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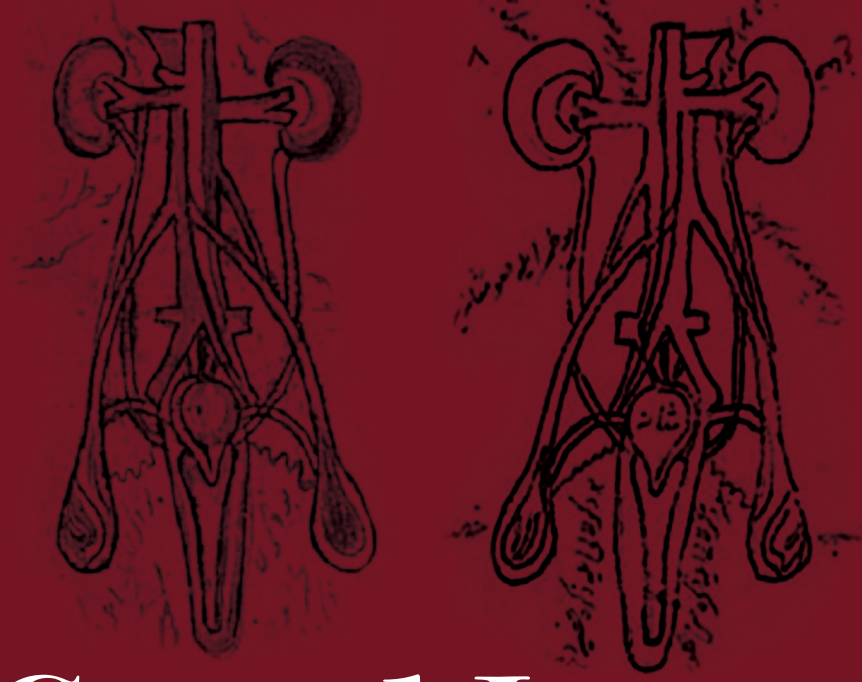

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Editorial

Dear colleagues,

I am honored to share with you the third issue of the Grand Journal of Urology (Grand J Urol) with the contributions of many respected researchers and authors.

Our journal has been indexed in Index Copernicus International (ICI), EuroPub and SciLit international databases since the second issue. Our applications to Ebsco Host and J Gate databases were also accepted and license agreements were signed mutually. The journal and its content will soon be included in the relevant databases. As of these achievements, the Grand Journal of Urology (GJU) has taken its place among the journals indexed by international databases. With this result, GJU was entitled to be included in the journals in category 1b defined in the application criteria for associate professorship.

In this third issue of our journal, there are many valuable articles under the subheadings of Female Urology, General Urology, Urolithiasis, Urological Oncology, Renal Transplantation, Andrology, Functional Urology, Neurourology and Genitourinary Radiology. I hope that these carefully prepared articles will make important contributions to valuable readers, researchers and the urology literature.

On this occasion, I would like to express my heartfelt gratitude to our authors who have contributed to our journal with their articles, to our reviewers who have meticulously evaluate the articles, to our designers and to our publisher.

Respectfully yours
September 2021
Assoc. Prof. Ekrem GUNER, MD
Editor-in-Chief

Original Article – Female Urology

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Our Minimally Invasive Sacrocolpopexy Experiences in Pelvic Organ Prolapse Treatment

Pelvik Organ Prolapsusu Tedavisinde Minimal İnvaziv Sakrokolpopeksi Deneyimlerimiz

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Abstract

Objective: We aimed to evaluate the results of our minimally invasive (laparoscopic and robotic) sacrocolpopexy operations in patients with pelvic organ prolapse (POP).
Materials and Methods: Demographic characteristics, intraoperative and postoperative data of 15 patients for whom we applied laparoscopic or robotic sacrocolpopexy due to symptomatic Grade 2 or higher apical POP based on POP-Q classification between September 2014 and September 2018. Treatment success was defined as Grade 0 or 1 POP in POP examination in the final surveillance.
Results: Mean age of the patients was 60.4 ± 8.3 (49-82) years. Four patients (26.7%) were operated using robotic and eleven patients (73.3%) using laparoscopic methods. Uterus conservative surgery was applied in all patients excluding one. Mean operative time was 183.3 ± 21.4 (145-220) minutes and mean hospital stay of the patients was 2.8 ± 0.7 (2-4) days. Intraoperative and postoperative complications developed in a total of two patients (13.3%). Mean duration of follow-up was calculated as 12.1 ± 4.8 (8-24) months. De novo urgency urinary incontinence developed in two patients and stress incontinence in one patient. Based on the physical examination in the follow-ups, 14 patients (93.3%) had Grade 0 and one patient had (6.7%) asymptomatic Grade 2 anterior POP.
Conclusion: Minimally invasive sacrocolpopexy is an efficient and safe surgical option for prolapse repair in symptomatic advanced stage POP cases.

