change in IIEF scores. We compared the datas [age, BMI (body mass index), PSA levels, prostate volume, periprostatic local anesthesia, pathologic results, post-biopsy complications] of these three groups. Postoperative complications were noted according to modified Clavien-Dindo classification system. Visual analog scale (VAS) questionnaire was directed to all patients after biopsy.

Statistical Analysis

IBM SPSS Statistics V22.0 was used for statistical analysis. The normal distribution of data was tested by the Kolmogorov-Smirnov, Shapiro-Wilk test. The Mann-Whitney U test was used for those who did not show normal distribution, and the Student's t-test was used for comparison of normally distributed data. The IIEF-5 score changes were compared using the paired t-test. Statistical significance was considered when the p-value was less than 0.001.

Results

A total of 207 patients were included in the study. The mean age of the patients was 64.7 (50-77) years, and the mean BMI was 27.6 (17.9-40.1). The mean serum PSA level was 14.9 (2.9-120) ng/mL and the mean prostate volume was 52.3 (10-140) cc. Forty-six (22.2%) patients had abnormal DRE findings. Mean VAS scores was 2.4 (0-8) (Table 1).

There were no serious complications during the procedures. According to the Clavien-Dindo classification system, grade-I complications developed in 43 patients and grade II complications in 12 patients after the procedure. There were no grade III or IV complications (Table 2).

The mean IIEF-5 score was 13.3 (5-25) before TRUS-Bx. One month after biopsy it was 13.5 (5-25). When prior to PB and after PB IIEF scores were compared, we found that 113 scores did not change, 44 scores increased, and 50 scores decreased. With

Table 1. Characteristics of the study population

Age* (years)	64.7 (±6.62)
BMI* (kg/m²)	27.6 (±3.87)
Abnormal DRE, n (%)	22.2 (46/207)
Serum PSA* (ng/mL)	14.9 (±21.1)
VAS scores*	2.4 (±1.77)
Prostate volume* (mL)	52.37 (±23.1)
Prior IIEF-5 score*	13.34 (±5.97)

*Mean ± standard deviation
BMI: Body mass index, DRE: Digital rectal examination, PSA: Prostate-specific antigen, ED: Erectile dysfunction, IIEF: International Index of Erectile Function, VAS: Visual analog scale

Table 2. Modified Clavien-Dindo classification system of after PB patients

Grade I [n=43]	Grade II [n= 12]
Fever (n=8)	Urinary tract infection (n=10)
Rectal pain (n=10)	Anemia (n=2)
Urinary retention (n=4)	
Hematuria (n=15)	
Erectile dysfunction (n=6)	

PB: Prostate biopsy, Grade IIIa, Grade IIIb, Grade IV not seen

these results we divided patients into 3 groups. In this group, age, PSA level, prostate volume, VAS scores, and complication rates were similar. PNB was performed in 134 patients (64.7%). There was no significant difference in the IIEF change. Between these groups, only the PCa ratio was statistically different (Table 3).

Sixty-five of 207 biopsies resulted in PCa (31.4%). Fifty-two (80%) of these had ED before PB. After 1 month, the number of ED patients increased to 56 (86.1%). When classified mild, mild to moderate, moderate and severe; pre-biopsy IIEF's were 19 (29.2%), 16 (24.6%), 13 (20%), 4 (6.1%) and post-biopsy IIEF's were 19 (29.2%), 18 (27.6%), 15 (23%) and 5 (7.6%) respectively (Table 4).

Before biopsy, ED was reported in 154 patients (74.3%) and 160 (77.2%) patients after PB. When IIEF was classified as mild, mild to moderate, moderate, and severe ED pre-biopsy, 56 (28.8%), 51 (24.6%), 41 (19.7%) and 6 (2.8%) patients, respectively. ED was reported as mild, mild to moderate, moderate, and severe in 56 (27%), 55 (26.6%), 42 (20.2%), and 7 (3.3%) patients, respectively, after 1 month (Table 4) (11).

Table 3. Mean IIEF scores before and after PB

	Pre-biopsy	1 month after	p-value
Mean IIEF	13.3	13.5	0.512
ED -	53	47	0.223
ED+	154	160	0.189
Mild	56	56	0.825
Mild-moderate	51	55	0.423
Moderate	41	42	0.321
Severe	6	7	0.612

IIEF: International Index of Erectile Function, ED: Erectile dysfunction, PB: Prostate biopsy

Discussion

PB is one of the most common urological procedures worldwide (2). ED is a common age-related medical problem that influences the quality of life and it has been reported following PB (12). The literature on ED after PB is heterogeneous, but this effect may be transient. In a systematic review in 2020, Frainberg et al. (9) found that 1 month after biopsy, the mean IIEF-5 scores had a statistically significant decrease, which appeared to resolve at 3 months. Most studies in the literature showed similar results, and we researched IIEF changes in the early period (first month) after biopsy in our study. In contrast, we did not find any association with ED after prostate biopsy in the early period. The mean IIEF-5 score was 13.3 (5-25) before TRUS-Bx in our study, after one month it was 13.5 (5-25) and this change was not statistically significant.

Chrisofos et al. (7) found a mean IIEF score of 15.9 prior to biopsy and 14.3 after 1 month biopsy. They mentioned that pre-biopsy ED had 38 patients, 18 mild, 9 mild- moderate, 7 moderate, and 4 severe. One month after PB, ED was reported by 42 patients (91.30%): Twelve patients with mild ED (26.08%), 14 patients with mild to moderate ED (30.43%), 9 patients with moderate ED (19.56%), and seven patients with severe ED (15.21%) (7). Kamali et al. (13) found a pre-biopsy ED rate of 76.2%, and these patients had 23 mild (28.8%), mild-modarate 21 (26.3%), modarate 17 (21.3%), and severe 0. Respectively, after 1 month, the ED subtypes were 23 (28.8%), 19 (23.8%), 18 (22.5%), and 5 (5%) patients. The mean IIEF before PB was 16.5 after 1 month 15,7 (13). Both authors found that the changes in IIEFs were not significant. In our study, similar to the mean IIEF score, the severity of ED did not change after PB. Before biopsy, ED was reported in 154 patients (74.3%) and 160 (77.2%) patients after PB. When IIEF was classified as mild, mild to moderate,

Table 4. Patient characteristics by IIEF score change

		Group 1 (raised IIEF) n=44	Group 2 (decreased IIEF) n=50	Group 3 (no change) n=113	p-value
Age (years) *		64.50 (7)	67.0 (15.75)	65 (9.75)	0.288
BMI (kg/m²) *		27.85 (3.43)	27.84 (6.18)	26.81 (6.83)	0.836
PSA (ng/dL) *		7.40 (3.48)	7.35 (21.12)	7.05 (5.02)	0.328
Prostate volume (mL) *		50 (24)	50 (20)	50 (38)	0.578
VAS score		2 (2)	2 (3)	2 (2)	0.457
PNB	+n (%)	32 (72.7)	33 (66.0)	69 (61.1)	0.380
	-n (%)	12 (27.3)	17 (34.0)	44 (39.9)	
PCa	-n (%)	36 (81.8)	24 (48.0)	82 (72.6)	**0.001**
	+n (%)	8 (18.2)	26 (52.0)	31 (27.4)	
Complication grade II or higher	-n (%)	40 (90.9)	48 (96.0)	107 (97.4)	0.544
	+n (%)	4 (9.1)	2 (4.0)	6 (5.3)	

*Mean ± standard deviation
BMI: Body mass index, PSA: Prostate-specific antigen, IIEF: International Index of Erectile Function, VAS: Visual analog scale, PNB: Periprostatic nerve block, PCa: Prostate cancer

and moderate ED pre-biopsy, 56 (28.8%), 51 (24.6%), 41 (19.7%) and 6 (2.8%) patients, respectively. ED was reported as mild, mild to moderate, moderate, and severe in 56 (27%), 55 (26.6%), 42 (20.2%), and 7 (3.3%) patients, respectively, after 1 month. No statistically significant difference was found in our study either (Table 3).

ED can occur more often after PB in PCa diagnosed patients. Helfand et al. (14) found that in 134 men evaluated after PB, PCa-diagnosed patients had an increased rate of ED as checked against men without PCa. They pointed out that men with PCa were 9.1 times more likely to have a decrease of 5 or more points in their total IIEF compared with men without cancer (14). In support of this finding, we found similar results to those of Helfand et al. (14) when pre- and post-biopsy IIEF scores were compared, 113 scores were not changed, 44 score were raised and 50 score were decreased. In these three groups, when the pathological outcomes were compared, the IIEF change was statistically significant in the PCa group (Table 4). This decrease in IIEF scores can be explained by three reasons; diagnosis of PCa, anxiety involved in the diagnosis of PCa, and possible choice of treatment for PCa (14).

The effect of PNB to erectile function is variant. Klein et al. (5) investigated whether PNB could result in ED after PB. In our study, there was no difference in terms of IIEF change between patients with and without PNB (Table 4). Klein et al. (5) reported that the decrease in IIEF-5 scores 1 month after PB recovered within 3 months. They found that ED might be associated with prostate biopsy regardless of PNB or number of cores, but that reduction was reversible within 3 months (5). In addition, we did not find any difference with PNB applied PB patients IIEF scores.

Although different rates of PCa are stated in various studies, in our study we found a PCa detection rate of 31.4% similar to that reported in the literature (65/207 biopsies). This rate ranges between 25.8% and 48% in different studies (15).

In our study, while investigating ED as a complication of prostate biopsy, we also noted and classified other complications. The complication rate of our study was 26.5% (55 of 207 biopsies), which was similar to the literature (16,17). There were modified Clavien-Dindo gradel 43 (20.7%) and 12 grade II (5.8%) complications, and we did not have any grade III or IV complications (Table 2). Prasetya and Renaldo (17) found an overall 98 complication events of 400 biopsies (24.75%), divided into 5 grades (I, II, IIIa, IIIb, and IV). Grade I was 20.5%, grade II was 3.25%, grade IIIa 0.25%, grade IIIb 0.25% and grade IV was 0.5% (16,17).

Conclusion

Various studies that aimed to show the relationship between PB and erectile function demonstrated that erectile function decreases in the early period after PB, and longer follow-up showed that these changes resolved back to baseline. In contrast, our study showed that PB did not affect erectile function 1 month after PB. However, ED is a possible complication after PB; therefore, potent patients should be informed.

Ethics

Ethics Committee Approval: The research was approved by the Ethics Committee of Hitit University Faculty of Medicine (protocol number: 447-07/04/2021, date: 29.03.2021).

Informed Consent: Written informed consent was obtained from all patients.

Authorship Contributions

Surgical and Medical Practices: M.Y., A.B., Concept: M.Y., A.B., Design: M.Y., A.B., Data Collection or Processing: M.Y., A.B., Analysis or Interpretation: M.Y., A.B., Literature Search: M.Y., A.B., Writing: M.Y., A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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Effects of Perioperative Fluid Management on Endothelial Glycocalyx in Radical Cystectomy: A Randomized Clinical Trial

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What's known on the subject? and What does the study add?

Major abdominal surgeries are known to cause large amounts of fluid shifts *in vivo*, occasionally depending on the fluid therapy modality. Theoretically, excessive fluid replacement leads to glycocalyx damage; however, it is not well established how to follow-up such damage and its clinical implications. In this study, biochemical degradation products of glycocalyx and their relationship with liberal fluid therapy are demonstrated, although there may not be any clear change in hemodynamic monitoring.

Abstract

Objective: The endothelial glycocalyx layer (EGL) is the interface between the blood and the endothelium that regulates permeability. This study compared the effects of liberal and restrictive fluid therapies on atrial natriuretic peptide (ANP) release and EGL products in radical cystectomy surgery. We hypothesized that a liberal regimen would damage the glycocalyx layer, resulting in a higher serum EGL product concentration than restrictive therapy.

Materials and Methods: Patients were randomized into two groups for restrictive (group R) or liberal (group L) regimens. Group R received 2 mL/kg/h Ringer's lactate and 2 mcg/kg/h norepinephrine infusion, whereas group L received only Ringer's lactate infusion at 10 mL/kg/h rate during the surgery. Preoperative and postoperative blood samples were obtained to evaluate ANP levels and glycocalyx degradation products. The stroke volume index, cardiac index, stroke volume variation, and systemic vascular resistance index parameters were recorded at 30-min intervals throughout the surgery. The length of stay in the hospital and intensive care unit and postoperative complications were recorded.

Results: The study was completed with 39 patients. Postoperative ANP levels were higher in group L in both between- and within group examination ($p<0.05$). EGL constituents; syndecan-1 and hyaluronan concentrations, were higher in group L ($p<0.05$). Advanced hemodynamic parameters indicated insignificant changes between the groups ($p>0.05$). Postoperative complications and length of stay data were similar ($p>0.05$).

Conclusion: ANP, hyaluronan, and syndecan-1 concentrations can be used as an indirect measurement method to show EGL damage and hypervolemia in major urologic surgeries. Advanced hemodynamic monitoring was ineffective for confirming hypervolemia.

Keywords: Fluid shifts, atrial natriuretic peptid, hemodynamic monitorization, liberal fluid therapy, radical cystectomy

Introduction

Major abdominopelvic surgeries are known to be extensive operations that cause large fluid shifts among the tissues and occasionally require high volume of intraoperative fluid replacement. Adopting proper perioperative fluid management is essential, but the correct therapy is still debated in the literature (1). Ongoing studies are now focusing on the micro

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level; investigating the dynamics of intravascular fluid by taking "endothelial glycocalyx" (EGL) into consideration, which may help define a suitable approach (2,3). An endogenous hormone, atrial natriuretic peptide (ANP), is secreted from the atrium of the heart due to mechanical wall stress which damages the EGL (4).

Conventionally, perioperative fluid therapy aims to provide adequate nutrient and oxygen delivery to the organs and tissues while avoiding hypotension, which may cause hypoperfusion. However, this approach may result in infusing quite large amounts of fluid with possible adverse effects on the organs (5). Organ perfusion disorders can be observed with hypovolemia, and when shifted to the hypervolemic side, complications such as pulmonary edema, prolonged mechanical ventilation, anastomotic leaks, and infection can be encountered (6).

The data regarding the fluid amount affecting EGL shedding is mostly investigated in critical care settings, and anesthesia-related results are yet to be investigated (7). We hypothesized that glycocalyx damage markers would be significantly higher in patients who receive liberal fluid therapy. The aim of this study was to investigate the relationship between liberal fluid replacement and EGL shedding during the perioperative period. Our primary outcome was the change in serum ANP concentrations, and secondary outcomes were structural EGL products (hyaluronic acid, heparane sulfat, syndecan-1) concentrations, advanced cardiac hemodynamic parameters, total usage of fluid, vasopressor, and blood products, length of intensive care unit (ICU) and hospital stay, and complications.

Materials and Methods

This prospective, single-center, double-blind, randomized trial was approved by the local Clinical Research Ethics Committee of İstanbul University, İstanbul Faculty of Medicine (2018/374) and registered at clinicaltrials.gov (NCT04780490). After obtaining informed consent, the study was performed on patients with American Society of Anesthesiologists physical status II-III who underwent radical cystectomy with urinary diversion under general anesthesia between April 2018 and June 2020. A computed system (www.graphpad.com) was used for randomization to generate numbers and divide patients into two groups, and the numbers were stored in opaque sealed envelopes by an external person. The exclusion criteria were hepatic dysfunction (impaired liver function tests), cardiac dysfunction (ejection fraction <35%), renal dysfunction (glomerular filtration rate <30 or creatinine >2 mg/dL), and known coagulapathies. Informed consent was obtained from all participants. The patients and postoperative data assessors were blinded to the groups.

Anesthesia Management

After arrival to the operating room, standard monitorization (electrocardiography, non-invasive blood pressure, and pulse oximetry) was performed on all patients. Before general anesthesia induction, an epidural catheter was inserted at T9-T10 level using a 16-gauge Tuohy needle in which the catheter placement was checked with a 3 mL 2% lidocaine (Jetmonal®, Adeka, İstanbul, Turkiye) test dose. In the postoperative period, 0.1% bupivacaine (Marcain®, Astra Zeneca, Cambridge, UK) infusion was administered to all patients via a PCA device (PCA Ambulatory infusion pump, CADD-legacy, Smiths Medical MD, Minnesota, USA), epidurally, for up to 48 h (basal infusion: 6 mL/h, PCA dose: 4 mL/h, lockout time: 30 min, 4-hour limit: 26 mL).

Standard anesthesia induction with midazolam (0.05 mg/kg IV, fentanyl 2 mcg/kg IV, propofol 2 mg/kg IV, and rocuronium (0.06 mg/kg IV) was provided. Controlled mechanical ventilation was set to keep $EtCO_2$ between 35 and 40 mmHg, positive end-expiratory pressure at 5 mmHg, and tidal volume at 6-8 mL/kg based on ideal body weight. Sevoflurane was used for maintenance to achieve a minimum alveolar concentration of 0.8-1.

Once safe induction and maintenance are provided; a pulse contour analysis device, the Vigileo™ system (Edwards Lifesciences LLC, Irvine, CA, USA) using the FloTrac™ Sensor via arterial cannulation, was installed in all patients. Using this monitor, advanced hemodynamic parameters like stroke volume index (SVI), cardiac index (CI), stroke volume variation (SVV), and systemic vascular resistance index values were recorded at 30-min intervals throughout the surgery. Despite this specific monitoring, the operating anesthetist was blinded to the parameters to follow our fluid protocol.

Fluid Management

Sealed envelopes were opened upon patient entry to the operating room. According to the randomization; restrictive fluid therapy group (Group R) was replaced with 2 mL/kg/h Ringer's lactate along with 2 mcg/kg/h norepinephrine IV infusion during the surgery. In case of a mean arterial pressure (MAP) drop below 65 mmHg, norepinephrine dosage was increased up to 8 mcg/kg/h. If further hypotension was observed, a 250 mL bolus of Ringer's lactate was administered. The liberal fluid therapy group (group L) was replaced with 10 mL/kg/h Ringer's lactate throughout the surgery. Similar to the other group; the hypotension periods were intervened with bolus Ringer's lactate (250 mL) without norepinephrine boluses or infusion. In case of observed hypotension after two consecutive fluid boluses, norepinephrine IV 0.1 mcg/kg bolus was administered to group L. Blood loss exceeding 500 cc was intervened with an equal

amount of colloid solution (voluven balanced®, Fresenius Kabi AG, Stans, Switzerland), and an erythrocyte suspension (ES) was transfused if the blood gas analysis reflected a hemoglobin drop below 8 g/dL (<9 g/dL for patients with ischemic heart disease) in both groups. In case of uncontrolled hypotension, the patients were excluded from the study.

Preoperative and postoperative 1st and 2nd day laboratory parameters, including hemoglobin (g/dL), hematocrit (%), albumin (g/dL), total protein (g/dL), urea (mg/dL), creatinine (mg/dL), and C-reactive protein (mg/dL), were recorded. The postoperative total amount of given crystalloid, blood products, and urine output were also recorded for secondary analyses. As a postoperative complication, acute kidney injury (AKI) occurrence was evaluated in the early postoperative period under KDIGO classification (8). Creatinine levels were also examined on the postoperative 6th month in order to observe chronic kidney disease occurrence. Length of hospital stay (LOS), gastrointestinal (constipation, ileus, anastomotic leak), cardiovascular, neurologic, and infectious complications were also recorded.

Determination of the ANP and Glycocalyx Constituents

Peripheral venous blood samples (10 mL) were taken before the induction of anesthesia and at the end of the surgery and were examined at the department of medical biology of the institute. The blood samples were centrifuged at 3500 RPM for 10 min, and the serum fraction was frozen and stored at 80 °C until required for the assay, which was thawed only once as appropriate. Serum levels of human syndecan-1/CD138, human heparan sulfate, human hyaluronic acid, and human ANP molecules were measured using an enzyme-linked immunosorbent assay (ELISAs kit, Invitrogen).

Statistical Analysis

Based on the assumption of a 30% change in serum ANP concentrations with liberal fluid therapy; and with a desired power of 0.8 and alpha error of 0.05, at least 17 participants were required for each group. Considering a possible drop-out ratio of 10%, 38 patients were planned to be enrolled in the current study. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 21.0. Categorical data were analyzed using descriptive statistics. Homogeneity of the data was assessed with Kolmogorov-Smirnov test, and the t-test or Mann-Whitney U test was used for between-group data comparison according to the normality of the data. Repeated measure analysis of variance (ANOVA) was performed for intragroup recurrent measurements. All categorical variables were compared for the study outcome using Fisher's exact test or the w2 test. A p-value of <0.05 was considered statistically significant.

Results

In each group, 22 patients were enrolled. However, one patient was excluded from group L because of intraoperative aberrant tachyarrhythmia, and four patients were excluded from group R because of missing follow-up data, including blood samples. Therefore, the current study was completed with 39 patients (Figure 1).