Keywords: pelvic organ prolapse, minimally invasive surgery, sacrocolpopexy, laparoscopy, robotic surgery

Öz

Amaç: Pelvik organ prolapsusu (POP) olan hastalarda minimal invaziv (laparoskopik ve robotik) sakrokolpopeksi operasyon sonuçlarımızı değerlendirmeyi amaçladık.
Gereçler ve Yöntemler: Eylül 2014- Eylül 2018 tarihleri arasında POP-Q sınıflamasına göre semptomatik evre 2 veya daha büyük, apikal POP nedeniyle laparoskopik veya robotik sakrokolpopeksi operasyonu uyguladığımız 15 hastanın demografik özellikleri, intraoperatif ve postoperatif verileri analiz edildi. Tedavi başarısı, nihai izlemde POP muayenesinde grade 0 veya 1 POP olarak tanımlandı.
Bulgular: Hastaların ortalama yaşları 60,4 ± 8,3 (49-82) idi. 4 hasta (%26,7) robotik, 11 hasta (%73,3) ise laparoskopik yöntemle opere edildi. Bir hasta hariç tüm hastalara uterus koruyucu cerrahi yapıldı. Ortalama operasyon süresi 183,3 ± 21,4 (145-220) dakika ve hastaların ortalama hastanede kalış süresi 2,8 ± 0,7 (2-4) gün idi. Toplamda 2 hastada (%13,3) intraoperatif ve postoperatif komplikasyon gelişti. Ortalama takip süresi 12,1 ± 4,8 (8-24) ay olarak hesaplandı. İki hastada de-novo urgency inkontinans, bir hastada ise stres inkontinans gelişti. Takiplerde fizik muayenede 14 hastada (%93,3) grade 0, bir hastada (%6,7) non-semptomatik grade 2 anterior POP mevcuttu.
Sonuç: Minimal invaziv sakrokolpopeksi semptomatik ileri evre POP olgularında prolapsus onarımı için etkin ve güvenli bir cerrahi seçenektir.

Anahtar kelimeler: pelvik organ prolapsusu, minimal invaziv cerrahi, sakrokolpopeksi, laparoskopi, robotik cerrahi

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Introduction

Pelvic organ prolapse (POP) affects nearly half of the female population [1]. Approximately 12.6% of women have a lifelong POP operation risk and this rate is considered to increase over years with aging, while importance was attached to quality life and the increasing awareness for pelvic base diseases [2]. Corrective restorative operations can be applied vaginally or abdominally in POP surgery. Higher rates of strength, and endurance of anatomic strcuctures are achieved using abdominal approach [3-5]. Thus abdominal sacrocolpopexy is regarded as the golden standard treatment method in the treatment of apical prolapse [6,7]. On the other hand, abdominal sacrocolpopexy is also associated with relatively longer operative times, delayed return to daily activities, higher morbidity, longer hospital stay and increased hospital costs compared to the vaginal approach [4].

Laparoscopic sacrocolpopexy was first defined by Nezhat et al in 1994 to overcome the present disadvantages of abdominal sacrocolpopexy [8]. With the developments in robotic surgery, robotic sacrocolpopexy was first applied by Di Marco et al in 2004 [9]. The studies showed that minimally invasive sacrocolpopexy had an equivalent efficiency compared to abdominal sacrocolpopexy [10-12]. Additionally, speeding up patient recovery and minimizing surgical morbidity have caused extensive use of minimally invasive sacrocolpopexy in recent years [13,14]. The objective of this study was to review our minimally invasive sacrocolpopexy experiences and present our results.

Materials and Methods

Fifteen patients who underwent minimally invasive sacrocolpopexy (laparoscopic sacrocolpopexy in 11 and robotic sacrocolpopexy in 4 patients) with symptomatic ≥ Grade 2 apical POP diagnosis based on POP-Q classification were retrospectively analyzed after obtaining local ethics committee approval (Dr. Sadi Konuk Training and Research Hospital Ethical Committee approval number: 2020/530) and also informed consent from all the patients for research.

Demographic data of all study patients such as age, parity, menopausal status, body mass index (BMI), previous pelvic operations (hysterectomy, pelvic base repair, etc.), comorbidities and ASA score were retrieved from medical records. Same preoperative protocol covering urogynecological history, physical examination, urinalysis, urination diary, stress test, measurement of postvoid residual urine volume was applied in all patients. Degree of prolapsus was evaluated using POP-Q quantification system in all patients [15]. Preoperative gynecological evaluation was performed in all patients who had conservative uterine-sparing surgery.

Perioperative period, estimated blood loss and duration of hospitalization were recorded. Low-molecular weight heparin and antithrombotic prophylaxis were given to risky patients. Antibiotic prophylaxis was applied in all patients. The difference between estimated blood loss and postoperative hemoglobin levels was calculated. Intraoperative and postoperative complications were recorded. The results were evaluated within postoperative 12 months. Surgical success was defined as POP-Q Grade 0 or 1 in the final follow-up examination.

Surgical Technique

Robotic Sacrocolpopexy: The patients were laid in dorsal lithotomy and 30° Trendelenburg position under general anesthesia. A 16 F Foley catheter was inserted. Pneumoperitoneum was created through umbilicus using a Veress needle and four robotic ports and one 12 mm assistant port were inserted through the same plane. Docking was performed using robotic system Da-Vinci-Xi (Intuitive Surgical Inc., Sunnyvale, CA, USA). Interchangeable 0° or 30° robotic optics were used. Vaginal retractor was used to push forward vaginal wall. Peritoneum was incised and dissected to reach first vesicouterine and then rectouterine space. Peritoneal incision was performed on sacral promontorium in aortal bifurcation and sacral dissection was performed up to the anterior longitudinal ligament and incision line was combined with vaginal stump posterior incision. Y shaped mesh prepared in advance was located in the abdomen. Starting from the most distal part, it was fastened using 2/0 vicryl in rectovaginal area starting from the most distal part towards proximal. The same procedure was performed also on the vesicovaginal dissection line. Peritoneal dissection was performed between the posterior region of uterus and vagina to form peritoneal tunneling at the lateral level of broad ligament of the uterus. Anterior and posterior meshes were sutured together at the anterior aspect of the uterus. T shaped mesh was used. One end of the mesh was stabilized on the promontorium using two no 0 prolene sutures after ensuring the suitable tension. The mesh covered with peritoneum, and was completely retroperitonized. One drain was inserted in the region.

Laparoscopic Sacrocolpopexy: 10 mm camera port was inserted through the umbilicus with the patient in robotic sacrocolpopexy position. 5 mm operation ports and one 5 mm suprapubic port were inserted in 4 cm lateral on both sides of this port. Surgical technique which was applied in robotic sacrocolpopexy was used. Laparoscopic tapper was used in some cases for mesh fixation.

Results

Mean age of the patients was 60.4 ± 8.3 years and mean BMI was 32.8 ± 2.5 kg/m2. Eight patients (53.3%) had previously undergone histerectomy. According to POP-Q, 10 patients (66.7%) had stage 2 and 5 patients (33.3%) had Grade 3 prolapse. None of the patients had a history of incontinence or urinary incontinence surgery. Occult stress urinary incontinence wasn't detected in any patient in the stress test performed through prolapse reduction. Demographic characteristics of the patients are summarized in **Table 1**.

Mean operative time was 183.3 ± 21.4 min (laparoscopic 190 min, and robotic 165 min). Mean estimated blood loss was 62 ± 30.6 mL. Mean hospital stay was 2.8 ± 0.7 days. Intraoperatively, serious intestinal injury occurred in a patient in laparoscopic sacrocolpopexy group which was repaired with laparoscopic suture and one patient had wound drainage and infection in postoperative early period which was treated using conservative methods. Mean follow-up period was 12.1 ± 4.8 months. Based on the POP-Q quantification in the physical examination during the follow-ups, 14 patients (93.3%)

Table 1. Preoperative and postoperative characteristics of the cases

	Age	Abdominal surgery history	POP-Q classification	Operative time (min)	Hospital stay (days)	Combined operation	Postoperative grade	Follow-up period (month)
1	57	Peptic ulcus perforation	Grade 2 cystocele	190	3	none	Grade 0	24
2	82	TAH	Grade 3 cystocele	205	4	Rectocele repair	Grade 0	21
3	57	None	Grade 2 cystocele	175	2	Hysterectomy	Grade 0	16
4	69	TAH, cholecystectomy	Grade 2 cystocele	210	4	None	Grade 0	14
5	68	TAH, cholecystectomy	Grade 2 cystocele	180	3	None	Grade 0	12
6	52	None	Grade 2 cystocele	170	3	None	Grade 0	11
7	59	TAH/BSO	Grade 3 cystocele	200	3	Rectocele repair	Grade 0	11
8	61	None	Grade 3 cystocele	185	2	Rectocele repair	Grade 2	10
9	62	TAH	Grade 2 cystocele	195	2	None	Grade 0	10
10	59	None	Grade 2 cystocele	220	3	none	Grade 0	10
11	61	TAH	Grade 3 cystocele	160	3	None	Grade 0	9
12	63	TAH	Grade 3 cystocele	150	3	None	Grade 0	9
13	57	TAH	Grade 3 cystocele	185	3	Rectocele repair	Grade 0	9
14	50	None	Grade 3 cystocele	180	2	None	Grade 0	8
15	49	None	Grade 2 cystocele	145	2	None	Grade 0	8

POP-Q: pelvic organ prolapse-quantification system; TAH: total abdominohysterectomy; BSO: bilateral salpingo-oophorectomy

had grade 0 and one patient had (6.7%) asymptomatic grade 2 POP. Postoperative de novo urgency urinary incontinence was detected in two patients in laparoscopic sacrocolpopexy group (13.3%) and stress urinary incontinence was detected in one patient in robotic sacrocolpopexy group (6.7%). Stress urinary incontinence was treated with midurethral sling surgery while urgency urinary incontinence was treated with lifestyle changes and pharmacotherapy. Intraoperative and postoperative data are summarized in **Table 2**.

Discussion

Abdominal and minimally invasive sacrocolpopexy were compared for many aspects in literature. Considering all data, it was observed that minimally invasive sacrocolpopexy had similar short term efficiency with abdominal sacrocolpopexy and with additional advantages of shorter hospital stays, and recovery period, llower postoperative pain, bleeding and transfusion rate [16-19]. Therefore minimally invasive sacrocolpopexy stand out and be preferred more often today due to all these favourable characteristics. We also prefer minimally invasive sacrocolpopexy in our clinic and minimally invasive sacrocolpopexy success rate was also high in our series in line with literature (93.3%).