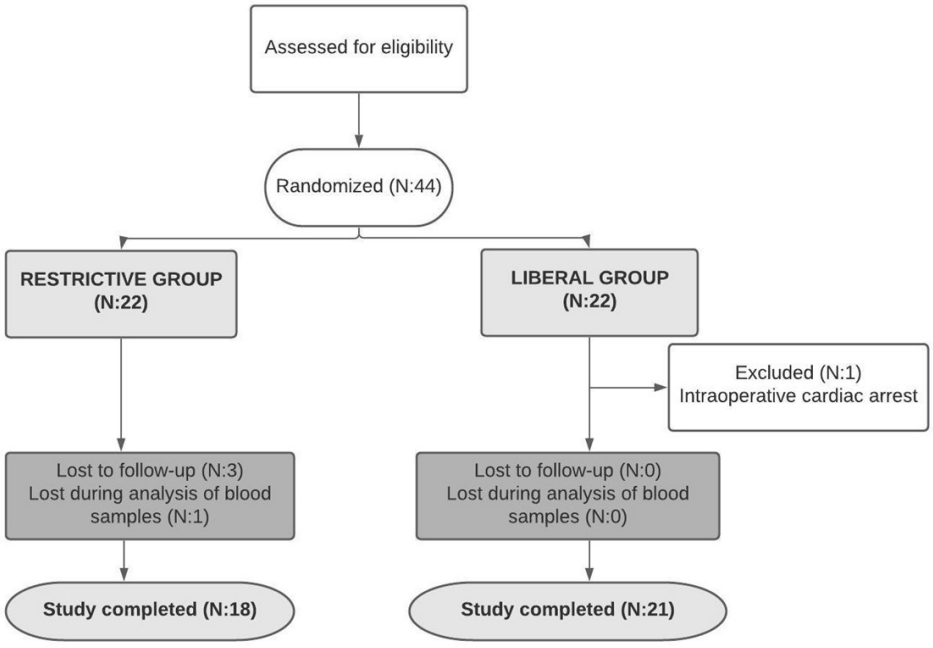

Figure 1. Study design flowchart (CONSORT diagram)

Demographic data were not different between the groups except for body weight. Anesthesia and surgical durations were also similar between the groups (p>0.05). Group R was given less fluid, which was compatible with the study design (1105 mL vs. 3790 mL, p<0.001). However, group L patients required a higher volume of colloid use (485 mL vs. 769 mL, p<0.05). The number of patients who required vasopressor use was significantly higher in group R, as expected; however, occasional vasopressor need was observed in group L, either (p<0.001). Intraoperative total amount of ES and fresh frozen plasma (FFP) consumption was similar between the groups (p>0.05) (Table 1). As summarized in "Table 2", intraoperative hemodynamic variables including cardiac output measurements were statistically similar at all predefined time points of the surgeries (p>0.05).

Postoperative laboratory parameters did not differ between the groups (p>0.05; Table 3). The situation was the same for postoperative 1st and 2nd day crystalloid replacement also (2846 mL vs. 3112 mL, 2482 mL vs. 2700 mL, respectively; p>0.05). Additionally, there was no difference in terms of the amount of ES and FFP replaced on the postoperative 1st and 2nd day (p>0.05). However, the urine output on both postoperative 1st and 2nd days was significantly lower in group R than in group L (1704 mL vs. 2481 mL, 1476 mL vs. 2304 mL, respectively; p<0.05). Six patients in group R and five patients in group L

Table 1. Demographic, clinical characteristics, intraoperative fluid parameters and postoperative complications of the groups

Characteristics	Group R (n=18)	Group L (n=21)	p
Sex (female/male)	3/15	4/17	0.3
Age (years)	62.29±9.52	64.41±10.66	0.5
Body weight (kg)	82.82±16.70	71.82±11.73	**0.02***
Height (cm)	171.35±9.99	167.23±7.09	0.1
BMI (kg/m²)	29.19±20.22	27.18±19.33	0.6
ASA II	13	15	0.8
ASA III	5	6	0.8
Hypertension (n)	10	10	0.4
Diabetes mellitus (n)	2	3	0.8
Ischemic heart disease (n)	2	2	0.8
COPD (n)	2	3	0.8
Active smoker (n)	10	13	0.9
Duration of anesthesia (min)	350.21±85.47	336.57±75.12	0.1
Duration of surgery (min)	322.5±80.14	296.76±69.81	0.1
Crystalloid infused (mL)	1105.88±319.12	3790.90±1078.75	**<0.001****
Colloid infused (mL)	485±209.56	769.23±330.11	**0.01***
Vasopressor usage (n)	18	4	**<0.001****
Length of ICU stay (hours)	19.7±8.4	21.4±6.15	0.8
Length of hospital stay (days)	11.3±8.4	12.1±7.3	0.7
Complications			
Gastrointestinal Anastomotic leak Constipation Ileus	 1 5 1	 2 3 3	0.7
Cardiovascular Ventricular tachycardia	 0	 2	0.4
Neurologic Seizure	 0	 1	0.9
Genitourinary Pyelonephritis Urosepsis Urinary tract infection Surgical wound infection	 0 1 4 3	 1 2 4 3	0.5
Exitus	1	1	1

ASA: American Society of Anesthesiologists, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, ICU: Intensive care unit, *: p<0.05, **: p<0.001, n: Number of patients

Table 2. Intraoperative hemodynamic parameters			
	Group R (n=18)	Group L (n=21)	p
HR (beats/min)			
Post-induction	77.11±17.84	76.72±12.53	0.9
30th min	73.00±14.72	70.72±12.53	0.6
60th min	68.41±15.35	68.50±13.26	0.9
90th min	69.05±14.23	69.40±13.26	0.9
120th min	76.76±13.65	68.77±11.33	0.4
End of surgery	78.31±6.77	82.82±10.71	0.1
MAP (mm Hg)			
Post-induction	88.17±19.16	92.45±25.90	0.5
30th min	83.41±15.67	84.68±13.87	0.7
60th min	79.23±12.57	85.27±13.65	0.1
90th min	83.58±11.62	84.54±16.08	0.8
120th min	84.00±8.97	81.40±15.84	0.5
End of surgery	71.43±14.94	75.82±11.85	0.3
SVI (mL/m²/beat)			
Post-induction	39.17±15.88	38.31±10.31	0.8
30th min	37.11±16.38	38.90±9.02	0.6
60th min	37.64±11.81	36.90±10.88	0.8
90th min	39.29±13.45	34.22±9.58	0.1
120th min	36.00±13.28	40.36±10.34	0.2
End of surgery	45.25±14.25	38.60±10.37	0.1
CI (L/min/m²)			
Post-induction	2.76±0.90	2.66±1.06	0.7
30th min	2.72±0.85	2.71±0.91	0.9
60th min	2.36±0.52	2.55±0.90	0.4
90th min	2.50±0.53	2.48±0.64	0.9
120th min	2.41±0.47	2.67±0.87	0.2
End of surgery	3.20±1.14	2.88±0.78	0.3
SVV (%)			
Post-induction	13.33±7.40	10.73±3.45	0.1
30th min	12.46±5.82	10.95±3.67	0.3
60th min	13.33±4.89	13.26±4.94	0.9
90th min	13.53±3.44	13.00±5.26	0.7
120th min	15.06±5.40	12.86±4.29	0.1
End of surgery	11.06±5.17	12.43±4.96	0.4
SVRI (dyne. s. cm⁻⁵/m²)			
Post-induction	32179.14±545.22	2222.56±738.27	0.8
30th min	2157.21±546.96	2182.76±674.84	0.9
60th min	2413.57±668.94	2193.30±616.37	0.3
90th min	2260.71±791.12	2392.30±838.92	0.6
120th min	2321.14±659.25	2270.39±659.25	0.8
End of surgery	1810.22±641.76	2049.22±626.60	0.2

HR: Heart rate, MAP: Mean arterial pressure, SVI: Stroke volume index, CO: Cardiac output, CI: Cardiac index, SVV: Stroke volume variation, SVRI: Systemic vascular resistance index

experienced creatinine elevation above 0.3 mg/dL in the early postoperative period, which was compatible with stage 1 AKI. However, none of the patients developed chronic kidney disease during the 6-month postoperative follow-up. Gastrointestinal, cardiovascular, neurologic, and infectious complications did not differ statistically among the groups (p>0.05). Accordingly; three of the group L patients experienced ileus and two experienced anastomotic leak, whereas one patient in group R experienced ileus and one other patient experienced anastomotic leak. It was similar on the wound infection aspect. Only one patient from each group developed a surgical wound infection (Table 1). The median length of ICU stay (19.7±8.4 hours in group R vs. 21.4±6.15 hours in group L, p>0.05) and hospital stay (11.3±8.4 days in group R vs. 12.1±7.3 days in group L, p>0.05) were similar (Table 1).

Our primary outcome; postoperative serum ANP concentrations were higher than preoperative values in group L (84.31±14.05 pg/mL and 55.64±15.38 pg/mL, respectively; p<0.05). The situation was the same for hyaluronan and syndecan-1 levels, also (p<0.05). Interestingly, restrictive therapy group postoperative ANP concentrations was quite close to the preoperative

Table 3. Preoperative, postoperative 1st and 2nd-day laboratory values			
	Group R (n=18)	Group L (n=21)	p
Preoperative			
Hemoglobin (g/dL)	12.24±2.34	12.15±2.19	0.9
Hematocrit (%)	37.36±7.12	36.22±6.32	0.6
Albumin (g/dL)	3.98±0.45	4.15±0.82	0.6
Total protein (g/dL)	6.67±1.01	6.58±1.10	0.6
Urea (mg/dL)	35.26±7.81	49.89±8.21	0.2
Creatinine (mg/dL)	1.02±0.25	1.29±0.45	0.8
C-reactive protein (mg/dL)	6.38±5.35	7.99±6.07	0.2
Postoperative 1st day			
Hemoglobin (g/dL)	10.21±1.69	9.92±2.24	0.9
Hematocrit (%)	30.92±5.18	28.98±4.28	0.1
Albumin (g/dL)	3.23±0.38	2.95±0.39	0.2
Total protein (g/dL)	5.60±0.76	5.01±0.46	0.1
Urea (mg/dL)	37.96±11.10	45.15±23.88	0.9
Creatinine (mg/dL)	1.23±0.35	1.30±0.51	0.8
C-reactive protein (mg/dL)	77.95±38.98	75.17±46.58	0.8
Postoperative 2nd day			
Hemoglobin (g/dL)	9.52±1.57	9.49±1.45	0.7
Hematocrit (%)	28.98±5.14	28.58±4.41	0.2
Albumin (g/dL)	3.08±0.38	3.06±0.50	0.8
Total protein (g/dL)	5.39±0.71	5.34±1.05	0.8
Urea (mg/dL)	46.17±19.36	46.72±25.68	0.4
Creatinine (mg/dL)	1.10±0.32	1.31±0.55	0.9
C-reactive protein (mg/dL)	160.00±62.74	165.91±102.16	0.6

values (55.81±9.98 pg/mL vs. 55.83±10.49 pg/mL; respectively; p>0.05). In line with this; postoperative serum hyaluronan and syndecan-1 concentrations were significantly lower in group R than in group L (14.19 ng/L vs. 19.45 ng/L and 3.99 pg/mL vs. 6.97 pg/mL; p<0.05, respectively). Of note, preoperative and postoperative comparison of heparan sulfate did not change significantly in both groups (p>0.05). Within-group analysis did not show any statistically significant change in ANP, heparan sulfate, hyaluronan, and syndecan-1 concentrations comparing the preoperative and postoperative values for group R (p>0.05) (Table 4).

Discussion

Our results support the relationship between the intraoperative liberal fluid regimen and EGL disintegration, which is attributed to elevated serum ANP concentration. As it was well demonstrated under "experimental" settings before; acute normovolemic hemodilution via limited colloid replacement is superior to excessive volume loading in terms of EGL protection (7). Although the data are quite sparse; clinical studies also exhibited similar outcomes. Belavić et al. (9) investigated three different groups as restrictive (1 mL/kg/h), low liberal (5 mL/kg/h), and high liberal (15 mL/kg/h) for minimally invasive surgeries and concluded that the high liberal crystalloid infusion group was associated with increased serum EGL constituents. Our current clinical study is consistent with the aforementioned findings. Accordingly, higher infusion rates causing hypervolemia are related to EGL damage regardless of the fluid (crystalloid or colloid) and surgery type (minimal invasive or open abdominal). Of note, only heparan sulfate did not increase with liberal therapy, which is compatible with the previous study (9). Heparanase enzyme is secreted from mast cells when activated by inflammation, and ANP receptors do not exist in the mast cell surface (10). Therefore, hypervolemia-induced ANP release may not affect heparan sulfate shedding into the circulation.

Table 4. Summary of preoperative and postoperative ANP, heparan sulphate, hyaluronan and syndecan-1 levels

	Group R (n=18)	Group L (n=21)	p**
ANP (pg/mL)			
Preoperative	55.83±10.49	55.64±15.38	0.6
Postoperative	55.81±9.98	84.31±14.05	**0.003**[a]
p*	0.4	**0.004**	
Heparan sulphate (ng/L)			
Preoperative	47.42±10.72	44.48±15.19	0.9
Postoperative	47.29±13.17	46.45±14.98	0.4
p*	0.4	0.2	
Hyaluronan (ng/L)			
Preoperative	13.93±6.21	13.00±3.56	0.7
Postoperative	14.19±5.19	19.45±5.99	**0.04**[b]
p*	0.09	**0.03**	
Syndecan-1 (pg/mL)			
Preoperative	4.04±1.69	4.76±1.97	0.8
Postoperative	3.99±1.55	6.97±1.87	**0.04**[a]
p*	0.6	**0.04**	

[a]: Student's t-test, [b]: Mann Whitney-U test. p*: ANOVA significance level within group analysis, p**: Significance level for between group analysis, ANP: Atrial natriuretic peptide

As seen in the revised starling equation, basic physiology has been evolving recently. Traditional capillary "reabsorption" is now a denied concept that was believed to protect intravascular fluid content initially. It is firmly underlined that the EGL layer is responsible for adjusting "the filtration" which occasionally preserves intravascular volume in case of hypovolemia or hypotension, and there is no "reabsorption" (3,11,12). Therefore, it is quite understandable why the EGL represents high importance. However, EGL cannot be the sole factor limiting hyperfiltration in cases of hyperhydration, which leads to "interstitial edema". Recent volume kinetics studies have shown that increased infusion rate is related to increased half-life in the peripheral space (13,14). High amounts of fluid retention may cause side effects in specific organ systems, such as pulmonary or urinary impairment (15).

MAP is one of the most important determinants of vascular filtration. Li et al. (16) clearly demonstrated that lower MAP is related to lower filtration, which causes more plasma dilution. Preserving individuals' hemodynamic parameters in a healthy window during surgery is a major concern in everyday anesthesiology practice. The tendency to replace higher amounts of fluid may arise due to the intention of avoiding hypotension. However; our results revealed that fluid restriction did not cause any significant drop in the MAP, SVI, CI, or SVV. Moreover; hyperhydration did not cause hypertension or increased cardiac output. These data are quite similar to Belavić et al.'s (9) study. As an exception, they demonstrated a relatively low MAP after anesthesia induction with restrictive fluid therapy compared with high liberal fluid therapy. Possibly, our restrictive regimen, which is supported with norepinephrine infusion, did not conduct the same situation because hypotension is due to vasodilation and norepinephrine is an alpha-1 adrenergic agonist. Note that Belavić et al. (9) did not exhibit any hypotension period with restrictive therapy, also. To our knowledge; data regarding intraoperative fluid regimen and its relation with advanced cardiac output measurement are quite sparse in the literature.

Clinical investigations that were presented in the early 2000s underline an observed lower postoperative complication rate, which may reach a 35% drop with intraoperative restrictive fluid therapy (17-21). Our current sample size was inadequate to compare postoperative complications; however, several studies

have demonstrated increased AKI incidence with restrictive regimen (22,23). Of note, long-term follow-ups did not exhibit chronic kidney disease in any patient who developed AKI in this study. Both restrictive and liberal fluid regimens have their own conflicts in terms of micro- or macrovascular complications. However, a quick return of bowel function and decrease in the LOS was achieved with enhanced recovery after surgery modalities for radical cystectomy patients in whom liberal fluid therapy is externalized (24,25). For this particular patient group, managing fluid therapy under the guidance of urine output is not possible because it is unmeasurable. Therefore, cardiac output measuring devices are considered valuable. However, we can only claim that advanced hemodynamic parameters may only prevent extreme fluid restriction, which eventually leads to low cardiac output, and as observed in this study; too much fluid replacement is not detectable with these hemodynamic variables occasionally. Therefore, biomarkers would be advantageous for recognizing excessive fluid replacement.

Study Limitations

This study represents a solid scientific basis since it is applied for major abdominopelvic surgery and examines biochemical findings along with advanced hemodynamic variables to evaluate the EGL structure. However, the total number of participants is a limitation for comparing postoperative clinical outcomes.

Conclusion

Compared with the restrictive fluid regimen, the intraoperative liberal fluid regimen causes elevated ANP secretion and EGL shedding in radical cystectomy patients without any significant change in static and dynamic hemodynamic parameters. Therefore, serum ANP concentrations may be used as an indicator of excessive fluid replacement. Further studies should focus on the clinical and laboratory effects of the chosen fluid regimen by considering recent physiological concepts such as the Revised Starling Equation, volume kinetics, and fluid distribution.

Ethics

Ethics Committee Approval: This prospective, single-center, double-blind, randomized trial was approved by the local Clinical Research Ethics Committee of İstanbul University, İstanbul Faculty of Medicine (2018/374) and registered at clinicaltrials.gov (NCT04780490).

Informed Consent: Informed consent was obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: F.S.O., Concept: H.Ş.Ç., K.M.T., Design: E.S.B., F.S.O., M.S.K., Data Collection or Processing: B.K.M., H.Ş.Ç., S.E., Analysis or Interpretation: H.Ş.Ç., K.M.T., F.S.O., T.M., M.S.K., Literature Search: B.K.M., E.S.B., T.M., Writing: B.K.M., E.S.B., K.M.T., F.S.O., M.S.K.

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ORIGINAL RESEARCH
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Long-term Surveillance Outcomes of Prostate Cancer Patients Eligible for Active Surveillance but Who Underwent Radical Prostatectomy

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What's known on the subject? and What does the study add?

Active surveillance has been introduced as an alternative to avoid unnecessary treatment and related side effects. No cancer-related deaths were observed in patients who is eligible for active surveillance but underwent radical prostatectomy. This may suggest that active surveillance criteria are suitable for detecting low-risk prostate cancer patients.

Abstract

Objective: We aimed to investigate the long-term surveillance outcomes (biochemical recurrance, survival) and adequacy of active surveillance criteria to detect low-risk prostate cancer patients who were eligible for active surveillance but underwent radical prostatectomy.

Materials and Methods: Data of patients who underwent radical prostatectomy for prostate cancer between January 2005 and January 2019 were retrospectively evaluated. Upstaging, upgrading, surveillance periods, and survival status of patients with clinical stage T1c and T2a, serum prostate-specific antigen below 10 ng/mL, International Society of Urological Pathology grade 1, number of tumor-positive cores in biopsy 2 and below, tumor percentage in tumor-positive cores 50 and below were inclusion criteria for active surveillance.

Results: The study included 606 patients. Of these patients, 184 (30.4%) met the inclusion criteria for active surveillance. Upgrading was detected in 77 (41.8%) patients and upstaging in 29 (15.8%) patients who met the criteria for active surveillance. The prostate-specific antigen (PSA) and PSA density values of the patients who met the active surveillance criteria were significantly lower than those of the other patients ($p<0.05$). The mean surveillance period was 127.6±49.6 (8-227) months, and 123 patients died during this period. Among them, 18 (3%) patients died because of related causes of prostate cancer. None of the patients who met the criteria for active surveillance died because of prostate cancer ($p=0.018$).

Conclusion: No cancer-related deaths were observed in patients who is eligible for active surveillance but underwent radical prostatectomy. This may suggest that active surveillance criteria are suitable for detecting low-risk prostate cancer patients.

Keywords: Active surveillance, prostate cancer, radical prostatectomy

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Introduction

Prostate cancer (PCa) has become an early-diagnosed disease with the common use of prostate-specific antigen (PSA) and has even led to overdiagnosis and overtreatment (1). Because curative treatment options for PCa carry the possibility of morbidity and mortality, active surveillance (AS) has been introduced as an alternative to avoid unnecessary treatment and related side effects (2). AS aims to monitor patients closely without losing the option of curative treatment (2). The inclusion criteria for AS are generally accepted as serum PSA less than 10 ng/mL, International Society of Urological Pathology (ISUP) grade 1, biopsy positive core less than 3, and involvement less than 50%. There are studies that include ISUP grade 2 patients with limited criteria (3).

There has been no randomized controlled study comparing AS with curative treatments. In AS studies, one-third of patients require reclassification and curative treatment (4). In one of the most extensive and longest-duration AS studies, curative treatment was required in 20% of the patients. Only 23% of the treated patients were ISUP grade 1 (5). In this study, which has the highest number of patients in the literature, the mean surveillance period was approximately 50 months, similar to other AS studies (4).

Screening for PCa reduces mortality, but this gain is associated with overdiagnosis and overtreatment (1). When we detect and treat insignificant PCa, overdiagnosis and overtreatment occur (1). Although AS protocols protect patients from overtreatment, upgrading in some patients and the delay and inability to predict this is important issues. Upgrading increases the risk of biochemical recurrence, and its rate is around 30-45% (6,7). In addition, the relatively short surveillance periods in the literature for a slowly progressive disease such as PCa should not be ignored. In our study, we aimed to investigate the long-term surveillance outcomes (biochemical recurrance, survival) and adequacy of active surveillance criteria to detect low-risk PCa patients who may be eligible for AS but who underwent radical prostatectomy (RP).