Apart from the advantages provided by minimally invasive surgery, laparoscopic sacrocolpopexy provides better visualization of the surgical field, more effective access to operation area and more accurate dissection. On the other hand, laparoscopic sacrocolpopexy has a vertical learning curve and longer operative times in addition to the classical disadvantages of laparoscopy such as limited degree of freedom and two-dimensional imaging [20]. Laparoscopic surgery is also related to more static head and neck posture, requirement for higher concentration and more mental stress for the surgeons compared to open surgery [21,22]. In the study by Tarr et al., comparing the ergonomic effects of laparoscopic sacrocolpopexy and robotic sacrocolpopexy, robotic sacrocolpopexy was reported to be related to lower neck, shoulder and back discomfort score [23]. Robotic surgery that overcomes the disadvantages of laparoscopy provides three-dimensional image through increased magnification, eliminates tremor of surgeon's hands, enables delicate and intuitional movements and provides more ergonomic surgery by improving manual skills thanks to wristed instruments [24].

Despite all these advantages, robotic surgery significantly limits buying, maintenance and repeated consumable price use. It especially results in low case volume and increased costs

Table 2. Intraoperative and postoperative data

	Laparoscopic sacrocolpopexy (n=11)	Robotic sacrocolpopexy (n:4)	Total (n:15)
Operative Time (min)	190 ± 18.2	165 ± 20.4	183.3 ± 21.4
Estimated Blood loss (ml)	70 ± 31.6	40 ± 12.9	62 ± 30.6
Perioperative Complication	1*	0	6.7%
Hospital stay (days)	2.9 ± 0.7	2.5 ± 0.6	
Follow-up period (months)	13.5 ± 4.9	8.5 ± 0.6	12.1 ± 4.8
Early complication	1**	0	6.7%
Late complication	2***	1****	20%
Postoperative POP-Q grade	10 (Grade 0) 1 (Grade 2)	4 (Grade 0)	14 (Grade 0) 1 (Grade 2)
Failure Rate	9.1%	0	6.7%

*Intestine serious injury; ** Wound drainage and infection; *** De novo urgency incontinence; **** Stress urinary incontinence

per case [24]. Two prospective randomized studies comparing laparoscopic and robotic sacrocolpopexy determined that robotic sacrocolpopexy was related to significantly higher costs [13,14]. While Anger et al., [13] reported purchase and maintenance cost of the robot as the cause of the higher cost of the procedure, Paraiso et al. [14] reported that robotic sacrocolpopexy was related to higher cost even if the purchase and maintenance cost of the robot is excluded. Cost of the robot is again an important limitation in our country and oncological surgeries are applied more frequently using the robotic approach. Thus, robotic sacrocolpopexy hasn't become popular in our country.

Prospective studies comparing laparoscopic sacrocolpopexy and robotic sacrocolpopexy have show that the success rates are comparable [13,14,25]. In the meta-analysis of the results of robotic sacrocolpopexy, Hudson et al. reported that this procedure has a success rate of 98.6% (defined as apical prolapse Grade ≤ 1) [26]. In our series high success rates were also achieved in both groups (robotic approach, 100%, and laparoscopic approach, 90.9% through). While Paraiso et al. [14] reported that robotic sacrocolpopexy was related to statistically significantly longer operative times (199 vs 265 min, p< .001), any statistically significant difference was not detected between two groups in terms of operative times [13,25]. Interestingly, in our series operative time was longer in the laparoscopic group (190 ± 18.2 versus 165 ± 20.4 min) compared to the robotic group which can be explained by high robotic surgery volume of our clinic. Oncology surgeries are extensively performed in our clinic and most of them (especially radical prostatectomy) are robotic surgeries. On the other hand, our sacrocolpopexy experience is limited and as anticipated, thanks to our accumulated experience, we perform faster surgeries using the robotic approach. In addition, while Seror et al., [25] reported robotic sacrocolpopexy to be related to statistically significantly lower amounts of bleeding (55 vs 280 mL, p= .03), Anger et al. [13] didn't detect any significant difference among the two groups. In our series, the average blood loss was found comparable between both groups.

Although sacrocolpopexy is the most effective procedure in apical POP treatment, the complications related to this operation constitute a significant problem. Although defecating disorders and stress urinary incontinence are the most common complications, presacral hemorrhage is the most life-threatening intraoperative complication. Also, dissection should be performed carefully to avoid the injury of sigmoid, presacral veins and right urethra during the leftward retraction of sigmoid and operating on sacral area [27]. Prospective studies comparing robotic sacrocolpopexy with laparoscopic sacrocolpopexy reported similar complication rates for both groups [13,14,25]. A retrospective study by Nosti et al., showed that the general complication rates in laparoscopic sacrocolpopexy are higher than robotic sacrocolpopexy (4.0% vs 0.4%, p < .01) [28]. On the contrary, another study reported that the robotic sacrocolpopexy was related to a higher rate of bladder injury [29]. Any serious early-term complication was not detected in our series apart from intraoperative small bowel injury in one patient (9.1%) and postoperative port site infection (9.1%) in one patient.

The main limitations of this study were its retrospective nature, limited number of patients especially in robotic sacrocolpopexy group, and relatively shorter patient follow-up.

Conclusion

Minimally invasive sacrocolpopexy is an efficient and safe surgical option for prolapse repair in symptomatic advanced grade POP cases. Prospective randomized studies with larger patient series are required.

Ethics Committee Approval: The study was approved by University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital Ethical Committee, Bakirkoy, Istanbul, Turkey (Approval Number: 2020/530).
Informed Consent: An informed consent was obtained from all the patients for research.
Publication: The results of the study were not published in full or in part in form of abstracts.
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Urological Pathologies and Their Incidence Rates Determined in Cases Applied to the Health Board

Sağlık Kuruluna Başvuran Olgularda Tespit Edilen Ürolojik Patolojiler ve Sıklıkları

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Abstract

Objective: Applications are made to health boards for age assessment, gender determination, employment in some occupational groups and detection of disability. The aim of our study is to determine the defined urological pathologies and their incidence rates in the patients who applied to the health board of our hospital.
Materials and Methods: Our study included patients who applied to the urology outpatient clinic of the health board between January 2015 and December 2020 for the purpose of employment in some occupational groups, determination of age, gender, disabilities and obtaining a general health report. Patients were investigated in two different groups, according to their indications for their applications as detection of disabilities and other indications, and the diagnoses were classified under the subheadings of stone diseases, malignancies, neurourology-incontinence, andrology and benign prostatic hyperplasia (BPH).
Results: A total of 1453 cases were included in the study. Hundred and fifty-one (10.4%) patients applied for the detection of disability. A total of 206 (17%) patients, including 70 (46.3%) cases in the disability detection group and 136 (10.4%) in the other group had a urological diagnosis. The most common pathology was malignancies with 65 (4.4%) cases, in order of frequency; testicular cancer (n=25: 38.4%), bladder cancer (n=15: 23%), prostate cancer (n=13: 20%), kidney cancer (n=11: 16.9%) and penile cancer (n=1: 1,5%). The second most frequently seen diagnostic group was the stone disease group (n=55: 3.7%), and 17 (30.9%) of them required further investigation after diagnosis. Consequently ESWL (n=6: 10.9%), and surgical intervention (n=4: 7.3%) were planned for the indicated number of patients.
Conclusion: Urogenital system malignancies and urinary tract stones have been identified as the most common pathologies in patients who applied to the health board. The fact that some diseases, especially urolithiasis were followed by further examination and treatment, shows the contribution of the health board examinations to the treatment as well as the health status determination feature.

Keywords: health board, disability evaluation, urologic diseases, medical examination, health check

Öz

Amaç: Yaş ve cinsiyet tespiti, özür tespiti ve bazı meslek gruplarında işe alınma gibi durumlarda sağlık kurullarına başvurular yapılmaktadır. Çalışmamızın amacı hastanemizin sağlık kuruluna başvuran olgularda tanımlanmış ürolojik patolojileri ve sıklıklarını belirlemektir.
Gereçler ve Yöntemler: Çalışmamız Ocak 2015- Aralık 2020 tarihleri arasında, bazı meslek gruplarının işe alınma, yaş ve cinsiyet tayini, özür tespiti ve genel sağlık raporu alınması amacıyla sağlık kurulu üroloji polikliniğine başvuran hastaları içermektedir. Hastalar başvuru nedenlerine göre; özür tespiti için başvuranlar ve diğer nedenlerle başvuranlar olmak üzere iki ayrı grupta incelenmiş ve tanılar; taş hastalıkları, maligniteler, nöroüroloji-inkontinans, androloji ve bening prostat hiperplazisi (BPH) alt başlıklarında sınıflandırılmıştır.
Bulgular: Toplam 1453 olgu çalışmaya dahil edildi. Özür tespiti için başvuran olgu sayısı 151 (%10,4) idi. Özür tespiti grubunda 70 (%46,3), diğer grupta 136 (%10,4) olmak üzere toplam 206 (%17) hastada ürolojik bir tanı mevcuttu. En sık tespit edilen patoloji 65 (%4,4) olgu ile maligniteleri, sıklık sırasıyla; testis kanseri (n=25: %38,4), mesane kanseri (n=15: %23), prostat kanseri (n=13: %20), böbrek kanseri (n=11: %16,9 ve penil kanser (n=1: %1,5). İkinci en sık görülen tanı grubu 55 (%3,7) hasta ile taş hastalıklarıydı, 17 (%30,9)'sinde tanı konulması sonrası ileri inceleme gerekti, bunun sonucu olarak 6 (%10,9) hastaya ESWL, 4 (%7,3) hastaya cerrahi planlandı.
Sonuç: Ürogenital sistem maligniteleri ve üriner sistem taşları sağlık kuruluna başvuran hastalarda en sık rastlanan patolojiler olarak tespit edilmiştir. Ürolitiazis başta olmak üzere bazı hastalıkların ileri tetkik ve tedavi edilmiş olması, sağlık kurulunun sağlık durumu tespiti özelliğinin yanında tedaviye katkısını da göstermektedir.