Materials and Methods

Following Dokuz Eylül University Faculty of Medicine Institutional Review Board Ethics Committee approval (decision no: 2023/34-02, date: 25.10.2023), the data of patients who underwent RP for PCa between January 2005 and January 2019 were retrospectively evaluated. The patients' ages at the time of surgery, preoperative PSA values (ng/mL), prostate volumes (mL), and PSA densities (PSADs) (PSA/prostate volume) were recorded. The number of cores sampled during biopsy, the number of positive cores, and the percentage of tumors in positive cores were evaluated. The biopsy and RP pathology results were evaluated according to the ISUP 2014 grading system (8).

Patients whose surveillance data were not available were excluded from the study. RP results were evaluated as upgrading if the ISUP grade was increased according to the biopsy pathology result, and upstaging if the RP result was T3a, T3b, or greater. The surveillance period was calculated in months by subtracting the date of RP from the date of death in patients who died and in months by subtracting the date of RP from January 2024, the date of the last surveillance in other patients. A PSA value >0.2 ng/mL after RP was considered a biochemical recurrence. Causes of death were determined from patient data.

Inclusion criteria for AS included clinical stage T1c and T2a, PSA below 10 ng/mL, ISUP grade 1, number of tumor-positive cores in biopsy 2 and below, and tumor percentage in tumor-positive cores 50 and below (3).

Statistical Analysis

The SPSS program was used for statistical analysis. In the study, numerical data were calculated as mean ± standard deviation, and categorical data were calculated as percentages. The significance between categorical groups was analyzed using the chi-square test. The difference between numerical data was evaluated with the Student's t-test. A value of $p<0.05$ was considered statistically significant.

Results

Seven hundred and thirteen patients underwent RP. One hundred and seven patients were excluded from the study because surveillance data were unavailable, and 606 patients were included. The mean age at the time of surgery was 63.1±6.5 years, serum PSA value was 8.8±7.5 ng/dL, number of biopsy cores was 11.5±2.2, prostate volume was 52.3±21.6 mL, and PSAD was 0.19±0.18. The mean surveillance period was 127.6±49.6 (8-227) months.

Of the 606 patients in the study, 184 (30.4%) met the inclusion criteria for AS. There was no statistically significant difference in age, surveillance period, prostate volume, and number of biopsy cores between patients who met the criteria for AS and other patients ($p>0.05$). The PSA, PSAD values, and number of positive biopsy cores of the patients who met the AS criteria were significantly lower than those of the other patients ($p<0.05$). A comparison of the preoperative data and surveillance periods of patients who met the AS criteria and other patients is given in Table 1.

Among patients eligible for AS, 77 (41.8%) patients had upgraded according to RP pathology. In other patients, upgrading was detected in 117 (27.7%) patients and downgrading in 63 (14.9%).

Upgrading was statistically significantly higher in patients who met the criteria for AS [$x^2(1)=35.467$ $p\leq0.001$]. Upstaging was detected in 29 (15.8%) patients eligible for AS and 234 (55.5%) in other patients. Among patients eligible for AS, 14.1% were T3a and 1.6% were T3b; among other patients, 41.9% were T3a and 13.5% were T3b. Upstaging was statistically significantly less in patients who met the AS criteria [$x^2(1)=82.168$ $p\leq0.001$]. Surgical margin positivity was statistically significantly lower in patients who met AS criteria [9.8% vs 30.8%; $x^2(1)=30.681$ $p\leq0.001$].

When the RP pathologies of patients who met the criteria for AS were evaluated, 58.2% were ISUP grade 1, 39.1% ISUP grade 2, 2.1% ISUP grade 3, 0.5% ISUP grade 4, and no patient had an ISUP grade 5 pathology result. When the RP pathologies of the other patients were evaluated, 12.6% were ISUP grade 1, 62.6% were ISUP grade 2, 14.2% were ISUP grade 3, 4.5% were ISUP grade 4, and 6.2% were ISUP grade 5.

While the biochemical recurrence rate was 2.7% in patients who met the criteria for AS, this rate was 16.1% in other patients, and this result was found to be statistically significant [$x^2(1)=20.457$ $p\leq0.001$]. When patient data were accessed, it was seen that 123 patients died. Eighteen (3%) of the deceased patients died because of PCa (progression of of and related complications). None of the patients who met the criteria of AS died of PCa [$x^2(1)=8.09$ $p=0.018$]. A comparison of the pathology and surveillance data of patients who met the criteria for AS and other patients is given in Table 2.

Discussion

Treatment of localized PCa can be likened to a double-edged knife; curative treatment can lead to morbidity, whereas if the disease is left untreated and progresses, we may have missed the chance of early treatment. The important point is to be able to predict which patients have a low risk of PCa.

The biopsy and final RP pathology results are only sometimes compatible and identical. In the literature, the rate of upgrading after RP is reported to be around 30-45% (6). The high probability of upgrading requires us to appropriately evaluate patients with AS and minimize this risk. In addition, upgrading increases the probability of biochemical recurrence of PCa (7). A recent systematic review investigating the risk factors for upgrading found that patient age, serum PSA value, prostate volume, PSAD, number, and percentage of biopsy-positive cores were significantly effective on upgrading (9). These risk factors form the basis of the inclusion criteria for AS. In our study, upgrading was found in 41.8% of patients who met the criteria for AS, which is similar to the literature. In other words, no matter how much we apply the risk factors for upgrading, this condition still develops at a high rate, and this risk should be reduced as much as possible in patients with AS. Upgrading in patients who were removed from AS and underwent RP varies between 14% and 51% (10).

The probability of positive surgical margin increases in the presence of extraprostatic extension or seminal vesicle invasion in the pathology result of RP (11). The risk of upstaging in low-risk PCa patients is approximately 25% (12). Upstaging increases the risk of biochemical recurrence (12). A meta-analysis investigating the importance of biochemical recurrence showed that the risk of distant metastasis and PCa-related death increased in patients with biochemical recurrence (13). In our study, upstaging was 15.8% in patients who met the active criteria, and a surgical margin positivity rate of 9.8% was observed in the same patient group.

The prostate does not have a true capsule but is surrounded by fibrous and muscular tissues (14). This situation complicates the work of imaging methods and makes local staging of PCa difficult (15). Current European Association of Urology guidelines recommend multiparametric magnetic resonance imaging (mpMRI) before biopsy in patients undergoing biopsy for the first time and systemic and targeted biopsy if a lesion is described on mpMRI (16). The patients in our study did not undergo mpMRI because mpMRI was not expected at that time, and these data were not yet accepted in the guidelines.

Table 1. Comparison of preoperative data and follow-up periods of patients eligible for active surveillance and other patients

	Eligible patients for active surveillance (n=184)	Other patients (n=422)	p-value
Age (years)	61.3±6.3	63.9±6.4	0.462
PSA (ng/mL)	6.1±2.0	9.9±8.6	<0.001
Duration of follow-up (months)	148.2±49.6	118.6±47.0	0.622
PV (mL)	57.3±21.3	50.2±21.3	0.241
PSAD (ng/mL²)	0.11±0.05	0.22±0.21	<0.001
Number of biopsy cores	11.1±1.7	11.7±2.4	0.136
Number of positive biopsy cores	1.35±0.47	3.93±2.50	<0.001

The difference between numerical data was evaluated with the Student's t-test
PSA: Prostate-specific antigen, PV: Prostate volume, PSAD: PSA density (PSA/prostate volume)

Table 2. Comparison of pathology data and follow-up data of patients who met the criteria for active surveillance and other patients

	Eligible patients for active surveillance (n=184)	Other patients (n=422)	Total (n=606)	p-value
Survival status				0.018
Death due to cancer	0	18 (4.3%)	18 (3.0%)	
Death from other causes	33 (17.9%)	72 (17.1%)	105 (17.3%)	
Alive	151 (82.1%)	332 (78.7%)	483 (79.7%)	
Upgrading	77 (41.8%)	117 (27.7%)	194 (32.0%)	<0.001
Upstaging	29 (15.8%)	234 (55.5%)	263 (43.4%)	<0.001
RP pathologies				<0.001
ISUP GRADE-1	107 (58.2%)	53 (12.6%)	160 (26.4%)	
ISUP GRADE-2	72 (39.1%)	264 (62.6%)	336 (55.4%)	
ISUP GRADE-3	4 (2.2%)	60 (14.2%)	64 (10.6%)	
ISUP GRADE-4	1 (0.5%)	19 (4.5%)	20 (3.3%)	
ISUP GRADE-5	0	26 (6.2%)	26 (4.3%)	
T stage				<0.001
T2	155 (84.2%)	188 (44.5%)	343 (56.6%)	
T3A	26 (14.1%)	177 (41.9%)	203 (33.5%)	
T3B	3 (1.6%)	56 (13.5%)	60 (9.9%)	
Positive surgical margin	18 (9.8%)	130 (30.8%)	148 (24.4%)	<0.001
Biochemical recurrence	5 (2.7%)	68 (16.1%)	73 (12.0%)	<0.001

The significance between groups was analyzed by chi-square test
ISUP: International Society of Urological Pathology

Adding mpMRI to AS criteria and surveillance protocols will make AS safer and more successful. In this way, both clinically significant PCa patients will be detected more efficiently, and local staging of the disease will be performed more accurately. We are waiting for the long-term results of ongoing studies using mpMRI. The results of these studies will perhaps make it easier for us to consider ISUP grade 1 as a benign condition (17).

Biomarkers such as prostate cancer antigen 3 or prostate health index used preoperatively are effective in showing the aggressiveness of PCa, but their costs leave question marks in terms of their cost-effectiveness (18). In a study by Gokce et al. (19), the neutrophil-to-lymphocyte ratio was a cheap and reliable method for predicting upgrading and biochemical recurrence. PSAD is also an important predictor used in risk calculations, and recent studies have shown that its combination with mpMRI significantly reduces unnecessary prostate biopsy (22). Although the cut-off value for PSAD is generally accepted as 0.15 ng/mL/cm^3, it is more effective when this value is reduced to 0.10 (20).

In the ProtecT study, 1643 patients were randomized into three groups and received RP, radiotherapy, or surveillance accordingly (21). Although the patients in this study did not fully comply with the current AS monitoring protocols, approximately 90% of the included patients met the current AS inclusion criteria (21). In this study, the 10-year cancer-specific survival rate of patients followed up without treatment was 98.8% vs. 99%, but the probability of metastatic progression was 6% vs. 2.6% (21). It should be kept in mind that metastases although rare, can be observed in AS protocols (4). In the ProtecT study, the authors also reported that 2/3 of AS patients received definitive treatment at the 7-year surveillance (21). Similarly, in the PRIAS study, no difference was found in the cancer-specific survival of patients in the low-risk group compared with those who received curative treatment (22). However, three-fourths of those in the AS group underwent curative treatment in this 10-year study (22). The mean surveillance period in our study was 127 months, indicating a long mean surveillance period of 10 years. During the surveillance period, which can be considered long enough for PCa, no cancer-related deaths occurred in the group of patients who met the criteria for AS.

While cancer-specific survival after RP was 80% in low- and intermediate-risk PCa patients in the pre-PSA era (23), this rate is 99% in the currently screened population (21). In our study, similar to the literature, cancer-specific survival was 100% in patients who met the criteria for AS. These data allow us to predict a high rate of success when low- and intermediate-risk PCa patients are treated with appropriate screening. High-risk PCa patients have a cancer-specific survival rate

of approximately 60% with RP and subsequent multimodal therapies (24). Therefore, it is necessary not to misclassify high-risk patients under AS as low-risk.

Study Limitations

Our study has some limitations, with the retrospective design being main. RP was not performed by a single surgeon, and there may be differences between surgeons' experiences over a 14-year period. In addition, because mpMRI, recommended before biopsy in current guidelines, was not routinely performed during the study, these data were not included in our study.

Conclusion

AS has an important place among the treatment strategies for PCa. Despite being in the low-risk group and meeting the criteria for AS, 41% of patients who underwent RP in our study had upgraded and 15% had upstaging. Patients should be informed about these risks when AS is recommended. In our study, no cancer-related deaths were observed in patients who is eligible for AS but underwent RP. This may suggest that active surveillance criteria are suitable for detecting low-risk prostate cancer patients.

Ethics

Ethics Committee Approval: This study was reviewed and approved by the Dokuz Eylül University Faculty of Medicine Institutional Review Board Ethics Committee approval (decision no: 2023/34-02, date: 25.10.2023). The study was performed in accordance with the most recent version of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Ş.O., V.Ş., B.T., K.Y., G.A., M.U.M., İ.C., Concept: Ş.O., A.E.S., S.H.B.Y., B.S., S.C., B.T., K.Y., M.U.M., Design: Ş.O., S.H.B.Y., S.C., V.S., B.T., K.Y., M.U.M., Data Collection or Processing: E.S., S.H.B.Y., B.S., Analysis or Interpretation: Ş.O., A.E.S., V.S., Literature Search: Ş.O., S.C., K.Y., M.U.M., Writing: Ş.O., V.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH
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Effect of Prilocaine Infiltration into the Nephrostomy Tract After Percutaneous Nephrolithotomy on Postoperative Pain

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What's known on the subject? and What does the study add?

It is known that there is serious pain after percutaneous nephrolithotomy surgery and that patients are given many painkillers accordingly. Due to this pain, the hospitalization period of the patients may be extended, and the cost increases. These can be prevented with local anesthetic applied to the operation area. We think that this simple application should be kept in mind and applied to patients routinely.

Abstract

Objective: To investigate the effect of local prilocaine infiltration on postoperative pain in patients undergoing percutaneous nephrolithotomy (PCNL).

Materials and Methods: The case-control study enrolled 137 patients who underwent PCNL at Çukurova University Balcalı Hospital from April 2022 to December 2022. These patients were categorized into two distinct groups: The case and control groups. While peritubal 2% 10 cc prilocaine local anesthetic infiltration was applied to the cases, local anesthetic was not applied to the control group. Pain was evaluated using an analog scale after surgery.

Results: In the study, which included 137 patients, local anesthesia was administered to 46 patients. Receiving local anesthesia was associated with the pain score ($p<0.001$). Pain scores were lower at the beginning and at the 4th minute in patients receiving local anesthesia ($p<0.001$ and $p=0.004$, respectively).

Conclusion: Infiltration of peritubal prilocaine has been shown to notably diminish pain following PCNL. Our hypothesis suggests that local anesthetic infiltration into the nephrostomy tract could present a superior alternative for postoperative pain control. Nevertheless, extensive and prolonged follow-up studies are imperative for advancing research in this domain.

Keywords: PCNL, pain, local analgesia

Introduction

Percutaneous nephrolithotomy (PCNL) is widely regarded as the gold standard for treating large kidney stones because of its less invasive and morbid nature compared with open surgery (1). PCNL has undergone significant evolution since Fernstrom and Johansson successfully planned and executed the first cases in 1976. Today, PCNL has emerged as the most favored surgical intervention for kidney stones (2,3). PCNL is indeed associated with lower morbidity and facilitates faster recovery compared with the open surgical method. However, it is important to note that while PCNL is less invasive, it is not without its own set of complication (4).

The placement of a nephrostomy catheter following PCNL is a standard practice in many clinics. While the nephrostomy catheter effectively ensures urine drainage during the healing

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phase, minimizes bleeding from the renal parenchyma, and allows room for secondary intervention procedures, it can also significantly contribute to postoperative pain. To mitigate this discomfort, the tubeless PCNL method has been introduced with the aim of alleviating postoperative pain by eliminating the nephrostomy tube. Recent studies on tubeless PCNL indicate a reduction in postoperative pain, thereby highlighting its potential advantages (2). Nevertheless, it is important to note that the tubeless PCNL procedure is applicable only in specific cases. Additionally, research suggests that pain tends to decrease as the size of the dilatation decreases (5).

Postoperative pain following PCNL represents a notable clinical challenge, primarily stemming from the stretching of the renal capsule and parenchyma. Furthermore, the movement of the access sheath induces severe discomfort by irritating the diaphragm, pleura, and retroperitoneum (6,7). Proper and sufficient management of pain after PCNL contributes to decreased morbidity rates, shorter hospital stays, and reduced costs. Analgesics, including nonsteroidal anti-inflammatory drugs and opioids, are commonly used to alleviate postoperative pain. Nonetheless, it is crucial to acknowledge that these medications come with potential side effects, and their use may be restricted in patients with underlying kidney issues (6). Another method for alleviating pain is peritubal local anesthetic infiltration.

Clear recommendations for optimal pain management after PCNL are currently lacking; however, the use of local anesthetics has demonstrated efficacy in providing analgesia. Prilocaine, classified as a medium-acting amide-type local anesthetic, finds application in various anesthesia techniques, particularly injection anesthesia and nerve blocks. Its half-life is approximately 1.6 h; however, individual variability in metabolism can influence this duration (8). Our study sought to assess the efficacy of a 2% prilocaine injection administered into the postoperative skin, subcutaneous tissue, muscle, and fascia layers in managing acute pain following PCNL.

Materials and Methods

The study included a total of 137 patients who underwent PCNL between April 2022 and December 2022. Patients under the age of 18 years were excluded from participation. Data regarding patients' preoperative age, body mass index, stone location, and stone burden were collected. The assessment of kidney stones was conducted using computed tomography. Of the patients, 65.7% were male and 34.3% were female. All percutaneous accesses were made from the subcostal region in the patients included in the study. Dilation was performed using an Amplatz set in all patients. After the Amplatz tube was placed, the stones were broken with the help of pneumatics or a holmium laser. Following the operation, 14 French reentry catheters were inserted in 136 patients, while one patient did not receive a tube. Subsequently, the patients were divided into two distinct groups. After the operation, 10 cc of 2% prilocaine was injected into the percutaneous access tract of 46 patients. Local analgesia was not administered to 91 patients. All patients received intravenous analgesia during surgery. The visual analog scale (VAS) assessed patient comfort and pain. The VAS scores at minutes 0 and 4 of the patients taken to the service after the operation were recorded here. The VAS scores range from 0 to 10, with 0 indicating no pain and 10 representing unbearable pain. Patients were monitored for any postoperative complaints. If no fever, hematuria, or opaque extravasation was observed after surgery, the nephrostomy tube was removed, and the patient was discharged.

The research was approved by the Çukurova University Faculty of Medicine Non-Invasive Clinical Research Board (approval number: 29, date: 14.07.2023).

Statistical Analysis

Statistical analysis was conducted using SPSS 13.0 (SPSS, Chicago, IL). Chi-square and independent sample tests were employed, with a p-value of <0.05 deemed statistically significant.

Results

A total of 137 patients underwent PCNL and were categorized into two groups: Those who received local anesthesia and those who did not. Table 1 presents the demographic and clinical characteristics of the patients. Among them, 90 were men and 47 were women. Right-sided PCNL was conducted on 56 patients, whereas left-sided PCNL was performed on 81 patients. No significant difference in patient characteristics was observed between the two groups ($p>0.05$) (Table 2). Changes in VAS pain scores are shown in Table 3 and Figure 1. In patients without local anesthesia, the average VAS score at minute 0 was 4.0 ± 2.4, while the average score at minute 4 was 1.1 ± 1.6, and this difference was statistically significant ($p<0.001$). In patients who underwent local anesthesia, the average VAS score at minute 0 was 1.3 ± 2.1, while the average score at minute 4 was 0.4 ± 1.3, which was statistically significant ($p=0.008$). Receiving local anesthesia was related to the time on pain score ($p<0.001$). Pain scores of patients receiving local anesthesia were lower at the beginning and at the 4th minute ($p<0.001$ and $p=0.004$, respectively) (Table 3). No major complications occurred during or after the surgery.