Anahtar kelimeler: sağlık kurulu, özür tespiti, ürolojik hastalıklar, tıbbi muayene, sağlık kontrolü

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Introduction

In Turkey, a health board report is issued every day for many patients due to various health problems. In addition to requesting a general health report in cases such as determination of age, and gender, and for employment in some occupational groups, applications to health boards for the determination of disability constitute also an important place among these applications.

The term "disabled" in the legislation; is defined as "the person who has difficulties adapting to social life and meeting his/her daily requirements due to the loss of his/her physical, mental, spiritual, sensory and social abilities to various degrees due to any reason, and needs protection, care, rehabilitation, counseling and support services" [1]. Disability Health Board consists of specialists in internal medicine, ophthalmology, ear-nose-throat diseases, general surgery or orthopedics, neurology or mental health and diseases [2]. The fact that urology is outside of these standard branches is due to the relatively lesser number of applications made regarding urogenital system-related pathologies. However, the branch of urology is included in the evaluation process in the health board in cases of employment for a number of professional groups, age and gender determination and declaration or determination of a urological pathology.

Many studies have been performed in different specialties related to pathologies detected in patients who applied to the health board for detection of disability and for other indications [1,3,4]. However, there is no published article investigating the applications to the health board in the field of urology. The aim of our study is to determine the defined urological pathologies and their incidence rates in patients who applied to our hospital's medical board.

Materials and Methods

Our study included patients who applied to the urology outpatient clinic of Dr. Sadi Konuk Training and Research Hospital for a health board report between January 2015 and December 2020 for the purpose of employment in some occupational groups (police, security guards, military, etc.), and also for determining the age, gender, and disability status. The ethical approval of the study was obtained from the ethics committee of the same hospital (Dr. Sadi Konuk Training and Research Hospital Ethical Committee approval number: 2021/187). Patients of all age groups were included in the study and their medical files were retrospectively examined. Patients were examined in two different groups, according to the indications for their applications as detection of a disability and for other indications (employment, obtaining a general health report, and determination of age or gender, etc.).

The gender and age of the patients were examined, and their urological diagnoses were scanned mainly through the International Classification of Diseases-10 (ICD-10) codes. Also medical histories, physical examination, and if available, radiological and ultrasonographic findings of the applicants registered in the system were investigated. The diagnoses found were classified under the subheadings of urinary tract stone diseases, malignancies, neurourology-incontinence, andrology and benign prostatic hyperplasia (BPH).

Patients in the group of stone diseases were examined for the need for further examination and intervention. Malignancies were classified as prostate, bladder, renal, testicular and penile cancers. Less frequently encountered pathologies were presented under the heading of "others"; such as renal cysts, testicular and renal agenesis and hypoplasia, ureteropelvic junction (UPJ) obstruction, vesicoureteral reflux (VUR), and urethral stenosis. Urogenital system infections were not included in the study by us because they were not considered as adverse conditions and were recorded at a low rate.

Statistical analysis

Statistical analyses were performed using Microsoft Excel 2013 (Microsoft, Redmond, WA, USA). Continuous data were described as mean and range. Categorical data was described as percentages.

Results

A total of 1484 cases with a health board urology examination record were detected. A total of 1453 cases were included in the study considering the first application records of those who applied more than once. The mean age of the patients was 29.5 ± 7.7 years, male patients constituted the majority (n=1381: 95%), and only 72 (5%) female patients included in the study. A total of 151 (10.4%) cases with a mean age of 54.8 ± 9.3 years including 129 (85.5%) male, and 22 (14.5%) female patients applied for the detection of disability. Patients presenting for the determination of disability were older than the general population, as expected. The remaining patients were classified under the heading of "other".

A total of 206 (14,3%) patients had received a urological diagnosis, including 70 (4,9%) patients in the disability detection and 136 (9,4%) cases in the other group. A urological pathology was identified in almost half of the patients in the disability detection group. The urological pathologies detected as a result of the study and their distribution among the groups are shown in **Table 1**.

The most common pathology was urogenital system malignancies with 65 (4.5%) cases. At least one malignancy had been diagnosed in one-fourth (37/151) of the disabled group. In the other group of admissions, the frequency of malignancy fell to the second rank with 1,9 percent. **Table 2** shows the distribution of detected uro-oncological diagnoses. The most common diagnosis in this group was testicular cancer (n=25: 38.4%) including 8 (32%) cases in the disability detection group and 17 (68%) in the other group. The mean age of these patients was 32.3 ± 9.7 years, and the most common pathological subgroup was pure seminoma with a rate of 40 percent. Bladder cancer was the second most common pathology, with a total of 15 (23%) cases including 11 (73.3%) patients in the disability detection group and 4 (26.7%) patients in the other group. The mean age of these patients was 56.2 ± 11 years, and 6 (40%) cases were cystectomized. Prostate cancer was the third most frequently encountered diagnosis with 13 (20%) cases. The mean age of the patients was 57.9 ± 7.5 years. There were 10 (76.9%) patients in the disability detection group and 3 (23.1%) patients in the other group. Five (38.5%)

Table 1. Urological pathologies and their distribution between groups

	Applications for the detection of disability n=151 (10,4 %)	Applications for other indications n=1302 (89.6%)	All applications n=1453 (100%)
Uro-oncological conditions	37 (2.6)	28 (1.9)	65 (4.5)
Urinary system stone disease	4 (0.3)	51 (3.5)	55 (3.8)
Neurourology-incontinence	10 (0.7)	4 (0.3)	14 (1)
BPH	9 (0.6)	4 (0.3)	13 (0.9)
Andrology	0 (0)	10 (0.7)	10 (0.7)
Others	10 (0.7)	39 (2.7)	49 (3.4)
Total diagnosis	70 (4.9)	136 (9.4)	206 (14.3)

BPH: benign prostatic hyperplasia

Table 2. Distribution of urogenital system malignancies

Testicular Cancer	
Number of patients (n;%)	25 (38.4)
Disabled	8 (32)
Other	17 (68)
Age (mean ± SD)	32.3 ± 9.7
Pathological subtypes (n;%)	
Pure Seminoma	10 (40)
Non-seminomatous	2 (8)
Mixed germ cell	11 (44)
Others	2 (8)
Bladder Cancer	
Number of patients (n;%)	15 (23)
Disabled	11 (73.3)
Other	4 (26.7%)
Age (mean ± SD)	56.2 ± 11
Prostate Cancer	
Number of patients (n;%)	13 (20)
Disabled	10 (76.9)
Other	3 (23.1)
Age (mean ± SD)	57.9 ± 7.5
Renal Cancer	
Number of patients (n;%)	11 (16.9)
Disabled	9 (81.8)
Other	2 (18.2)
Age (mean ± SD)	53.5 ± 7.2
Gender (M/F)	8/3
Pathological subtype (n;%)	
Clear cell carcinoma	7 (63.6)
Papillary cell carcinoma	2 (18.2)
Chromophobe cell carcinoma	1 (9.1)
Urothelial carcinoma	1 (9.1)
Penile Cancer (n;%)	1 (1.5)
Total number of patients (n)	65

Table 3. Distribution of urinary system stone diseases

Disabled	4 (7.3)
Other	51 (92.7)
Age (mean ± SD)	28.5 ± 9.3
Gender (n;%)	
Male	6 (10.9)
Female	49 (89.1)
Patient undergoing further examination (n;%)	17 (30.9)
Conservative follow-up	7 (12.7)
ESWL	6 (10.9)
Surgical intervention	4 (7.3)
Number of patients (n;%)	55

HUN: hydrureteronephrosis; ESWL: extracorporeal shockwave lithotripsy

patients were in the metastatic stage of the disease. Kidney cancer was present in 11 (16.9%) patients including 9 (81.8%) patients in the disability determination group, and 2 (18.2%) cases in the other group. The most common renal pathology was clear cell carcinoma. The mean age of these patients was 53.5 ± 7.2 years, and three (27.2%) of them had metastatic disease at admission. One (1.5%) patient had a diagnosis of penile cancer.

The second most common diagnostic group was stone diseases with 55 (3.7%) patients and when the disability detection group was excluded from the assessments it ranked on top with an incidence rate of 3.9 percent. The mean age of the patients was 28.5 ± 9.3 years, and the majority of them were male patients (n= 49: 89.1%). In 17 (30.9%) of these patients, further examination was required after the diagnosis, and as a result, ESWL was planned for 6 (10.9%) and surgery for 4 (7.3%) patients. The group characteristics of the stone patients are given in **Table 3**.

The neurourology-incontinence diagnosis group ranked third in frequency with 14 (0.9%) cases. The mean age of these patients was 39.7 ± 12.6 years, and 10 (71.4%) patients were receiving treatment with the diagnosis of neurogenic bladder. Almost half of these patients (n=4: 40%) had a traumatic etiology. Thirteen (0.89%) cases with a mean age of 58.3 ± 7.6

years had a diagnosis of BPH. There were 10 (0.68%) patients in the andrology group, and all of these patients had a diagnosis of varicocele. The mean age of the patients was 27.2 ± 7.1 years, and none of them were in the disability detection group.

There were 49 (3.4%) patients in the other group, and the majority of them were (n=23: 46.9%) patients with solitary/single-functioning kidney including 9 (39.1%) patients with renal agenesis, and 7 (34.7%) with renal atrophy/hypoplasia. Seven (30.4%) patients had a solitary kidney due to previous nephrectomy. Patients who underwent nephrectomy with the diagnosis of renal cell carcinoma were included only in the group of 'malignancies'. The diagnoses determined in the patients applied with other indications are given in **Table 4**.