Table 1. Demographic and clinical data	
	n=137
Local analgesia, n (%)	
None	91 (66.4)
Yes	46 (33.6)
Old	48.3±14.1 48.0 (18.0-75.0)
Gender, n (%)	
Male	90 (65.7)
Woman	47 (34.3)
BMI	27.3±4.8
Side, n (%)	
Right	56 (40.9)
Left	81 (59.1)
Postoperative pain 0 min	4.0 (0.0-8.0)
Postoperative pain 4 min	0.0 (0.0-6.0)
Supin	4 (2.9)
Prone	133 (97.1)
GSS, n (%)	
1	44 (32.1)
2	41 (29.9)
3	30 (21.9)
4	22 (16.1)
Renax size	24.0 (14.0-30.0)
Tubeless n (%)	
None	136 (99.3)
Yes	1 (0.7)
Postoperative complication, n (%)	
None	136 (99.3)
Yes	1 (0.7)
Residue, n (%)	
SF	99 (72.3)
CSRF	19 (13.9)
CIRF	19 (13.9)
Discharge day	3.0 (2.0-14.0)
Karnofsky performance score	100.0 (60.0-100.0)
BMI: Body mass index	

Table 2. Comparison of features by groups			
	Local analgesia		**p-value**
	None (n=91)	**Yes (n=46)**	
Old	48.0 (38.0-59.0)	50.5 (35.3-63.0)	0.547
Gender, n (%)			0.211
Male	56 (61.5)	34 (73.9)	
Female	35 (38.5)	12 (26.1)	
BMI	26.0 (24.0-29.0)	25.5 (24.0-30.0)	0.505
Side, n (%)			0.911
Right	38 (41.8)	18 (39.1)	
Left	53 (58.2)	28 (60.9)	
Supin/prone, n (%)			0.300
Supin	4 (4.4)	-	
Prone	87 (95.6)	46 (100.0)	
GSS, n (%)			0.682
1	27 (29.7)	17 (37.0)	
2	30 (33.0)	11 (23.9)	
3	19 (20.9)	11 (23.9)	
4	5 (16.5)	7 (15.2)	
Renax size	22.9±3.7 24.0 (24.0-24.0)	23.0±3.6 24.0 (24.0-24.0)	0.844
Residue, n (%)			0.696
SF	67 (73.6)	32 (69.6)	
CSRF	11 (12.1)	8 (17.4)	
CIRF	13 (14.3)	6 (13.0)	
Discharge day	3.3±0.9 3.0 (3.0-3.3)	3.6±2.0 3.0 (3.0-4.0)	0.848
Karnofsky performance score	98.0±6.6 100.0 (100.0-100.0)	99.4±3.3 100.0 (100.0-100.0)	0.243
BMI: Body mass index			

Table 3. Comparison of local anesthetic administration			
Local analgesia	**0 minute**	**4 minute**	**p-value**
None	4.0±2.4 4.0 (0.0-8.0)	1.1±1.6 0.0 (0.0-6.0)	<0.001
Yes	1.3±2.1 0.0 (0.0-6.0)	0.4±1.3 0.0 (0.0-6.0)	0.008
P-value	<0.001	0.004	

Discussion

Conditions like obesity, diabetes, hypertension, and metabolic syndrome elevate the risk of stone formation. Moreover, the presence of stones intensifies hypertension, kidney disease, and other ailments. Currently, the management of symptomatic kidney stones predominantly revolves around minimally invasive techniques. These methods mitigate surgical complications, minimize tissue damage, enhance stone clearance rates, and improve the overall quality of life. In particular, PCNL is the primary treatment modality for large kidney stones. It holds significant importance, particularly in the management of stones larger than 2 cm and staghorn kidney stones (9). Treatment of kidney stones has made significant progress, especially with the application of PCNL. Large kidney stones are effectively and safely treated with PCNL. Although kidney stone treatment has less morbidity than open surgery, patients still complain of postoperative pain and require adequate analgesia (3). Postoperative pain represents a significant challenge following surgical procedures. It significantly impairs the patient's quality of life during the recovery phase, manifesting in various adverse

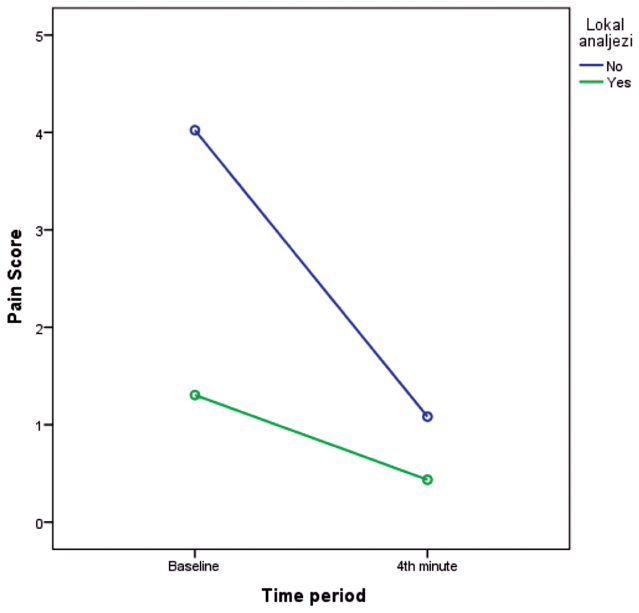

Figure 1. Pain scores of groups according to time periods

outcomes, including anxiety, delayed ambulation, increased risk of postoperative complications, and prolonged hospitalization. Recent developments in postoperative pain management have stemmed from a deeper understanding of acute pain physiology, the introduction of novel analgesic medications, advancements in analgesia administration methods, and the refinement of local anesthetic infiltration techniques (10). Pietrow et al. (11) determined that employing a smaller nephrostomy catheter (10 Fr pigtail catheter) rather than the conventional 22 Fr catheter resulted in reduced pain scores during the early postoperative phases. However, they did not establish a statistically significant advantage. Bellman et al. (12), through the implementation of tubeless PCNL, concluded that this approach diminishes postoperative patient discomfort, reduces the need for analgesics, shortens hospital stays, and lowers overall patient costs. Traditional management of postoperative pain involves the use of opioid analgesics; however, these drugs have associated side effects. Combining lower doses of opioid analgesics with non-opioid analgesics may mitigate these adverse effects. Multiple studies have illustrated the efficacy of acetaminophen, both alone and in combination with opioids, in managing postoperative pain (10). Maghsoudi et al. (13) documented the beneficial impact of intravenous acetaminophen within a multimodal analgesia strategy for managing postoperative pain after PCNL. Their study revealed that 50 patients administered 1 g of intravenous acetaminophen exhibited significantly lower visual analog scores at 6 and 24 h postoperatively compared with those receiving a placebo. Moreover, meperidine consumption was notably reduced in the paracetamol group (54.40 mg vs 77.60 mg, $p<0.001$) (13). Another approach to alleviate pain post-PCNL, besides intravenous and oral analgesics, involves the infiltration of local anesthetic into the subcutaneous and percutaneous access tracts. Andreoni et al. (14) observed that preoperative subarachnoid spinal analgesia combined with a single dose of morphine and bupivacaine infiltration into the nephrostomy canal led to a statistically significant decrease in the need for parenteral analgesics post-surgery. Uğras et al. (15) examined the impact of postoperative pain on lung function after PCNL. Their study revealed that enhanced pain management and reduced analgesic demands were achieved by combining ropivacaine installations with meptazinol compared with the use of meptazinol alone. Jonnavithula et al. (16) administered 0.25% peritubal bupivacaine (20 mL) from the skin to the renal capsule. Their study revealed that patients in the study group experienced significantly lower analgesic requirements during the initial 24-h period. In a prospective randomized study, Parikh et al. (4) demonstrated that pain scores at rest and during coughing, along with the need for rescue analgesia in the initial 24 h, were notably lower in the bupivacaine group than in the control group. Their conclusion suggested that peritubal infiltration with 0.25% bupivacaine effectively alleviated postoperative pain following PCNL (4). Gökten (2) studied the infiltration of levobupivacaine throughout the entire nephrostomy tract, supplemented with intravenous acetaminophen infusion for postoperative pain control. Their findings indicated significantly reduced opioid requirements during the initial 24-h period (2). This study evaluated the effect of medium-term effective local anesthetic (prilocaine 2%). The disadvantage of prilocaine is that it does not have a long-term impact. Its effect lasts a maximum of 6 h after injection. Therefore, it is thought that prilocaine may only play a role for treating acute pain after PCNL (8). We believe that the pain in the first hours of this surgery is more severe than that in the later hours; therefore, this study demonstrates the effect of 2% prilocaine on the acute management of post-PCNL pain.

Conclusion

In our study, we observed that local anesthetic infiltration around the nephrostomy pathway resulted in significant postoperative analgesia compared with the control group (those without local anesthetic infiltration). We posit that local anesthetic infiltration into the nephrostomy tract could be a superior option for managing postoperative pain. However, further research necessitates significant and long-term follow-up studies to validate and explore its efficacy.

Ethics

Ethics Committee Approval: The research was approved by the Çukurova University Faculty of Medicine Non-Invasive Clinical Research Board (approval number: 29, date: 14.07.2023).

Informed Consent: Written informed consent was obtained from all patients.

Authorship Contributions

Surgical and Medical Practices: N.A., M.D., Concept: N.A., İ.A.A., Design: N.A., İ.A.A., Data Collection or Processing: N.A., M.D., İ.Ö.Y., S.S.K., Ş.Y., Analysis or Interpretation: S.S.K., S.P.Y., Literature Search: İ.Ö.Y., S.S.K., Writing: N.A., S.S.K.

Informed Consent: All patients signed a written consent form before the operation.

Financial Disclosure: The authors declare that they have no relevant financial.

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ORIGINAL RESEARCH
Urooncology

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Correlation of Transrectal Ultrasonography Guided Prostate Biopsy Gleason Score Results with Prostate Volume in Patients with Prostate Specific Antigen Level Between 2.5-10 ng/mL

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What's known on the subject? and What does the study add?

To investigate the correlation between prostate volume and Gleason score results obtained by systematic transrectal prostate biopsy in patients with a prostate-specific antigen value between 2.5 and 10 ng/mL.

Abstract

Objective: To investigate the correlation between prostate volume (PV) and Gleason score (GS) results obtained by systematic transrectal prostate biopsy in patients with a prostate-specific antigen value between 2.5 and 10 ng/mL.

Materials and Methods: A total of 904 patients who underwent transrectal prostate biopsy at our institution were divided into four groups based on PV calculated by transrectal ultrasonography. Group 1 had a PV ≤35 cc, group 2 had a PV ranging from 36 to 55 cc, group 3 had a PV between 56 and 75 cc, and group 4 had a PV >75 cc. Subgroups were based on biopsy-proven prostate carcinoma patients within each group in the same PV intervals, and prostate cancer detection rates and GSs were calculated for each group and subgroup.

Results: The prostate cancer detection rate was 78.5% in group 1 and decreased to 17.2% in group 4. GS ≥8 also decreased from 16.4% in group 1 to 2.5% in group 4. However, there was no statistically significant difference between GS ≥8 in the subgroups, with the results of 20.9% in group 1a and 15% in group 4a.

Conclusion: Our study results suggest an inverse relationship between PV and cancer detection rates. Although GS ≤6 rates in biopsy-proven prostate carcinoma patients increased and GS of 7 decreased in larger prostates, it was not obvious in patients with GS ≥8. Further prospective studies with large volumes of patients are required to confirm our results.

Keywords: General urology, pathology, urooncology

Introduction

Prostate cancer (PCa) and benign prostate hyperplasia (BPH) are two of the most frequently diagnosed urological diseases affecting aging men, and transrectal ultrasound-guided prostate biopsy (TRUS-PB) remains the commonly applied diagnostic procedure to detect them (1,2).

Although diagnostic multiparametric prostate magnetic resonance imaging (mpMRI) before biopsy has increased over the past decade and assisted biopsy indication in patients with suspicious lesions on mpMRI, the same is not valid for patients without lesions on mpMRI. Current guidelines recommend targeted and systematic biopsy for patients with suspicious lesions on mpMRI, but there is no consensus on patients with negative mpMRI (3). In addition, no suspicious lesion was detected in up to 30% of patients who underwent pre-biopsy mpMRI (4). Therefore, in cases where mpMRI cannot be performed, or the results are negative, classical biopsy parameters are still needed.

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Traditionally, elevated levels of prostate-specific antigen (PSA) and abnormal digital rectal examination (DRE) were the sole parameters for deciding on a biopsy, given that TRUS-PB was conveniently performed in outpatient clinics. But PSA and DRE tests have limited ability to detect PCa, leading to overdiagnosis and overtreatment (5). For that reason, various PSA-dependent measures have been studied to improve the detection rate of PCa while minimizing the number of unnecessary biopsies. These variables include the free-to-total PSA ratio (f/t PSA), PSA velocity, PSA density (PSAD), age-referenced PSA, and transition zone PSAD (6,7). However, several studies have highlighted a significant inverse correlation between prostate volume (PV) and PCa. Clinical studies have demonstrated that patients diagnosed with PCa typically demonstrate comparatively lower PV than those diagnosed with BPH (8,9).

The Gleason score (GS) remains the essential grading system for evaluating PCa, and it plays a crucial role in determining the prognosis and treatment options for patients diagnosed with PCa (10). In addition, studies have shown that for patients with larger prostates, needle biopsy and radical prostatectomy (RP) pathology results have not only yielded lower detection rates of PCa but also resulted in more favorable GS results (11-13).

In this study, we aimed to determine the correlation between PV and PCa detection rate and the correlation of GS with PV in which TRUS-PB pathology results were taken as a reference point in patients with a PSA level between 2.5 and 10 ng/mL. Second aim was to compare diagnostic value of PV to other classical parameters and eligible cut-off value of PV in predicting PCa.

Materials and Methods

The study was conducted in line with the principles of the Declaration of Helsinki and the local ethics committee accepted this single-center retrospective study conducted between January 2016 and October 2023 (Local Ethics Committee of Karabük University, approval number: 2024/1633, date: 07.02.2024), we reviewed the medical records of 1337 patients undergoing TRUS-PB at our tertiary hospital between January 2016 and October 2023. The biopsy criteria included abnormal DRE, PSA ≥4 ng/mL, previous suspicious pathology, and suspicious lesions on mp-MRI. Following a comprehensive evaluation, 307 patients with PSA levels outside 2.5-10 ng/mL, 13 patients with fewer than 10 cores, 91 with atypical small acinar proliferation (ASAP) pathology, 11 with high-grade prostatic intraepithelial neoplasia results, and 11 with a known PCa diagnosis were eliminated. The final study comprised 904 eligible patients meeting all criteria.

TRUS-PB was performed in the same outpatient room with the same ultrasonography equipment and an automatic single-use 18 gauge- 24 cm biopsy needle with local anesthesia in the left decubital position.

The pathology doctors at our hospital evaluated the pathology results. Prostate intraepithelial neoplasia and BPH results were accepted as BPH, whereas GS ≥6 (stated by the International Society of Urological Pathology) was taken as PCa (14).

The study evaluated parameters of patient's age, PSA, free PSA (f PSA), PV measured by TRUS, f/t PSA ratio, PSAD, number of biopsy cores, patients with previous negative pathology (PNB) results, DRE results, biopsy pathology result, number of cores taken, and GSs. Although 455 patients had pre-biopsy mp-MRI, the PV measured by TRUS according to the ellipsoid formula (height × width × length × 0.52) was used for all patients for standardization.

According to the PV values, the patients were divided into four groups. Group 1 (PV ≤35 cc, 140 patients), group 2 (PV 36-55 cc, 287 patients), group 3 (PV 56-75 cc, 245 patients), and group 4 (PV ≥76 cc, 232 patients). Main pathological results and GS results were evaluated for each group. Then, within each main group, additional four subgroups were created for patients who were diagnosed with PCa through TRUS-PB, and the GS results were compared within each subgroup. These subgroups were group 1a (110 PCa patients, PV ≤35 cc), group 2a (112 PCa patients, PV=36-55 cc), group 3a (49 PCa patients, PV=56-75 cc), and group 4a (40 PCa patients, PV ≥76 cc). For our second aim we conducted receiver operating characteristic (ROC) curve analysis to determine the optimal cut-off value of PV for predicting PCa and compared its diagnostic value with other parameters.

Statistical Analysis

The suitability of numerical variables for normal distribution was tested with the Shapiro-Wilk test. Kruskal-Wallis and Dunn tests compared non-normally distributed variables in the four groups. Relationships between categorical variables were tested using the chi-square test, and multiple comparisons were tested using the Bonferroni test. Factors affecting PCa were tested by univariate and multivariate binary logistic regression analysis. ROC curve analysis was used to calculate and compare the area under the curve (AUC) of the variables. The analyses used the SPSS 22.0 Windows version package program and the MedCalc 19.7.1 version package program. $P<0.05$ was considered significant.

Results

Table 1 provides a concise overview of the parameters and pathological results of the 904 patients who were divided into four groups depending on PV. The mean age, PSA level, PV, PSAD, and f/t PSA ratio were 65.3 years, 6.3 ng/mL, 64.9 cc, 0.12 ng/mL/cc, and 0.23, respectively. Seven hundred and ninety-six patients (88.0%) had a primer biopsy, while 108 (11.9%) had a

PNB. The overall PCa detection rate was 34.4%, with a mean of 12.1 biopsy cores.

Group 4 had a higher age than group 2 and group 3. PSA levels were lower in group 1 and group 2 than in groups 3 and 4. PSA was lower in group 1 compared to all other groups. Similarly, f/t PSA was lower in group 1 and group 2 than in other groups. PSAD was lower in group 4 compared to all other groups. Anormal DRE was higher in group 1 and group 2 than group 3 and group 4. PNB was higher in group 3 and group 4 compared to group 1 and group 2. The PCa detection rates for groups one through 4 is 78.6%, 39%, 20%, and 17.2%, respectively. Detailed statistical analysis were shown in Supplementary Table 1, and Figure 1 demonstrates the distribution of BPH, PCa, GS ≤6, GS=7 and GS ≥8 according to groups.

When we compared patients with biopsy-proven PCa across subgroups, the percentage of low-grade PCA (GS ≤6) increased progressively from 27.2% in group 1a to 55.1% in group 1c (p=0.004) and further to 62.5% in group 1d (p=0.001). For patients with GS 7 (considered high-grade PCa), the percentage decreased from 51.8% in group 1a to 22.5% in group 4b (p=0.008). However, no statistically significant difference was observed between the subgroups when comparing the results for GS ≥8 (Table 2 and Figure 2).

Our second aim was to compare the diagnostic value of PV, which demonstrated the second-highest AUC in ROC analysis, following PSAD. The parameter AUC rankings, from highest to lowest, are PSAD (0.797), PV (0.757), f/t PSA (0.742), abnormal DRE (0.696), age (0.609), PSA (0.608), and PNB (0.552) (Supplementary Table 2).

Using the Youden J index to evaluate PV, it was found that a value of ≤49 cc resulted in a sensitivity of 63.6% and a specificity of 80.1%. Based on this cutoff, the detection rate of PCa was 62.6% (198/316). Further classification according to the GS showed that for PV ≤49 cc, GS ≤6 accounted for 18.9% (60/316), GS=7 for 30.3% (96/316), and GS ≥8 for 13.2% (42/316) (Supplementary Table 3).

Discussion

Our study results demonstrated that patients with a PSA value of 2.5-10 ng/mL have a 78.5% PCa detection rate when their PV ≤35 cc, whereas that rate drops to 17.2% in patients with a PV >75 cc. These results were similar to those of previous studies in which PV inversely correlates with the incidence of PCa; as PV increases, the detection rate of PCa decreases (8-13). The reference pathology used in these studies was obtained by TRUS-PB, targeted MRI-fusion, or RP. In two studies similar to ours, where PV was measured via TRUS and biopsies were taken with TRUS-PB, the PCa rate was calculated as 65% when PV <38 cc (15) and 66% when PV <35 cc (16). The same studies calculated the PCa rate as 20% when PV >72 cc and 40% when PV >65 cc. In other studies, in which RP pathology results were taken as a reference, Briganti et al. (13) found a direct correlation between PV and high-grade PCa when PV <45 cc but an inverse correlation when PV >45 cc. Meanwhile, Freedland et al. (17), demonstrated inverse relationship between PV and high-grade PCa when PV <20 cc, compared to PV ≥100 cc. Similarly, in a study by Kassouf et al. (18), the incidence of low-grade PCa was reported to be 17.9% in patients with a PV <25 cc compared to 45.3% in those with a PV >50 cc (p<0.01).

Some authors hypothesize that the low incidence of PCa in large prostates is due to sampling error. However, a study conducted by Elkhoury et al. (19) found that cancer detection rates are inversely related to PV despite the performance of both targeted and systematic biopsies. Specifically, the study

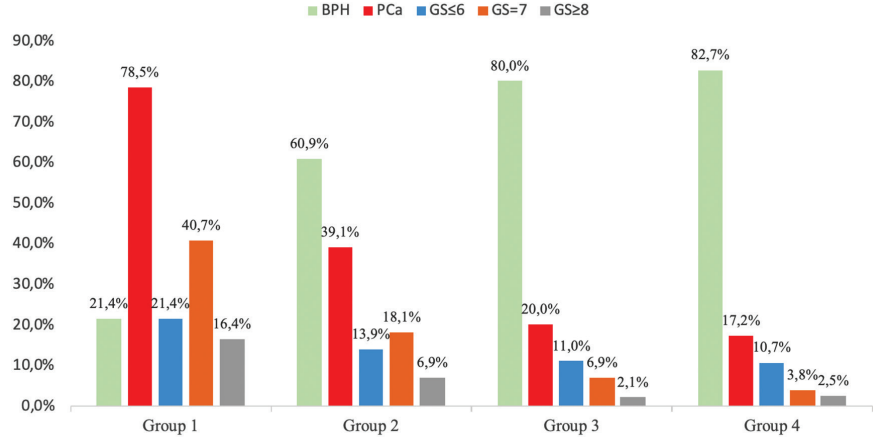

Figure 1. Classification of biopsy pathology results according to groups. Group 1; 140 patients with prostate volume ≤35 cc. Group 2; 287 patients with prostate volume between 36-55 cc. Group 3; 245 patients with prostate volume between 56-75 cc. Group 4; 232 patients with prostate volume ≥76 cc

BPH: Benign prostate hyperplasia, GS: Gleason score, PCa: Prostate carcinoma

Table 1. Main characteristics of groups

	Overall	Group 1	Group 2	Group 3	Group 4	p<0.05
No of patients	904 (100)	140 (15.5)	287 (31.7)	245 (27.1)	232 (25.7)	
Age mean, SD	65.3±6.6	65.29±7.39	64.37±6.91	65.22±6.32	66.56±5.77	0.005†
PSA mean, SD	6.38±1.89	6.16±2.19	5.99±1.72	6.51±1.75	6.87±1.91	0.001†
f PSA mean, SD	1.46±0.75	0.93±0.5	1.21±0.52	1.61±0.64	1.94±0.87	0.001†
f/t PSA mean, SD	0.23±0.1	0.16±0.08	0.21±0.09	0.25±0.08	0.28±0.11	0.001†
PSAD mean, SD	0.12±0.07	0.22±0.09	0.13±0.04	0.1±0.03	0.06±0.02	0.001†
Anormal DRE n, (%)	329 (36.4)	89 (63.6)	119 (41.5)	58 (23.7)	63 (27.2)	0.001ǂ
PNB n, (%)	108 (11.9)	5 (3.6)	25 (8.7)	41 (16.7)	37 (15.9)	0.001ǂ
No. of cores mean, SD	12.12±0.64	12.09±0.66	12.18±0.74	12.09±0.49	12.08±0.64	0.265†
GS results						
GS ≤6 n, (%)	122 (13.4)	30 (21.4)	40 (13.9)	27 (11)	25 (10.7)	0.001ǂ
GS=7 n, (%)	135 (14.9)	57 (40.7)	52 (18.1)	17 (6.9)	9 (3.8)	0.001ǂ
GS ≥8 n, (%)	54 (5.9)	23 (16.4)	20 (6.9)	5 (2.0)	6 (2.5)	0.001ǂ
Main pathology results						
BPH n, (%)	593 (65.6)	30 (21.4)	175 (61)	196 (80)	192 (82.8)	0.001ǂ
PCa n, (%)	311 (34.4)	110 (78.6)	112 (39)	49 (20)	40 (17.2)	0.001ǂ

†: Kruskal Wallis and Dunn tests, ǂ: Chi-square test, BPH: Benign prostate hyperplasia, DRE: Digital rectal examination, f PSA: Free prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, GS: Gleason score, PCa: Prostate carcinoma, PNB: Previous negative biopsy, PSA: Prostate specific antigene, PSAD: Prostate specific antigene density, PV: Prostate volume, SD: Standard deviation, Group 1; 140 patients with prostate volume ≤35 cc. Group 2; 287 patients with prostate volume between 36-55 cc. Group 3; 245 patients with prostate volume between 56-75 cc. Group 4; 232 patients with prostate volume ≥76 cc

Table 2. The classification of GS in patients with biopsy-proven prostate carcinoma according to subgroups

GS results	Group 1a (PV ≤35 cc)	Group 2a (PV = 36-55 cc)	Group 3a (PV= 56-75 cc)	Group 4a (PV ≥76 cc)	p<0.001
No. of patients	110	112	49	40	
GS ≤6, n, (%)	30 (27.2)	40 (35.7)	27 (55.1)	25 (62.5)	Group1a vs. Group 1c p=0.004* Group 1a vs. Group 1d p=0.001* Group 1b vs. Group 1d p=0.020*
GS=7, n, (%)	57 (51.8)	52 (46.4)	17 (34.6)	9 (22.5)	Group 1a vs. Group 1d p=0.008* Group 1b vs. Group 1d p=0.020*
GS ≥8 n, (%)	23 (20.9)	20 (17.8)	5 (10.2)	6 (15)	No statistical difference

*: The chi-square test and Bonferroni test, GS: Gleason score, PCa: Prostate carcinoma, PV: Prostate volume, Group 1a, 110 PCa patients with PV ≤35 cc; Group 2a, 112 PCa patients with PV=36-55 cc; Group 3a, 49 PCa patients with PV=56-75 cc; Group 4a, 40 PCa patients with PV ≥76 cc

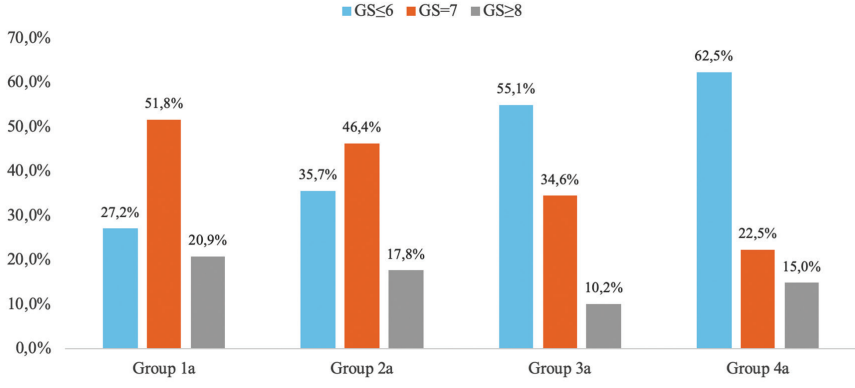

Figure 2. The classification of GS results in patients with biopsy-proven PCa according to subgroups. Group 1a, 110 PCa patients in PV ≤35 cc; group 2a, 112 PCa patients in PV=36-55 cc; group 3a, 49 PCa patients in PV= 56-75 cc; group 4a, 40 PCa patients in PV ≥76 cc

GS: Gleason score, PCa: Prostate carcinoma, PV: Prostate volume

revealed that 77% of men with low volumes (20-30 cc) had PCa, whereas only 42% of men with high volumes (60-100 cc) had PCa. Notably, no significant difference was found between the biopsy methods employed. Another study supporting it demonstrated that the MRI fusion biopsy technique detected 77% of PCa cases in PV <30 cc. However, this detection rate decreased to 34% for PV >55 cc (20). Finally, a meta-analysis in which the correlations between PV and MRI fusion prostate biopsy samples were analyzed also indicated that PCa reduces as PV increases, as demonstrated by prior TRUS biopsy-based research (21).

In contrast, Kulkarni et al. (12) conducted a study to compare biopsy and RP pathology results with PV, which differed from other studies findings. Based on the biopsy results, the study showed an inverse relationship between PV and high-grade PCA. However, the same relationship could not be observed between the RP pathology results, which were taken as a reference point. Karakiewicz et al. (22) also examined the biopsy yield in 10 cc gland-volume intervals in another study. They discovered that cancer detection decreased in larger glands using a traditional sextant biopsy approach, but there were no differences in Gleason grade among the gland-volume intervals.

In our study, we also studied patients with biopsy-proven PCa, subgrouping them on the basis of the same PV intervals, and no statistically significant difference was observed among subgroups with a GS ≥8. This finding aligns with a study by Kassaouf et al. (18), where biopsy pathology results were used as a reference. Specifically, the GS ≥8-10 rate was 13% for PV <25 cc and 11% for PV >50 cc with no statistically significant difference. However, a statistically significant difference was observed when comparing results concerning RP pathology. In another study, in which mpMRI fusion biopsy was used, the PCa detection rate decreased from 71.1% to 30.4% (PV <40 cc vs PV >116 cc), whereas the rate of PCa patients with GS ≥8 was not changed according to PV groups (23).

Two primary theories suggest an inverse correlation between PCa and PV. The first theory posits the hormonal theory that lower levels of dihydrotestosterone in small prostates may lead to the development of high-grade PCa (17). The second theory pertains to the mechanical impact of enlarged prostate tissue in the transitional zone. Histological studies have demonstrated that BPH growth in the transitional zone of larger prostate exerts mechanical pressure on the peripheral zone, where 80% of PCa originates. This pressure can result in glandular tissue atrophy and scarring in the peripheral zone, leading to thickening of the prostate capsule. Histological studies have shown that the thickness of the prostate capsule, gland atrophy, and scarring of glandular epithelial cells in the peripheral zone are positively associated with PV (24,25).

Our study also prioritized parameters for PCa detection. In the ROC curve analysis, PSAD showed the highest AUC value (0.797), followed by PV (0.757) and f/t PSA (0.742). However, PSAD and f/t PSA depended on the PSA level, which had a second-to-last AUC value of 0.608. It is worth noting that PSA levels can increase in various conditions, BPH (26), and f PSA is accused of being unstable (27), whereas PV emerged as a more stable predictor of PCa. In addition, PSAD appeared to be more valuable in only small- and medium-sized prostates (28).

Study Limitations

Our study has two main limitations. First, the study was conducted retrospectively in a single center with a relatively small number of patients. Therefore, the results should be interpreted cautiously due to the limited number of patients with biopsy-proven PCa results. Second, we used transrectal prostate biopsy pathology reports as the basis for the study. However, it is known that 30-40% of these pathologies are upgraded after pathological examination of the RP material.

Conclusion

Our study results suggest an inverse relationship between PV and PCa detection rates. Although, in biopsy-proven PCa patients, the GS ≤6 rate increased and the GS=7 rate decreased in larger prostates, it was not clearly observed in patients with GS ≥8. However, this needs to be confirmed by conducting additional prospective studies with a considerable number of patients.

Ethics

Ethics Committee Approval: The study was conducted in line with the principles of the Declaration of Helsinki and the local ethics committee accepted this single-center retrospective study conducted between January 2016 and October 2023 (Local Ethics Committee of Karabük University, approval number: 2024/1633, date: 07.02.2024).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: C.B., K.E., Concept: C.B., K.E., Design: C.B., K.E., Data Collection or Processing: C.B., K.E., Analysis or Interpretation: C.B., K.E., Literature Search: C.B., K.E., Writing: C.B., K.E.

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Supplementary Table 1. Detailed statistical analysis for pathological results between groups (a), for parameters (b)

a) Detailed statistical analysis for pathological results between groups

Group 1 (A)		Groups				
		Group 2	Group 3	Group 4	p-value	
		(B)	(C)	(D)		
GS results	≤ 6	C (p=0.034) D (p=0.030)				Group 1 to Group 3 p=0.034* Group 1 to Group 4 p=0.030
	=7	B (p=0.001) C (p=0.001) D (p=0.001)	C (p=0.001) D (p=0.001)			Group 1 to Group 2 p=0.001* Group 1 to Group 3 p=0.001* Group 1 to Group 4 p=0.001* Group 2 to Group 3 p=0.001* Group 2 to Group 4 p=0,001*
	≥ 8	B (p=0.014) C (p=0.001) D (p=0.001)	C (p=0.045)			Group 1 to Group 2 p=0.001* Group 1 to Group 3 p=0.001* Group 1 to Group 4 p=0.001* Group 2 to Group 3 p=0.001*
Main pathology results	BPH		A (p=0.001)	A (p=0.001) B (p=0.001)	A (p=0.001) B (p=0.001)	Group 1 to Group 2 p=0.001* Group 1 to Group 3 p=0.001* Group 1 to Group 4 p=0.001*
	PCa	B (p=0.001) C (p=0.001) D (p=0.001)	C (p=0.001) D (p=0.001)			Group 1 to Group 2 p=0.001* Group 1 to Group 3 p=0.001* Group 1 to Group 4 p=0.001*

* The chi-square test and Bonferroni test, GS: Gleason score, BPH: Benign prostate hyperplasia, PCa: Prostate carcinoma

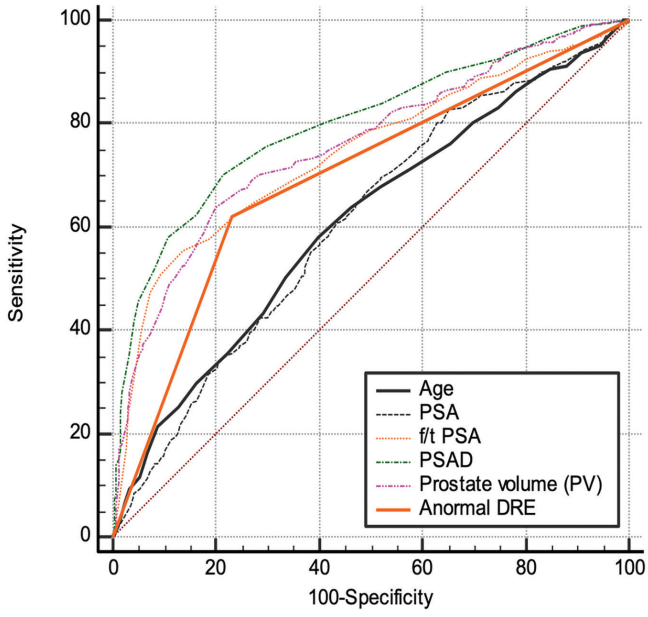
b) Detailed statistical analysis for parameters between groups

Age	p-value	PSA	p-value	f PSA	p-value
Group 2-Group 3	0.139	Group 2-Group 1	0.515	Group 1-Group 2	0.001*
Group 2-Group 1	0.120	Group 2-Group 3	0.001*	Group 1-Group 3	0.001*
Group 2-Group 4	0.001*	Group 2-Group 4	0.001*	Group 1-Group 4	0.001*
Group 3-Group 1	0.765	Group 1-Group 3	0.029*	Group 2-Group 3	0.001*
Group 3-Group 4	0.044*	Group 1-Group 4	0.001*	Group 2-Group 4	0.001*
Group 1-Group 4	0.153	Group 3-Group 4	0.081	Group 3-Group 4	0.001*

f/t PSA	p-value	PSAD	p-value
Group 1-Group 2	0.001*	Group 4-Group 3	0.001*
Group 1-Group 3	0.001*	Group 4-Group 2	0.001*
Group 1-Group 4	0.001*	Group 4-Group 1	0.001*
Group 2-Group 3	0.001*	Group 3-Group 2	0.001*
Group 2-Group 4	0.001*	Group 3-Group 1	0.001*
Group 3-Group 4	0.003*	Group 2-Group 1	0.001*

*The chi-square test and Bonferroni test, f PSA: Free prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, GS: Gleason score, PCa: Prostate carcinoma, PSA: Prostate specific antigene, PSAD: Prostate specific antigene density

Supplementary Table 2. ROC curve analysis and AUC values of parameters including age, PSA, f/t PSA, PSAD, PV and anormal DRE for risk factors of PCa (a), for parameters including age, PSA, f/t PSA, PSAD, PV and PNB (b)

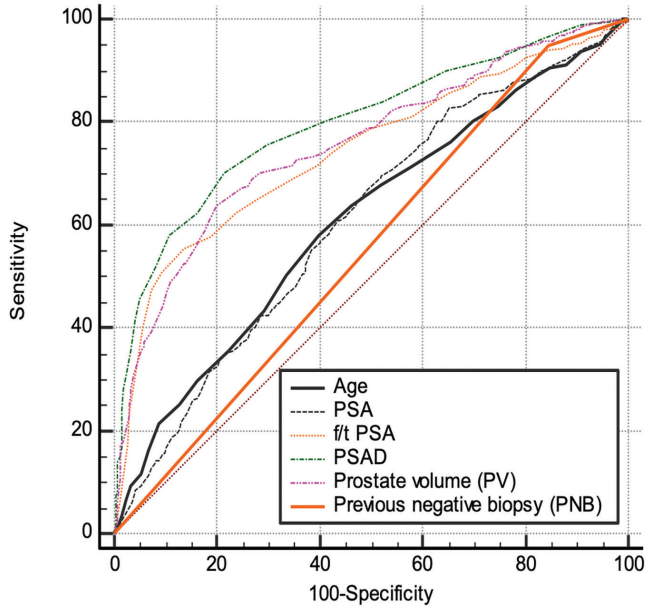


PSA: prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, PSAD: Prostate specific antigene density, PV: Prostate volume, DRE: Digital rectal examination

Variables	AUC	SE[a]	95% CI[b]
Age	0.609	0.0200	0.576 to 0.641
PSA	0.608	0.0196	0.576 to 0.640
f/t PSA	0.742	0.0185	0.712 to 0.770
PSAD	0.797	0.0165	0.770 to 0.823
Prostate volume	0.757	0.0176	0.727 to 0.784
Anormal DRE	0.696	0.0190	0.664 to 0.725

[a] Hanley & McNeil, 1982, [b] Binomial exact, AUC: Area under the curve, SE: Standard error, CI: Confidence interval, PSA: prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, PSAD: Prostate specific antigene density, DRE: Digital rectal examination

a) For parameters including age, PSA, f/t PSA, PSAD, PV and PNB



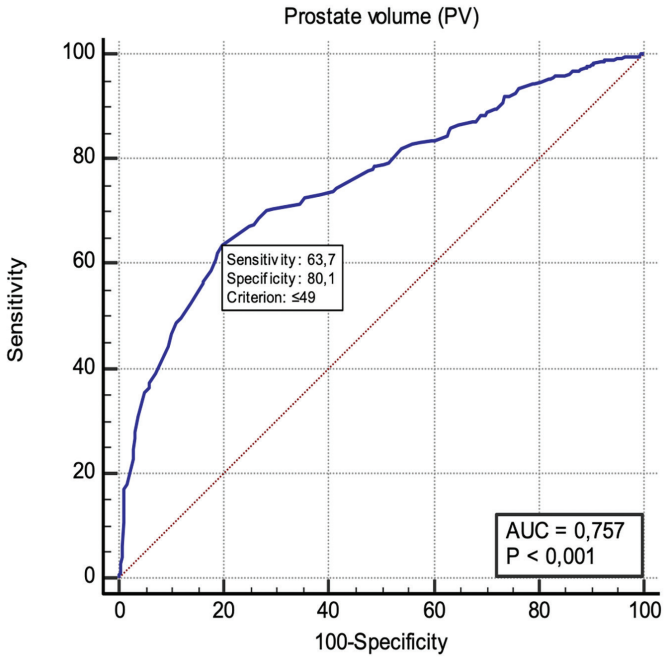
PSA: Prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, PSAD: Prostate specific antigene density, PNB: Previous negative biopsy

Variables	AUC	SE[a]	95% CI[b]
Age	0.609	0.0200	0.576 to 0.641
PSA	0.608	0.0196	0.576 to 0.640
f/t PSA	0.742	0.0185	0.712 to 0.770
PSAD	0.797	0.0165	0.770 to 0.823
Prostate volume	0.757	0.0176	0.727 to 0.784
Previous negative biopsy	0.552	0.0196	0.519 to 0.585

[a]Hanley & McNeil, 1982, [b]Binomial exact, AUC: Area under the curve, SE: Standard error, CI: Confidence interval, PSA: prostate specific antigene, f/t PSA: Free total prostate specific antigene ratio, PSAD: Prostate specific antigene density, DRE: Digital rectal examination

Supplementary Table 3. AUC value of prostate volume with sensitivity and specificity for prostate carcinoma (a), pathology results according to prostate volume cut-off value of ≤49 cc

a)



Area under the ROC curve (AUC)	0.757
Standard error[a]	0.0176
95% confidence interval[b]	0.727 to 0.784
Z statistic	14.584
Significance level P (area=0.5)	<0.0001

Youden index J	0.4377
Associated criterion	≤49
Sensitivity	63.67
Specificity	80.10

Criterion	Sensitivity	95% CI	Specificity	95% CI
≤49	63.67	58.0-69.0	80.10	76.7-83.2
CI: Confidence interval				

b)

Pathology results	PV ≤49 cc
No. of patients	316
GS ≤6 n, (%)	60 (18.9)
GS=7 n, (%)	96 (30.3)
GS ≥8 n, (%)	42 (13.2)
BPH n, (%)	118 (37.3)
PCa n, (%)	198 (62.6)
PV: Prostate volume, GS: Glason score, BPH: Benign prostate hyperplasia, PCa: Prostate carcinoma	

ORIGINAL RESEARCH
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Satisfaction and Quality of Life of Elderly Women with Pelvic Organ Prolapse Undergone Colpocleisis

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What's known on the subject? and What does the study add?

Pelvic organ prolapse (POP) is common in elderly women. This condition affects patients' quality of life. The lifetime risk of having POP surgery is 18.7% in an 80-year-old woman and 21.5% in older women. Colpocleisis is an underrated but effective surgical treatment option for POP. POP and urinary incontinence were significantly decreased after colpocleisis surgery. There was a significant relationship between quality of life (social functioning) and the stage of prolapse after surgery. The quality of life of patients in the four investigated dimensions, including physical functioning, role limitations, social functioning, and emotional role limitations, was significantly higher than the mean.

Abstract

Objective: Pelvic organ prolapse (POP) affects the quality of life of elderly women. This study aimed to investigate the satisfaction, recovery, and recurrence of symptoms in patients with POP who underwent colpocleisis.

Materials and Methods: This retrospective cohort study included elderly women (106 cases with an average age of 74.49±6.07) suffering from stage III or higher POP who underwent partial or total colpocleisis. Pre- and post-operative POP-Q, urinary symptoms, and the level of patient satisfaction were the outcome measures.

Results: POP and urinary incontinence significantly decreased after surgery ($p<0.001$). There was a significant relationship between quality of life (social functioning) and the stage of prolapse after operation ($p<0.01$). In addition, the patient's quality of life in the four investigated dimensions, including physical functioning, role limitations, social functioning, and emotional role limitations, was significantly higher than the mean and average ($p<0.01$).

Conclusion: Colpocleisis is a procedure characterized by high subjective and objective success, low regret, and low risk of complications. Therefore, colpocleisis is a minimally invasive and effective treatment method for elderly women. However, further clinical research is needed to evaluate the efficacy of this procedure.

Keywords: Colpocleisis, pelvic organ prolapse, quality of life, patient satisfaction

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Introduction

Pelvic organ prolapse (POP) is a syndrome of pelvic floor and pelvic organ prolapse either alone or in combination, which severely affects the quality of life of patients. POP affects approximately 40% of women worldwide, and this proportion is likely to increase as the population ages (1). Colpocleisis is a surgical procedure used to treat POP, a condition in which pelvic organs such as the uterus, bladder, or rectum protrude into the vaginal wall due to weakened pelvic floor muscles (2,3). There are many risk factors for POP, among which parity, vaginal delivery, aging, and body mass index (BMI) can be mentioned (4). In a systematic review that investigated the risk factors for POP recurrence following colpocleisis, the findings revealed that both the preoperative and postoperative genital hiatus lengths were significantly longer in the recurrence group. Additionally, the postoperative total vaginal length was significantly longer in the recurrence group. Women with previous POP surgery were also more likely to experience recurrence following colpocleisis. However, the patient's age and previous hysterectomy did not affect recurrence rates. These findings emphasize the importance of appropriate patient selection and surgical technique in minimizing the risk of recurrence following colpocleisis (5). The surgical management of POP includes reconstructive and obliterative procedures. Reconstructive surgery corrects the prolapsed vagina and aims to restore normal anatomy, whereas obliterative surgery is defined as an operation to obliterate the vagina in elderly women who do not have sexual activity or who wish to have future intercourse. These procedures include colpectomy and Le Fort colpocleisis (6). For patients with severe POP who cannot be treated with conservative methods and for whom long surgery is not possible because of physical condition, this method is a suitable choice (7). The obliterative technique is an effective alternative for correcting advanced apical prolapse (8). The potential benefits of the obliterative method compared with the reconstructive approach include decreased operation time, blood loss, and recovery time (7). Patient satisfaction and quality of life are crucial aspects of any medical intervention, including colpocleisis. The main purpose of this study was to investigate patient satisfaction, quality of life, symptoms before and after surgery, and postoperative complications in women who underwent colpocleisis.

Materials and Methods

This retrospective cohort study was conducted from 2017 to 2022. In this study, all women with POP grades 3 and 4 were evaluated. The study population included all women aged 60-85 years with a history of POP who underwent colpocleisis surgery at the Taleghani and Al-Zahra Hospitals of Tabriz University of Medical Sciences. At each of these two medical centers, colpocleisis was performed by a single expert surgical team. The Ethics Committee of Tabriz University of Medical Sciences approved the study (decision no: IR.TBZMED.REC.1400.1018, date: 12.01.2022).

Study Population and Sample Size Calculation

In this research, 106 participants were selected based on the size of the original sample using a simple sampling method. Assuming a recurrence probability of 50%, power of 80%, type 1 error of 0.05, and maximum tolerable error of 0.01 and using the formula to determine the prevalence of the sample size, 96 patients were estimated in this study. Assuming a probability of missing 0.1, a sample size of 106 people was considered.

Evaluation of POP Severity

We used the pelvic organ prolapse quantification (POP-Q) system developed in 1996 as the severity criteria to evaluate the severity of apical prolapse (9). In this study, four questionnaires were used: A demographic questionnaire, a World Health Organization standard quality of life questionnaire, a POP-Q, and a urinary symptom questionnaire comprising urinary frequency, nocturnal urination, urinary urgency, and urinary incontinence. The demographic and clinical characteristics questionnaire included questions on age, level of education, employment status, income, parity, number of living children, age at the time of first delivery, and method of delivery. The questionnaire of the POP-Q, including standard examination with the POP-Q system, was administered in the lithotomy position, and points were measured using a spatula calibrated in centimeters. In this system, 9 special places were measured, of which 6 points along the length of the vagina were related to the hymen ring. The anatomical location of these 6 points should be expressed in centimeters either proximal to the hymen (negative numbers) or distal to the hymen (positive numbers), with the hymen having a score of 0. The three other measurements in the pelvic organ prolapse examination include the genital hiatus, perineal body, and total vaginal length. All measurements except for the total vaginal length were performed in the state of maximum thrusting (10). The Short Form 36 Health Survey Questionnaire (SF-36) is a self-administered questionnaire containing 36 items. It measures health on eight multi-item dimensions, covering functional status, well-being, and overall health evaluation (11,12). For regular postoperative follow-up, patients were referred for outpatient visits or follow-up via telephone.

Statistical Analysis

All data were analyzed using SPSS 22 statistical software, and the values are presented as means ± standard deviation (SD), medians, or percentages, depending on the variable. A linear regression test (single variable and multivariable) was used to control for confounding variables. The independent t-test

was used to compare the data before and after surgery. In all stages of the study, α=0.05 and a confidence interval of 95% were considered. A p-value of less than 0.05 was considered statistically significant.

Results

All patients were categorized as stage III or IV according to the definition of the POP-Q system. The median age of the patients was 74.49 (60-85) years. There was no significant correlation between the BMI of patients and the stage of POP before surgery (p>0.01). The baseline characteristics of the participants are presented in Table 1.

The most common comorbidity was hypertension (71.02%), and 30.8% of patients had two or more comorbidities. The most frequent pregnancies were 7-8 pregnancies, which were observed in 18.6% and 20.9% of the women studied. The results showed that 26.7% of the patients experienced 6 natural vaginal delivery, whereas 77.9% had no experience of cesarean section. The status of pregnancy, childbirth, and abortion in the women studied are presented in Table 2. The results showed that 14% of the women studied had undergone previous prolapse surgery, whereas 86% had no history of prolapse surgery. Mean and SD follow-up duration was 36.7±24.18 (range: 12-60) months.

There were no POP cases over stage II on outpatient examination. Thus, anatomical recurrence was not observed in our study. The evaluation of the quality of life of the patients showed that the average of the different dimensions of the patient's quality of life, based on the SF 36 questionnaire, was significantly higher than the median (p>0.001) (Table 3). Comparison of the POP stage before and after surgery was performed using the Wilcoxon signed-rank test. The results obtained from the statistical analysis showed that the degree of prolapse after surgery was significantly decreased compared to before operation (Z=-8.244; p<0.001). No recurrence was observed during clinical evaluation. The results of prolapse surgery performed in the studied women before and after surgery are presented in Table 4.

In this study, urinary incontinence was significantly decreased after surgery compared with pre-operation (p<0.001). Urinary incontinence before surgery was observed in 11 cases (10.37%) patients and in only 5 cases (4.71%). Before the operation, 7 patients had stress urinary incontinence (SUI) and 4 had urgency urinary incontinence; after the operation, 4 patients had SUI and 1 had urinary incontinence due to neurological disease. Two patients with SUI also had stress incontinence before surgery, but this relationship was not significant (p>0.01). In total, 4 patients underwent colpocleisis and urinary incontinence surgery at the same time, and none experienced urinary symptom recurrence (Table 5).

Discussion

According to the National Health and Nutrition Examination Survey, approximately 3% of women in the United States have symptoms of vaginal bulging. Colpocleisis is a popular and durable procedure for prolapse or incontinence with success rates of 98-100%. It is ideal for women who are no longer sexually active or who cannot tolerate extensive procedures (13). In a review, the prevalence of POP based on reported symptoms was much lower (3-6%) than that identified by examination (41-50%) (14). POP is a progressive herniation of pelvic organs through the urogenital diaphragm (15). This condition is often

Table 1. Clinical and demographic characteristics of the study participants (n=106)

Baseline characteristics	n (%)
Non-smoking	103 (97.1)
Previous hysterectomy	6 (5.66)
Previous prolapse surgery	12 (11.32)
Previous anti-incontinence surgery	4 (3.77)
POP-Q stage	
Stage III	27 (25.47)
Stage IV	59 (55.66)
Marital status	
Married	87 (82.08)
Widowed	19 (17.92)
Divorced/separated/single	0

POP-Q: Pelvic organ prolapse quantification system

Table 2. Status of pregnancy, childbirth, and abortion in the women

Score	Gravid	Parity	Alive	Abortion	NVD	CS
0	0	0	0	40.7	0	77.9
1	0	0	0	18.6	0	22.1
2	4.7	5.8	9.3	24.4	5.8	-
3	7	8.1	9.3	8.1	11.6	-
4	9.3	20.9	16.3	1.2	19.8	-
5	7	9.3	9.3	0	12.8	-
6	11.6	20.9	24.4	2.3	26.7	-
7	18.6	30.2	26.7	4.7	19.8	-
8	20.9	4.7	4.7	0	3.5	-
9	15.1	0	0	0	0	-
10	0	0	0	0	0	-
11	0	0	0	0	0	-
12	0	0	0	0	0	-
13	5.8	0	0	0	0	-

The data are presented as percentages (%)
NVD: Normal vaginal delivery, CS: Caesarean section

Table 3. Quality of life of patients based on the SF-36 questionnaire			
Summary measure	**Scale**	**Means ± SD**	**p-value**
Physical functioning	Physical functioning	24.50±2.25	<0.001
	Role limitations (physical)	29.53±2.36	<0.001
Mental functioning	Social functioning	12.15±1.16	<0.001
	Role limitations (emotional)	21.83±1.77	<0.001
The data are presented as the means ± standard deviation (SD), SF-36: The Short Form 36 Health Survey Questionnaire			

Table 4. Stage of pelvic organ prolapse		
Pelvic organ prolapse	**Pre-operation**	**Post-operation**
0	-	83 (91.6)
I	-	3 (8.4)
II	-	-
III	27 (31.4)	-
IV	59 (68.6)	-
The data are presented as n (%)		

Table 5. Urinary incontinence before and after surgery				
Time	**Stress urinary incontinence**	**Urgency urinary incontinence**	**Others**	**Total**
Pre-operation	7 (63.63)	4 (36.36)	-	11
Post-operation	4 (80)	-	1 (20)	5
The data are presented as n (%)				

accompanied by symptoms such as urine leakage during coughing or physical activities such as exercise, which are known as SUI (4). Of course, in some women, prolapse prevents urinary incontinence, and SUI may be revealed only after the replacement of prolapsed organs. SUI may also occur after surgical treatment of prolapse (14). Our findings suggest that in the long term, colpocleisis remains a good option for elderly patients with multiple comorbidities and advanced POPs (16,17). This method has been obliterated; as a result, it is more suitable for those who do not like having intercourse in the future (18). In addition, obliterative procedures are appropriate for people who have failed reconstructive methods (19). This approach can be a good option for elderly women with advanced POP because of its simplicity, reported good anatomical outcomes, minimal anesthesia requirements, short operative time, and less blood loss compared with the reconstructive procedure (17,18). In the present study, 106 women with POP who underwent colpocleisis were examined. The results showed that the stage of prolapse after surgery was significantly decreased compared with pre-operation. In our study, none of the patients experienced symptoms of prolapse recurrence, which is a great success for this surgical method. However, in a study by DeLancey and Morley (20), 3% of patients who underwent colpocleisis experienced recurrence of prolapse (20,21). Similarly, Song et al. (22) reported outcomes for patients who underwent LeFort colpocleisis and found no POP recurrences. In similar studies, the success rate of this surgical method, defined as POP-Q stage ≤1 ranged from 62.5 to 100% (23). Eisenberg et al. (24) reported an anatomical success rate of 62.5% (POP-Q ≤1), but the success rate increased to 100% when the definition was extended to POP-Q ≤2. In a study by Ng and Chen (25), 14 patients (87.5%) had successful postoperative results, and 93.8% of the patients were satisfied with the operation. Our anatomical success rate was similar to that of previous studies (16,17,22). It was also observed that the BMI of patients with POP ranged from overweight to obese. This indicates that weight loss can play an important role in preventing pelvic organ prolapse. However, a systematic review by Zenebe et al. (26) did not show a significant effect of BMI on the development of pelvic organ prolapse. However, a recently published systematic review and meta-analysis by Giri et al. (27) obtained similar results to our findings. They reported an association between degrees of obesity and POP. Estimates of the effects of POP in obese women (BMI ≥30 kg/m^2) range from negative to a 2.5-fold increase in risk when compared with women of normal weight (28,29).

In our study, patients generally reported high levels of satisfaction. Fortunately, none of the patients complained about lack of intercourse. However, in the present study, only 5 (4.71%) cases of urinary incontinence were observed after surgery, with 4 cases having SUI and 1 case being due to neurological causes. Two patients had *de novo* SUI, but the difference was not statistically significant. In our patients, the desire for re-operation was not observed, except in two

cases. The request for re-surgery in these two patients was due to SUI, which symptoms did not exist at the time of the last operation. The symptoms of these patients developed after colpocleisis surgery. In total, 4 cases of the patients underwent simultaneous colpocleisis and mid-urethral sling (MUS) surgery, none of whom had urinary symptoms. Our present study showed that urinary incontinence significantly decreased after surgery compared with pre-operation. These results demonstrate the positive effect of colpocleisis in women with POP. Wheeler et al. (30) showed a significant improvement in the quality-of-life questionnaires assessing impact, and lower urinary tract symptoms were decreased after colpocleisis with MUS or other anti-incontinence procedures. The results of Hullfish et al.'s (30) study were also similar. Although colpocleisis is an option for older women who do not have sexual function, there are concerns that this procedure, which significantly changes the female genital anatomy and vaginal function, may negatively impact body image, lead to patient dissatisfaction, and result in regret about treating their prolapse. Colpocleisis is a safe procedure with a high rate of anatomical and subjective success. In conclusion, the present study showed that the levels of satisfaction, quality of life, and the absence of POP symptom recurrence were significantly improved after colpocleisis. Le Fort partial colpocleisis is a procedure in which the uterus is preserved during prolapse repair, involving cervix denudation and vaginal wall suturing. Normal cervical cytology, human papillomavirus testing, and endometrial evaluation are documented before surgery. Total colpectomy procedures denude the entire vaginal epithelium, and suburethral plication or midurethral sling is recommended to reduce postoperative SUI and prolapse risk (14).

Study Limitations

A limitation of this study was the lack of a control group or comparison with alternative surgical interventions for POP treatment. Without a comparative analysis, it is challenging to determine whether the observed improvements in POP and urinary incontinence outcomes are specifically attributable to colpocleisis or whether similar results could have been achieved with other surgical approaches. This limitation limits the ability to assess the relative effectiveness and safety of colpocleisis compared with alternative treatments for POP in menopausal women. Reliance on self-reported symptoms to determine the prevalence of POP may underestimate the true prevalence because reported symptoms may not always align with clinical examination findings. The small sample size of women in the present study may limit the generalizability of the findings to a larger population. Moreover, the variability in the definitions of success across studies evaluating colpocleisis outcomes may hinder direct comparisons and interpretations of overall effectiveness.

Conclusion

Our study demonstrated that colpocleisis effectively reduced the degree of prolapse and improved patient quality of life. The absence of anatomical recurrence and the significant decrease in urinary incontinence after surgery highlight the success of the procedure. These findings suggest that colpocleisis interventions were beneficial in addressing both POP and urinary incontinence, leading to positive patient outcomes. However, considering the risk of occult urinary incontinence, MUS or other procedures should be performed simultaneously with colpocleisis.

Ethics

Ethics Committee Approval: The Ethics Committee of Tabriz University of Medical Sciences approved the study (decision no: IR.TBZMED.REC.1400.1018, date: 12.01.2022).

Informed Consent: Retrospective cohort study.

Authorship Contributions

Surgical and Medical Practices: F.R., F.M., L.S., H.S.P., Concept: F.R., F.M., L.S., H.S.P., Design: F.R., F.M., L.S., H.S.P., Data Collection or Processing: F.R., F.M., L.S., H.S.P., Analysis or Interpretation: F.R., F.M., L.S., H.S.P., Literature Search: F.R., F.M., L.S., H.S.P., Writing: F.R., F.M., L.S., H.S.P.

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ORIGINAL RESEARCH
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Guy's, S.T.O.N.E., CROES Nomograms in Percutaneous Nephrolithotomy Can Predict the Stone-Free Rate Similarly: A Retrospective Study of Thousand Patients

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What's known on the subject? and What does the study add?

Some scoring systems are known to predict stone-free percutaneous nephrolithotomy. All three of the Guy's stone score, S.T.O.N.E. and CROES nomograms predicted stone-free percutaneous nephrolithotomy.

Abstract

Objective: To compare the Guy's, S.T.O.N.E, and CROES nomograms for predicting stone-free status in patients who underwent percutaneous nephrolithotomy for renal stones.

Materials and Methods: The data of 1114 patients who underwent percutaneous nephrolithotomy for renal calculi between 11/2008 and 08/2018 in our clinic were retrospectively reviewed. Various parameters evaluated by preoperative computed tomography and the scoring systems of the patients and postoperative stone-free status were compared.

Results: Out of 1000 patients who met the study criteria. Gender, body mass index, and stone density were not statistically different between the group with residual stones and the stone-free group. However, stone size, number of renal accesses, duration of fluoroscopy usage, duration of operation, number of stones, and complication rate were significantly higher in the group with residual stones than in the stone-free group. A statistically significant correlation was found between the postoperative stone-free rate and scoring systems. The applicability and preoperative prediction ability of all three systems were evaluated by receiver operating characteristic analysis. The area under the curve (AUC) was detected in the Guy's, CROES, and S.T.O.N.E scoring system (AUC: 0.642, 0.665, 0.592 respectively).

Conclusion: In this study, where the perioperative and postoperative results of 1000 patients were evaluated, we found that all three scoring systems could predict the stone-free rate. "We believe that the use of these scoring systems before surgery can guide surgeons."

Keywords: Complications, endourology, kidney stone

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Introduction

There are many invasive and non-invasive methods in the current treatment of urinary system stone disease. Because of advances in endoscopic approaches together with developing medical technology, open surgery is required in a very small proportion of urinary system stones. Today, minimally invasive treatments are mostly used in urinary system stones (1,2). In the 1950s, with the use of percutaneous needle aspiration treatment and antegrade pyelography in kidneys with hydronephrosis, percutaneous interventions on the kidney became widespread (3,4). Percutaneous nephrolithotomy (PNL) for the treatment of kidney stones was first described by Fernström and Johansson in 1976 (5).

Despite advances in surgical techniques and technology, there is an increase in the number of complications in parallel with the number of surgeries (6,7). There have been ongoing studies for years on preoperative variables that can predict PNL success and complication rates. However, there is no preoperative variable that can be accepted as a standard yet (8-10).

Until recently, there were no useful scoring systems that could predict success and complication rates in PNL. Guy's stone score (GSS), stone size, tract length, obstruction, number of involved calices, andessence/density (S.T.O.N.E), and the Clinical Research Office of the Endourological Society (CROES) nomograms have been recommended as preoperative assessment tools since 2011 (11-13). It has been shown in these studies that nomograms inform the surgeon about the stone-free rate and complication ratio. In addition, different studies have yielded results showing nomograms' use in daily practice. We conducted this study to contribute to the literature because it is one of the studies with the largest patient population in the literature and is a tertiary reference hospital.

In this study, we aimed to investigate the predictive ability and superiority of GSS, S.T.O.N.E, and CROES nomograms in a retrospective extensive patient group.

Materials and Methods

This study was conducted after the Ethics Committee approval of University of Health Sciences Turkiye, İzmir Tepecik Education and Research Hospital (IRB no: 2019/9-13). Informed consent was obtained from all patients. A total of 1114 patients who underwent PNL in our clinic between November 2008 and August 2018 were screened. Patients younger than 18 years of age with a solitary kidney or horseshoe kidney anomaly and who underwent endoscopic combined retrograde intratrenal surgery (eCIRS) were excluded from the study. The remaining 991 patients were included in the study.

A detailed anamnesis was taken from all patients before surgery, and physical was examined. An informed consent form was obtained from the patients before the procedure. Complete blood count, biochemical tests (kidney and liver function tests and electrolyte levels), bleeding parameters, and urine culture were evaluated. The medications of the patients using anti-aggregant or anticoagulant were discontinued in consultation with the relevant units, and appropriate treatment (low molecular weight heparin) was initiated when necessary. All patients were evaluated with a kidney-ureter-bladder X-ray and non-contrast enhanced computed tomography (NCCT) preoperatively. These protocols were routinely applied to all stone patients. All stone protocol NCCT were evaluated according to the S.T.O.N.E, GSS, and CROES nomograms. In the GSS, the location of the stone, number of stones, presence of partial or complete staghorn stones, and presence of anomalies in the kidney anatomy were evaluated and scored between 1 and 4 (Figure 1). In the CROES nomogram, six parameters including stone burden, stone location, previous intervention history, presence of staghorn stone, number of stones, and number of annual cases were evaluated (Figure 2). In the S.T.O.N.E nomogram, five parameters including the size of the stone (size), the distance of the stone from the skin (tract of length), the presence of hydronephrosis (obstruction), the number of calices in which the stone is located (number of calices), and the density of the stone (essence) were evaluated (Figure 3).

All procedures were performed under general anesthesia. A 6F open-ended ureteral catheter was inserted into the ureter in the lithotomy position. The patients were then placed in the prone position on a table compatible with the C-arm. Using fluoroscopy, the appropriate calyx was accessed with the triangulation technique using an 18G percutaneous access needle. A single-step Amplatz dilation technique was used. A 26-F nephroscope (Karl Storz GmbH, Tuttlingen, Germany) was used through the 30F Amplatz sheath, and the stones were broken with the help of a pneumatic and/or ultrasonic lithotripter. The residual stone status was evaluated by perioperative fluoroscopy. After the operation, a nephrostomy tube was placed and the procedure was terminated.

Operation time, number of percutaneous accesses, fluoroscopy time, intraoperative and postoperative complications, duration of nephrostomy catheterization, and length of hospital stay were evaluated. Residual stone status was assessed by perioperative fluoroscopy and NCCT 1 month after surgery. After PNL, residual fragments of 4 mm that did not cause obstruction or infection were considered "stone-free". Patients were evaluated according to three nomograms. Stone-free were defined as group 1, and residual stone was defined as group 2.

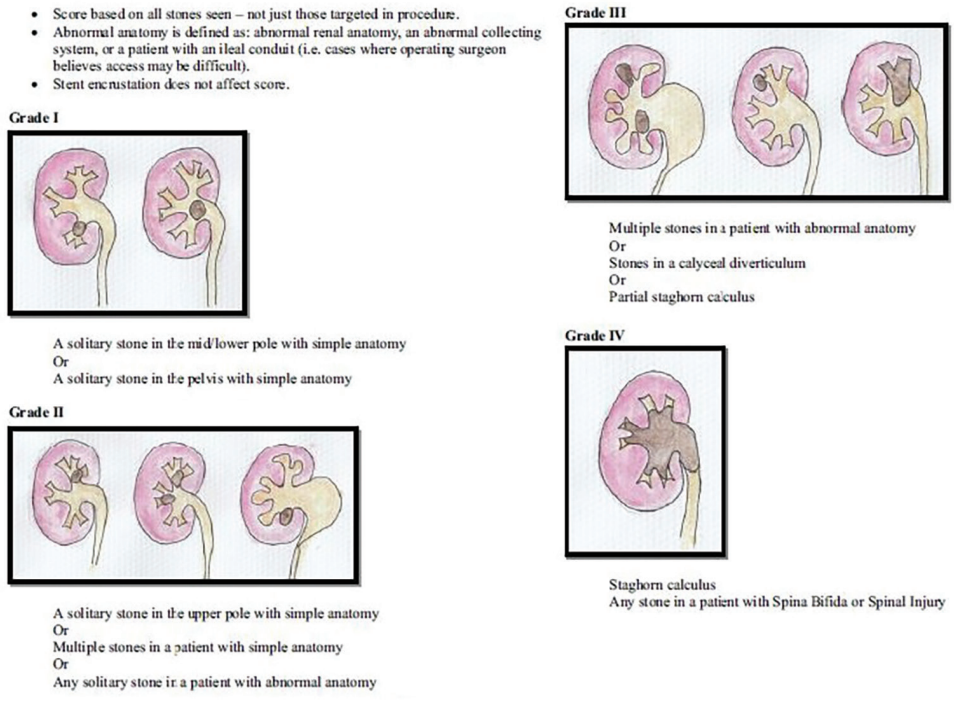

Figure 1. Guy's stone score

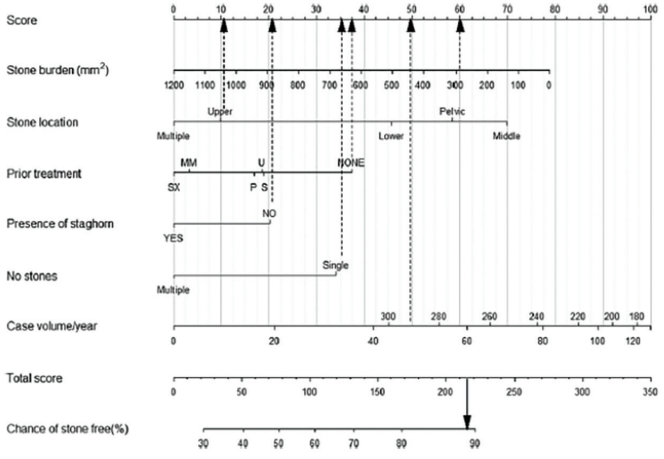

Figure 2. Nephrolithometry nomogram to predict treatment success using KUB after PCNL. Instructions for use: Draw 3 vertical lines to score axis to determine score attributable to each observed radiological characteristic. Sum scores for all radiological characteristics. Locate calculated sum of scores on total score axis. Draw vertical line to chance of stone-free axis to determine predicted chance of treatment success. Note that staghorn stones are scored under multiple group in stone location axis. Stone burden is estimated from stone dimensions in mm using formula Σ (0.785 + length$_{max}$ + width$_{max}$) (10). Example shows patient with no prior stone treatment and 1 upper calyceal stone with estimated stone burden of 300 mm² at center with average case volume of 45 patients per year. Total stone score of 212 predicts 87% chance of treatment success

MM: Multiple stone treatment modalities, U: Ureteroronoscopic stone treatment, SX: Pyelolithhotomy, P: PCNL, S: Extracorporeal shock wave lithotripsy, PCNL: Percutaneous nephrolithotomy

Statistical Analysis

The SPSS 15.0 package program (SPSS for Windows, 15.0, SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. Independent sample t-test, chi-square test, receiver operating characteristic (ROC) curve test, and correlation analysis were used to analyze the data. A $p<0.05$ was considered statistically significant.

Results

In our study, the patients' mean age was 49+13.2 (standard) years. 59% of the patients were male. The mean body mass index (BMI) was 28.3 (23-38). Hypertension, hyperthyroidism, and diabetes mellitus were detected in 16%, 11%, and 4% patients, respectively.

Perioperative and postoperative data of the patients and postoperative stone-free status are shown in Table 1. While the mean stone size of the patients before the operation in the stone-free group was 265 mm², it was calculated as 563 mm² in the patients with residual stones. The stone size was found to be statistically higher in patients with residual stones ($p<0.001$). According to the number of stones, a statistically significant difference was found between the groups ($p<0.001$). The mean stone density was not statistically significant difference between groups (Table 1).

The overall stone-free rate of the patients was 81.6%. When stone-free rates were evaluated according to GSS grades, the

stone-free rate was 89.6% in grade 1, 77.2% in grade 2, 72.5% in grade 3, and 71.4% in grade 4. While the stone-free rate was 84.8% in the group with S.T.O.N.E score of 5-7, it was 74.4% in the group with 8-10 and 60.9% in the group with 11-13. In the CROES scoring system, stone-free rates were 92.7% in the 276-340 score, 89.7% in the 211-275 score, 76.6% in the 146-210 score, and 71.3% in the 80-145 score (Table 2).

S.T.O.N.E	1 Point	2 Point	3 Point	4 Point
Size	0-399	400-799	800-1599	≥1600
Tract of Lenght	≤100	>100		
Obstruction	None or light	Moderate or severe		
Number of Calyx	1-2	3	Staghorn	
Essence (HU)	≤950	>950		
Total Score				

Figure 3. S.T.O.N.E. nephrolithometry score

S.T.O.N.E: Stone size, tract length, obstruction, number of involved calices, andessence/density, HU: Hounsfield unit

Scoring systems and the relative risk of residual calculi were evaluated as risk groups.

The GSS was determined as grade 1 low, grade 2 moderate, grade 3 high, and grade 4 very high-risk groups. With the S.T.O.N.E nephrolitometry score, 5-7 were determined as low risk, 8-10 as medium risk, and 11-13 as high risk. The CROES nephrolitometry score was also divided into four groups according to the risks. It was determined as low risk between 276 and 340, medium risk between 211-275, high risk approximately 146-210 and very high-risk group between 80 and 145 (Table 3). All Three scoring systems were found to be significant on logistic regression analysis. The odds ratio and confidence index are shown in Table 3.

Table 1. Demographic, perioperative and postoperative data of the patients and their postoperative stone-free status

	Total	Stone free % (n)	Residual calculi % (n)	p
Patients (n)	991	807	184	
Age mean (year), STD	49+**13.2**	48.6**+13.3**	50.2**+12.7**	0.082[¢]
Sex	0.044*			
Male	596	83.6 (498)	16.4 (98)	
Female	385	78.5 (310)	19.5 (75)	
BMI (mean) kg/m^2, STD	28.3+**45.7**	28.8**+44.6**	25.8+**50.5**	0.598[¢]
Stone size (mm^2)	320**+544.9**	265**+366.3**	563**+973.2**	<0.001[¢]
Stone density (HU)	825**+528.7**	822**+534.0**	838**+505.5**	0.295[¢]
Number of tracts	<0.001			
1	866	83 (719)	17 (147)	
2	105	67.6 (71)	32.4 (34)	
3	20	90 (18)	10 (2)	
Fluoroscopy time (second)	153.1+**161.6**	147+**147.2**	177**+213.3**	0.034[¢]
Operation time (min.)	63.4+**51.8**	59.4+**48.1**	81+**62.8**	<0.001[¢]
Number of stone	<0.001*			
Single	416	90.6 (377)	9.4 (39)	
Multiple	575	75 (431)	25 (144)	
Stone location	<0.001*			
Calix	223	171	52	
Renal pelvis	312	287	25	
Both	456	350	106	
Clavien classification	<0.001*			
0	816	688	128	
1	73 (7.3%)	56	17	
2	75 (7.5%)	43	32	
3a	5 (0.5%)	4	1	
3b	4 (0.4%)	2	2	
4a	18 (1.8%)	14	4	

[¢]: Independent sample t-test, *: Chi-square test, STD: Standard, HU: Hounsfield unit, BMI: Body mass index

All stone nomograms gave statistically significant results in predicting stone-free status. GSS p<0.001 [95% confidence interval (CI) 0.598-0.686, area under the curve (AUC): 0.642], S.T.O.N.E p<0.001 (95% CI 0.544-0.640, AUC: 0.592), CROES p<0.001 (95% CI 0.622-0.708, AUC: 0.665). A comparison of scoring systems for stone-free status is shown in Table 4. Simultaneously, the predictive capabilities of the scoring systems were compared by calculating the area under the curve with ROC analysis (Figure 4). The optimal cut-off score values, AUC, sensitivity, and specificity score are shown in Table 4.

Considering the complications, fever was observed in 73 patients, bleeding or urinary leakage not exceeding 12 h in 75 patients, pneumothorax requiring intervention in 5 patients, arteriovenous fistula in 4 patients, and colon injury in 18 patients. The overall complication rate was 17%. The complication rates according to Clavien classification are given in Table 1.

Discussion

Since its definition, PNL has become the first-line treatment option for large, complex, and staghorn stones. The main goal for treating kidney stones is to provide maximum benefit with minimal harm. Although there are many scoring systems predicting stone-free status after PNL, there is no standard method that is widely accepted.

Table 2. Stone free rate and scoring system groups

		Stone free	Residual calculi	Stone free rate
GSS	**Grade 1**	397	46	89.6%
	Grade 2	244	72	77.2%
	Grade 3	111	42	72.5%
	Grade 4	55	22	71.4%
S.T.O.N.E.	**5-7**	617	110	84.8%
	8-10	166	57	74.4%
	11-13	25	16	60.9%
CROES	**276-340**	51	4	92.7%
	211-275	334	38	89.7%
	146-210	296	90	76.6%
	80-145	127	51	71.3%

GSS: Guy's stone score, CROES: Clinical Research Office of the Endourological Society, S.T.O.N.E: Stone size, tract length, obstruction, number of involved calices, andessence/density

Table 3. Scoring systems and relative risk for residual calculi and risk group

		p	Odds ratio (95% CI)	Risk group
GSS	**Grade 1**	<0.001		Low
	Grade 2	**<0.001**	**2.547 (1.702, 3.810)**	Intermediate
	Grade 3	**0.001**	**2.046 (1.360, 3.078)**	High
	Grade 4	**0.047**	**1.704 (1.007, 2.883)**	Very high
S.T.O.N.E.	**5-7**	**<0.001**		Low
	8-10	**<0.001**	**2.469 (1.549, 3.936)**	Intermediate/high
	11-13	**0.943**	**0.987 (0.685, 1.421)**	Very high
CROES	**276-340**	<0.001		Low
	211-275	0.016	4.514 (1.322, 15.412)	Intermediate
	146-210	0.033	3.711 (1.113, 12.365)	High
	80-145	0.954	1.037 (0.300, 3.583)	Very high

CI: Confidence interval, GSS: Guy's stone score, CROES: Clinical Research Office of the Endourological Society, S.T.O.N.E: Stone size, tract length, obstruction, number of involved calices, andessence/density

Table 4. Area under the curve of the three scoring systems predicting stone-free status

	AUC	Cut-off value	Sensitivity	Specificity	p	95% CI
GSS	0.642	2	74.4%	50.7%	<0.001	0.598, 0.686
S.T.O.N.E.	0.592	7	41%	75%	<0.001	0.544, 0.640
CROES	0.665	206.5	81.5%	47.5%	<0.001	0.622, 0.708

GSS: Guy's stone score, CROES: Clinical Research Office of the Endourological Society, AUC: Area under the curve, CI: Confidence interval, S.T.O.N.E: Stone size, tract length, obstruction, number of involved calices, andessence/density

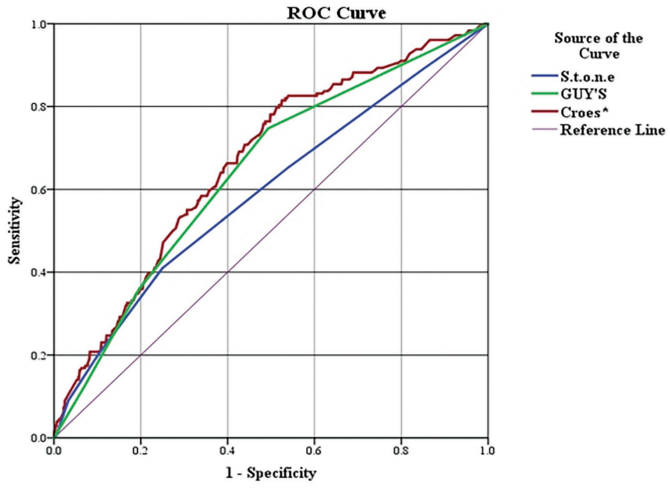

Figure 4. ROC curve for stone-free predicting, Guy's stone score, S.T.O.N.E., and CROES nomogram

ROC: Receiver operating characteristic, S.T.O.N.E: Stone size, tract length, obstruction, number of involved calices, andessence/density

Among these scoring systems, GSS, S.T.O.N.E, CROES, Seoul National University Renal Stone Complexity and acute angle, complicated calyx and stone size are frequently discussed in the literature. In recent years, the importance of systematic and standard reporting of results after various endourological surgeries, including PNL, has been emphasized (14-16). GSS, CROES, and S.T.O.N.E are the nomograms most frequently used recently.

Many factors have been defined that predict the stone-free rate after PNL, such as stone burden, stone type, number and location of the stone, HU, BMI, stone skin distance, and abnormal kidney anatomy. However, a single parameter that predicts stone-free status has not yet been identified. Therefore, nomograms in which many factors are combined have been developed by the authors (15-17). Numerous studies have attempted to validate these scoring systems. However, most studies are retrospective, and the stone size definition of residual stone, method, and timing of imaging after PNL are different. This has made it impossible for scoring systems to be accepted as a standard (18-25).

Although the parameters evaluated by the scoring systems are different from each other, all of them can help the surgeon in predicting stone-free status and operation-related complications. There are several important differences between the aforementioned scoring systems. While S.T.O.N.E is based entirely on data from preoperative NCCT, GSS and CROES also include patient variables. Because the definition of full staghorn or partial staghorn is not clear and subjective, its effects on scoring systems are suspicious. Some authors classify staghorn stones as follows: "borderline", stones filling the pelvis and calyx; "partial", stones filling the pelvis and extending into the two calyces; "complete", stones filling ≥80% of the pelvicalyceal system, extending to the pelvis and all major calyces; and "huge", stones filling the entire pelvicalyceal system accompanied by dilatation (26,27). Since the number of calyx filled by the stone is one of the parameters in the S.T.O.N.E scoring system, it can evaluate the staghorn stone status more objectively than other systems.

Spina bifida or spinal injury history of the patient, stone burden, and calyceal anatomy were evaluated using GSS (15). Studies have reported that GSS is important for predicting stone-free status. In addition, the stone-free rate was found to be associated with an increase in GSS grade (GSS grade 1 81%, GSS grade 2 74.2%, GSS grade 3 35%, GSS grade 4 29%). However, no significant correlation was found between GSS and postoperative complications.

The GSS symptom score has some limitations. The use of different imaging methods other than CT in the evaluation of stone-free status can be considered as a weakness of the scoring system because the sensitivity of imaging methods in showing residual stones is not the same. In our study, all patients were evaluated with NCCT postoperatively, and GSS could again predict stone-free status significantly.

In the S.T.O.N.E. scoring system, 4-5 were defined as low, 6-8 as medium and 9-11 as high-risk groups, and it was shown that the success of the operation decreased as the S.T.O.N.E score increased. In the study, the S.T.O.N.E score was the best predictor of stone-free status, whereas the second most effective factor was found to be stone size. Complication rates were given in the study, and it was determined that only stone size was associated with complications. The small number of complications prevented detailed analysis of the complications (28). In our study, it was observed that the success rate decreased with the increase in the number of scores. In the S.T.O.N.E scoring system, calyx stones and pelvis stones affect the scoring system equally, with a score of "1". However, the stone-free rates of pelvic and calyx stones are not the same in the literature (29).

In addition to stone parameters and patient characteristics, the experience of the clinic was evaluated using the CROES nomogram (30). When the stone volume calculation in the CROES study is used as maximum length maximum width x π x 0.25, it is valid for round and oval stones, but unfortunately it is not possible to give the same exact result for large, complex, staghorn stones. Similar to stone burden, HU is not applicable to large/staghorn stones. The reason for this is that the density is different in the periphery and center of the stone because of its lamellar structure.

Stone scoring systems are also used in solitary kidney stone disease. The authors concluded that stone burden was associated with SFR and complication rate. Moreover, the CROES score was

the only independent factor associated with SFR status in their study. Also, this study has shown correlation with the literature (31).

Unlike the GSS, the CROES nomogram is difficult and time consuming for clinical applicability. However, in our study, it was shown that the AUC in CROES is better than the GSS and S.T.O.N.E scores (Table 4).

Our study was retrospective. In addition, evaluation of scoring systems by a single urologist and performing surgeries by different surgeons are limitations of our study. However, the evaluation of a larger patient population than that of many studies in the literature can be shown as the strength of the study.

Conclusion

It was determined in our study with a large patient population that the three scoring systems could predict stone-free rates significantly. Because of the weak correlation with the complication rates, a clear opinion on this issue could not be declared yet. However, it is possible to say that all three methods are suitable and usable for preoperative planning in PNL. For scoring systems to be widely used in daily practice, there is a need for large prospective studies and elimination of their weaknesses.

Ethics

Ethics Committee Approval: The research was approved University of Health Sciences Turkiye, İzmir Tepecik Education and Research Hospital (IRB no: 2019/9-13, date: 23.05.2019).

Informed Consent: Written informed consent was obtained from all patients.

Authorship Contributions

Surgical and Medical Practices: T.Ç., M.Y.Y., Ç.B., T.S., Concept: T.Ç., M.Y.Y., M.H.Ö., E.K., H.B., Design: T.Ç., Ç.B., H.B. T.S., G.K., Data Collection or Processing: T.Ç., M.Y.Y, M.H.Ö., T.S., E.K., G.K., Analysis or Interpretation: H.B., Literature Search: T.Ç., M.H.Ö., Ç.B., E.K., G.K., Writing: T.Ç.

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VIDEO ARTICLE
General Urology

Doi: 10.4274/jus.galenos.2024.2024-4-6
J Urol Surg 2024;11(3):187-188

Minimally Invasive Thulium Laser Enucleation of the Prostate

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Abstract

The goal of Minimal Invasive Laser Enucleation of Prostate (MiLEP) surgery is to reduce complication rates and risk of urethral trauma, while providing similar success rates by using smaller caliber instruments. Enucleation was performed with 22 Ch outer resectoscope sheath, a rotatable 19 Fr inner sheath, a 2.9 mm 30 degrees telescope (Tontarra - Germany). In this surgery, a 100 W pulse thulium YAG laser (Dornier Thulio® High Power Laser) with a 550 µm fiber laser was used. Enucleation was performed at 2 J & 50 Hz (enucleation mode), and coagulation at 0.4 J & 75 Hz (soft tissue mode). The total surgical time was 32 minutes. The enucleation duration was 17 minutes, and morcellation took 11 minutes. No intraoperative complications were observed. MiLEP surgery aims to provide similar efficacy to standard endoscopic laser enucleation of the prostate while using smaller endoscopic instruments and reducing postoperative complications.

Keywords: MiLEP, enucleation, benign prostat hyperplasia

Introduction

Anatomic endoscopic enucleation of the prostate is an effective surgical alternative for relief of lower urinary tract symptoms in patients with benign prostatic hyperplasia (1). The goal of minimal invasive laser enucleation of prostate (MiLEP) surgery is to reduce complication rates and risk of urethral trauma, while providing similar success rates by using smaller caliber instruments (1). This video presents unedited real-time recordings of MiLEP surgery performed in a 66-year-old male patient with a pre-diagnosis of benign prostatic hyperplasia.

Case Presentation

A 66-year-old male patient with lower urinary tract symptoms for approximately 7 years presented to our outpatient clinic. He was under tamsulosin medication, but his symptoms worsened. In uroflowmetry, the Q_{max} was 8.5 mL/sec, and postvoid residual volume was 110 milliliters. The total prostate-specific antigen level was 3.5 ng/mL, and ultrasound estimates the prostate weight to be 65 milliliters. Therefore, the patient was scheduled for MiLEP with pulse Thulium-YAG laser.

Discussion

Enucleation was performed with 22 Ch outer resectoscope sheath, a rotatable 19 Fr inner sheath, a 2.9 mm 30 degrees telescope (Tontarra-Germany). For morcellation, a morsescope with a working channel of 5 mm for morcellation, compatible with all available morcellators was used. The morcellator fits the outer sheath of the resectoscope, eliminating the need to change the outer sheath intraoperatively. In this surgery, a 100-W pulsed thulium YAG laser (Dornier Thulio® High Power Laser) with a 550 µm fiber laser was used. Enucleation was performed at 2 J and 50 Hz (enucleation mode) and coagulation at 0.4 J and 75 Hz (soft tissue mode).

Surgical Equipment

22 CH Laser resectoscope set (Tontarra)

Laser: Pulse Thulium YAG laser (Dornier Thulio® High Power Laser)

Fiber: 550 µm

Laser Settings

Enucleation: Enucleation Mode - 2 J & 50 Hz

Coagulation: Soft tissue Mode - 0.4 J & 75 Hz

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J Urol Surg,
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Result

The total surgical time was 32 minutes. The enucleation duration was 17 min, and morcellation took 11 min. No intraoperative complications were observed, and the postoperative catheterization period was 2 days. Following catheter removal and spontaneous urine passage, the patient was discharged without complications. At the 1-month postoperative follow-up, Q_{max} was 24 mL/sec, and postvoid residual was 25 milliliters. There were no early-onset urinary incontinence issues.

Conclusion

MiLEP surgery aims to provide similar efficacy to standard endoscopic laser enucleation of the prostate while using smaller endoscopic instruments and reducing postoperative complications.

Video 1.

Ethics

Informed Consent: The patient featured in the video article has been appropriately informed and consented to publication.

Authorship Contributions

Surgical and Medical Practices: M.İ.G., Concept: M.İ.G., Design: A.F.Ö., Analysis or Interpretation: M.İ.G., Literature Search: A.F.Ö., Writing: M.İ.G., A.F.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT
Urooncology

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Penile Metastasis from Anal Canal Carcinoma: A Case Report

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Abstract

Penile metastases are exceptionally rare and are associated with poor prognosis. Herein, we report the case of a 74-year-old man with previously treated squamous cell carcinoma of the anal canal who was referred with a painless penile lump. Biopsy identified a similar squamous cell carcinoma. Imaging studies excluded other sites of metastases. It was considered a solitary metastasis, and a total penectomy was performed. The patient was free of metastases for four years until the disease progressed, and he is currently under palliative chemotherapy with 5 years of follow-up. This is the second worldwide case of anal canal carcinoma with penile metastasis.

Keywords: Penile metastases, anal canal carcinoma, total penectomy

Introduction

Penile metastases are rare and were first described by Eberth in 1870 (1,2). Since then, many reports have been made, with more than five hundred patients reported (2). The most common primary tumor origins are the bladder and prostate, with approximately 30% each, and 10-20% for rectosigmoid tumors (1-5). The most common clinical presentation is a painless penile mass; other symptoms include malignant priapism, pain, voiding symptoms, and hematuria (4-6). The prognosis is abysmal, irrespective of the treatment choice (1). We present a case of a patient with penile metastasis from an anal canal carcinoma treated surgically and briefly review the literature.

Case Presentation

A 74-year-old man arrived at the outpatient clinic with a complaint of a penile lump. The patient had a history of squamous cell carcinoma of the anal canal, classified as T4N0M0, two years ago. This tumor presented as an anal mass complicated with a perianal abscess. The perianal abscess was conservatively treated with antibiotics. Subsequently, chemoradiation (54 Gy/30 F on both tumor and regional lymph nodes and two cycles of mitomycin C plus 5-fluorouracil) with curative intent was performed with complete response. No surgical approach was applied to this tumor. However, a small liquid collection remained (10x5 mm) with small fistulous tracts. No biopsy or treatment was performed on this collection or the fistulous tracts.

Upon physical examination, we palpated two painless, round, hard masses on both cavernous bodies from the glans to the shaft, without skin or glan invasion. We performed a core biopsy that revealed a squamous cell carcinoma with histological characteristics similar to those of the previous tumor. The patient was screened using computed tomography and magnetic resonance imaging and had no other primary site tumor, neither local nor distant recurrence (Figure 1).

A multidisciplinary team considered a solitary penile metastasis of the anal canal carcinoma and proposed a total penectomy with palliative intent. The procedure was performed, and the anal canal was biopsied to exclude local relapse. The pathology report identified a squamous cell carcinoma histologically similar to the previous anal canal tumor (Figure 2), and the biopsies were negative. The total penectomy specimen had a

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tumor of 16 cm distancing 2.5 cm from the base with negative surgical margins.

The patient remained on follow-up without complaints or evidence of recurrence for four years. Subsequently, the patient recurred with perineal cutaneous metastases, inguinal, iliac, and aortic lymph nodes, and pulmonary metastases. Palliative chemotherapy with paclitaxel and carboplatin was initiated. The patient is alive and has five years of follow-up with partial response to chemotherapy.

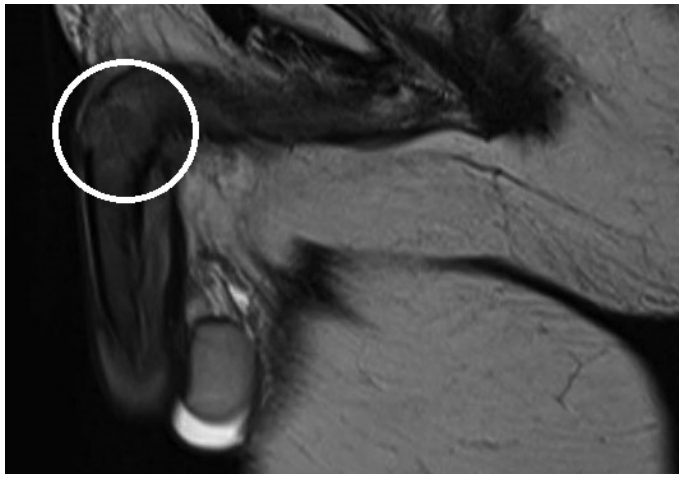

Figure 1. MRI image of the left cavernous body with a suspected lesion at referral (white circle)

MRI: Magnetic resonance imaging

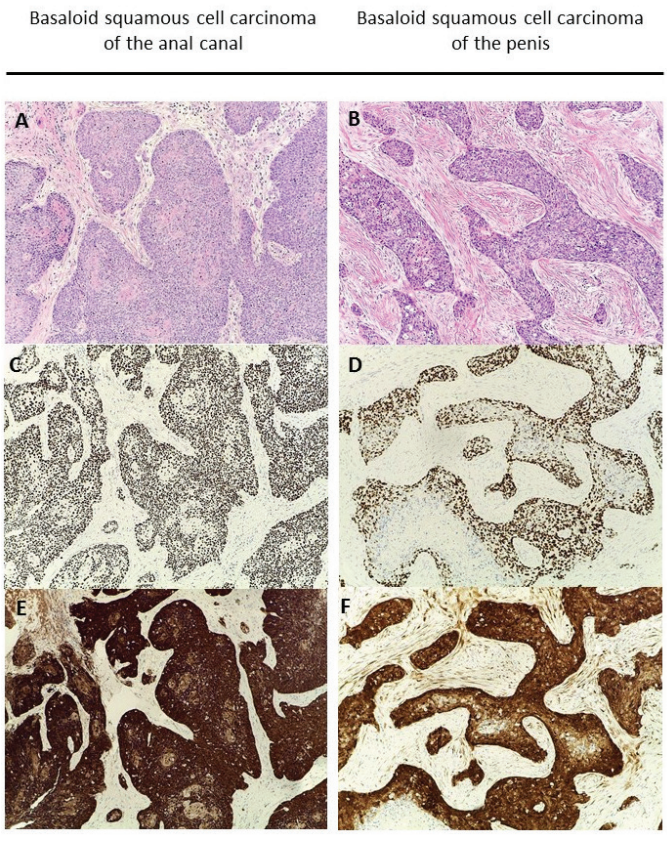

Figure 2. Histological comparison of the squamous cell carcinoma of the anal canal to the squamous cell carcinoma of the penis. A and B. Hematoxylin and eosin stain, 100x; C and D. Immunohistochemistry study positive for p40, 100x; E and F. Immunohistochemistry study positive for p16, 100x

Discussion

Secondary metastatic penile cancer is rare despite its rich and interconnected vasculature (1-4). The most common origins are the neighboring pelvic tumors: bladder, prostate, and rectosigmoid, with approximately 75% (1-5). Other tumor origins include the kidney, testis, and lungs, among others (1-5). There is only one report of an anal canal primary carcinoma (7). Therefore, to the best of our knowledge, this is the second report of penile metastasis of an anal canal carcinoma.

There is uncertainty regarding the metastatic mechanism, and several hypotheses have been proposed: The retrograde venous route, retrograde lymphatic route, arterial embolism, direct extension, and implantation secondary to instrumentation (1-5). The retrograde venous route is the most commonly acknowledged and results from refluxing cancer cells through the pelvic venous plexus to the penile dorsal vein (1-5). This route explains pelvic tumors' higher incidence of secondary malignancy (1-5). The retrograde lymphatic route results from the spread from the iliac to the inguinal nodes and then to the penis, explaining the involvement of the penile skin but not the corpora or glans (1,2,4,5). Direct extension results from highly locally invasive and aggressive tumors that invade the base and proximal shaft (1,2,4,5). Arterial embolism and implantation secondary to instrumentation are uncommon (1,2,4,5).

The two most probable hypotheses in our report are direct extension and retrograde venous spread. Direct extension relies on evidence of liquid perineal collection with fistulous tracts. However, to counter it, the tumor did not evolve to the base of the penis, and negative surgical margins were obtained. Hence, the most probable metastatic mechanism is the venous retrograde route.

The most common clinical presentation is a painless penile mass in 60-80% of cases, involving the corpora bilaterally in 60-70% (2-4). Isolated glans is less common, 10-24%, and skin and prepuce evolvement are rare, 5-6% (2,4,5). Malignant priapism is a prominent feature present in up to 40% of patients (1-3,5) and portends a poor prognosis (6). Other clinical features include pain, hematuria, and voiding symptoms (1-3,5).

The diagnosis is made through a lesion biopsy or fine needle aspiration (1,5). The pathological examination confirms and excludes differential diagnoses such as other primary penile

tumors, Peyronie's disease, tuberculosis, and other inflammatory and suppurative diseases of the penis (1,2,5).

Management varies according to the patient's general health status, primary tumor response to treatment, extent of metastases, and symptoms presented (1-3,6,8). Chemotherapy, radiotherapy, and surgical excision, including total penectomy, are all possible treatments (1,2,5,8). Most patients have disseminated systemic disease and poor performance status (1,2,4,5,7,8). The prognosis is abysmal irrespective of treatment options, and survival is usually less than one year (1,2,4). Surgical treatment with total penectomy is performed with palliative intent to alleviate intractable pain and voiding symptoms in patients with good general health (2-3,8). However, there are reports of prolonged survival in patients who underwent total penectomy with metastasis confined to the penis (7,8).

In our report, because it was a unique metastasis, a total penectomy was performed to prevent the symptom development and delay the metastatic spread. The patient was followed up for five years and asymptomatic until the fourth year, when recurrence was diagnosed. Although penectomy had no curative intent, this radical surgery successfully resulted in a significant survival benefit with preserved quality of life.

Conclusion

The anal canal carcinoma as the primary tumor site and the significant delay and survival benefit obtained from the total penectomy contribute to the singularity of this case.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices: A.M.P., F.P., S.D., E.F., G.B., F.G., A.B., S.R., A.S., A.F., F.R., P.C., F.F., Concept: A.M.P., A.B., A.S., F.R., P.C., F.F., Design: A.M.P., A.B., S.R., A.S., A.F., F.R., P.C., F.F., Data Collection or Processing: A.M.P., F.P., S.D., E.F., G.B., F.G., Analysis or Interpretation: A.M.P., F.P., S.D., E.F., G.B., F.G., S.R., A.S., A.F., P.C., Literature Search: A.M.P., S.D., E.F., G.B., F.G., A.B., F.R., P.C., Writing: A.M.P., F.P., S.D., E.F., G.B., F.G., S.R., A.F., F.R., P.C., F.F.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT
General Urology

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A Rare Coexistence: Gangrenous Cystitis and Necrotizing Fasciitis

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Abstract

Gangrenous cystitis is an exceedingly uncommon diagnosis characterized by bladder mucosa and submucosal necrosis. The presence of non-specific symptoms and signs complicates the diagnostic process. Necrotizing fasciitis is a rare infection affecting the deep soft tissues, causing progressive destruction of the muscle fascia and rapid systemic spread. This study aimed to elucidate the atypical presentation of rare gangrenous cystitis in the literature, highlighting its potential to lead to necrotizing fasciitis. An 82-year-old female patient was admitted with abdominal and pelvic pain complaints. Computed tomography of the lower abdomen revealed free air-fluid densities in the pelvic region, raising the suspicion of intestinal perforation. Exploratory laparotomy diagnosed the patient with gangrenous cystitis and necrotizing fasciitis. Pathological examination confirmed the presence of necrosis. In patients presenting with acute abdominal symptoms, when free air-fluid levels are observed in imaging studies of the pelvis, rare diagnoses such as gangrenous cystitis should not be overlooked, even if the patient's history indicates anuria.

Keywords: Gangrenous cystitis, necrotizing cystitis, necrotizing fasciitis, acute abdomen, peritonitis

Introduction

Gangrenous cystitis, characterized by necrosis of the bladder mucosa and submucosa, can progress to involve the entire bladder wall and result in spontaneous rupture (1). Its etiology includes infections, chemical and physical irritations, and conditions leading to circulatory disturbances. It primarily affects patients with comorbidities such as diabetes, stone disease, spinal cord injuries, and pelvic malignancies (2). The rarity of this disease contributes to challenges in diagnosis, often leading to delayed identification and increased mortality. Researchers have explored the etiology, presentation, and management of gangrenous cystitis in the current literature, emphasizing the significance of prompt and aggressive surgical intervention (3). Necrotizing soft tissue infections are infrequent yet rapidly advancing bacterial infections with high morbidity and mortality rates (4). Necrotizing fasciitis, an uncommon yet life-threatening infection affecting the skin, soft tissue, and muscle, spreads along fascial planes at a rate of 2-3 cm/h, causing fascial destruction (5). This study contributes a unique clinical, radiological, and histological case of the coexistence of gangrenous cystitis and necrotizing fasciitis to the medical literature.

Case Presentation

An 82-year-old female patient presented to the emergency department with a 2-day history of abdominal pain. The patient had chronic kidney failure and had been anuric for 20 years, requiring dialysis. In addition, she had diabetes mellitus and chronic atrial fibrillation. Physical examination revealed no evident wounds or signs of infection on the skin. Abdominal examination demonstrated guarding and rebound tenderness. Laboratory results indicated an elevated C-reactive protein level of 424 mg/L and a white blood cell count of 7.31 10^3/µL. Computed tomography revealed diffuse intestinal dilation and air-fluid levels. Suspecting mesenteric ischemia and accompanying intestinal perforation, exploratory laparotomy was scheduled (Figure 1).

The surgical procedure revealed necrotic sections in the lower part of the rectus abdominis, rectus fascia, and parietal peritoneum extending superiorly to the bladder. Consultation with a urologist confirmed extensive necrosis in the superior,

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right lateral, and posterior bladder walls (Figure 2). Further debridement was performed to preserve viable tissue margins. The patient underwent cystectomy, and tissue samples were sent for pathological and microbiological assessment. Histological analysis indicated fat necrosis and an inflammatory cell infiltrate rich in polymorphonuclear leukocytes on a necrotic fibrotic background (Figure 3). Despite early surgical intervention and antibiotic therapy, the patient succumbed to cardiopulmonary arrest due to septic shock 2 days after surgery.

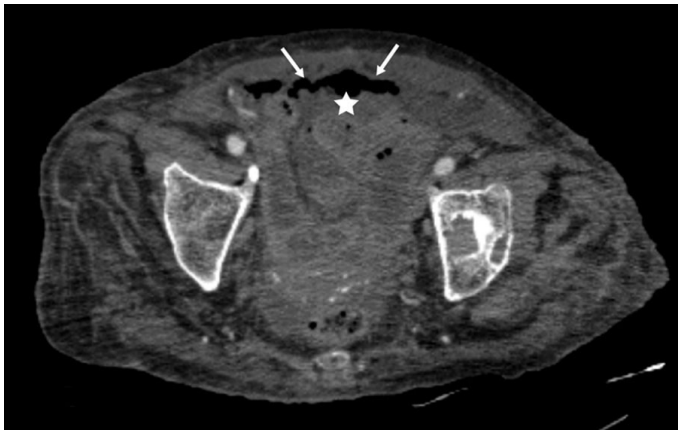

Figure 1. Air-fluid levels in the pelvic region

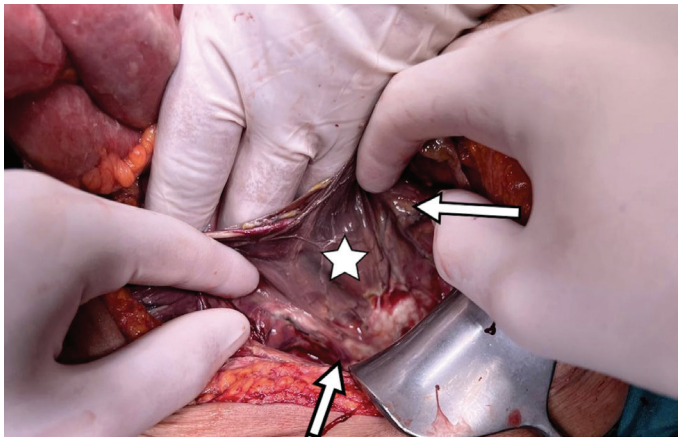

Figure 2. Intraoperative view of the bladder

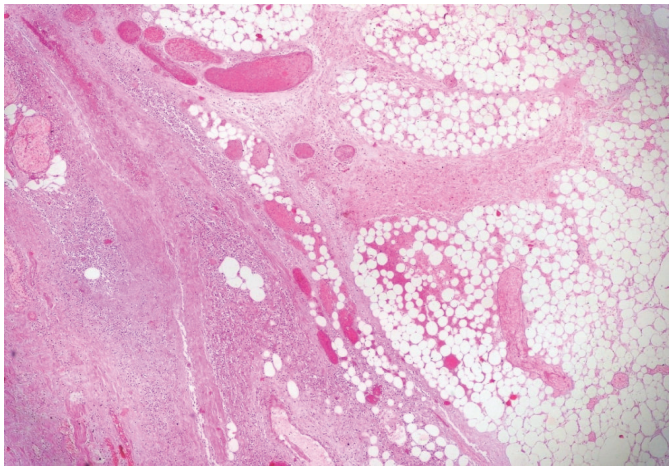

Figure 3. Diffused necrosis and inflammation, x40

Discussion

Gangrenous cystitis was initially documented by Willis (6) in 1650. The advent of broad-spectrum antibiotics has significantly reduced its incidence. It involves necrosis of the bladder mucosa and submucosa, potentially leading to spontaneous perforation and secondary acute peritonitis (7). The prognosis remains unfavorable, with a mortality rate of approximately 35%. Etiological factors include infections causing bladder wall ischemia, vascular obstruction, chronic urinary retention, radiation and chemotherapy, prior surgeries, and trauma. Comorbidities, such as diabetes mellitus, are frequently associated with bladder wall ischemia (8). Diagnostic challenges arise from a lack of distinctive symptoms. Common manifestations include lower abdominal pain, dysuria, hematuria, and pyuria (2,9), which may progress to acute abdomen or urosepsis.

Imaging techniques, including ultrasound, computed tomography, cystography, and cystoscopy, aid in diagnosis. Early surgical debridement is generally imperative, and there is a potential need for urinary diversion (10). Partial cystectomy is considered if the trigone is intact, whereas advanced cases may necessitate radical cystectomy (10).

In this case, despite the patient's anuria, a bladder-derived infection may have triggered gangrenous cystitis although histological confirmation is lacking. In addition, vascular obstruction from the patient's underlying conditions might have compromised bladder blood flow. The aggressive surgical approach involved extensive debridement and partial cystectomy. Delays in presentation, advanced sepsis, and comorbidities likely contributed to the unfavorable outcome.

Conclusion

In patients presenting with acute abdominal symptoms, when free air-fluid levels are observed in imaging studies of the pelvis, rare diagnoses such as gangrenous cystitis should not be overlooked, even if the patient's history indicates anuria.

Ethics

Informed Consent: Verbal and written informed consent was obtained from the patient for the study.

Authorship Contributions

Surgical and Medical Practices: M.B., G.A., E.E., Concept: M.B., Y.Y.K., E.E., Design: M.B., Data Collection or Processing: G.A., Y.Y.K., Analysis or Interpretation: G.A., Y.Y.K., E.E., Literature Search: M.B., Writing: M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

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