Table 4. Distribution of diagnoses in the other group

Solitary/Single-functioning kidney number of patients (n;%)	23 (46.9)
Disabled	7 (30.4)
Other	16 (60.6)
Etiologies	
Agenesis	9 (39.1)
Atrophy/Hypoplasia	7 (30.4)
Surgery*	7 (30.4)
UPJ obstruction	7 (14.2)
Renal angiomyolipoma	4 (8.2)
Renal cyst	4 (8.2)
Urethral stenosis	3 (6.1)
Horseshoe kidney	3 (6.1)
Ectopic kidney	2 (4.1)
VUR	2 (4.1)
Testicular agenesis	1 (2)
Prostatic cyst	1 (2)
Bladder diverticulum	1 (2)
Solitary testis**	1 (2)
Total number of patients (n;%)	49

UPJ: ureteropelvic junction VUR: vesicoureteral reflux; * nephrectomies performed with benign indications; ** orchiectomized due to orchitis

Discussion

When we grouped the diagnoses seen in the patients who applied to the health board according to the subspecialty areas of urology, the most common disease group was determined as genitourinary system cancers. A total of 65 uro-oncological pathologies were detected in 63 different cases. In order to determine the prevalence of serious cancer types at a national level in our country, cancer records are collected by the Cancer Control Department of the Ministry of Health, and evaluations are made on the data obtained by considering gender and demographic data of the patients. The data have shown that the incidence of cancer is increasing every year [5]. According to the report of Turkey Cancer Statistics, prostate cancer is the most common cancer (13%) in men in all age groups in Turkey after lung and respiratory tract cancers. While bladder cancer takes the fourth (8,1%), and kidney tumors the sixth place (2,9%). Testicular cancer is not in the top ten in all age groups. In women, on the other hand, none of the urological cancers are found in the top ten [6].

In our study, testicular cancer patients constituted the majority (39.1%) of the cancer patients who applied to the health board. Although its frequency is low among urological cancers, testicular cancer was the most common urogenital cancer detected in our study which seems to be due to our relatively young patient population. In addition, the conditions that increase the reasons for admission, such as compulsory military service examination of the patients orchiectomized due to testicular tumor seem to increase the number of cases with testicular cancer applying to the disability health board. Testicular cancers account for 1% of all adult malignancies and 5% of urological tumors [7]. The most common cancer in men in the 15-24 age group in Turkey is testicular cancer with a rate of 24.3 percent [6]. The peak incidence is seen in the third decade of life for non-seminomatous and mixed germ cell tumors, and in the fourth decade for pure seminoma [7]. As a result of the sensitivity of testicular cancer to chemotherapy, development of cisplatin-based treatment modalities, multidisciplinary approaches, close patient follow-ups, and increased salvage treatment options, long-term survival rates are between 80-90%, even in metastatic disease [8].

The second most common oncological diagnosis in our patient group was bladder cancer. Bladder cancer is the seventh most frequently diagnosed cancer in the male population worldwide and the tenth most common cancer for both sexes. It is approximately four times more common in men than in women [9]. At the time of diagnosis, in one-third of the patients, the disease is limited to the mucosa (Ta, carcinoma in situ) or submucosa (T1) [10]. These patients have much better survival rates than patients with T2-T4 tumors [9]. T stages of the patients were not examined in our study, but it was found that 40% of them were cystectomized. Since it is a surgical procedure that causes organ loss and some degree of disability, this rate is expected to be high. The reason why bladder cancer was found in the second frequency in our study was the applications made for the detection of disability due to this morbid surgical procedure.

Prostate cancer is the second most common cancer in men in Turkey and in the world. It is the most common urogenital cancer [6,11]. In 2012 alone, 1.1 million people were diagnosed with prostate cancer worldwide, which corresponds to 15% of all diagnosed cancers for that year [11]. In Western societies, it is relatively more common, and its frequency is increasing with the widespread use of prostate-specific antigen (PSA) screenings [11]. In an epidemiological study conducted by Zorlu et al., in 2014 covering 12 cities, the incidence of prostate cancer in Turkey was found to be 35/100,000, with the highest rate in Istanbul with 43.7/100,000 and the lowest in Edirne with 17.7/100,000 [12]. It can be thought that prostate cancer was seen less frequently in our study compared to its incidence in the literature, besides its definitive treatment was relatively less morbid with lower incidence of metastatic diseases resulting in decreased need for health board applications. The reason why a

significant portion of the patients (38.7%) who applied had the metastatic disease can be explained by the fact that most of the patients (76.9%) applied for the detection of disability.

Kidney tumors are usually asymptomatic, and their incidence has increased in recent years due to incidental diagnosis with radiological examinations [13]. Renal cell carcinoma represents about 3% of all cancers, with the highest incidence in Western countries. The highest incidence rates in Europe and worldwide are detected in the Czech Republic and Lithuania [14]. It is the most common solid lesion of the kidney and represents 90% of all renal malignancies. As for renal malignancies, men have a 1.5:1 dominance compared to women, and a higher incidence is noted in the elderly population [15]. In our study, a total of 11 cases including 8 (72.7%) male patients had renal tumors, and all but one had renal cell carcinoma. This rate was consistent with the literature.

Urinary system stones were the second most common urological disease group in patients applied to the health board. Although urolithiasis is more frequently seen in some regions, it is a common public health problem all over the world [16]. Its incidence ranges from 1% to 20% depending on the genetic, environmental factors, and dietary habits [17].

In epidemiological studies conducted in our country, prevalence rates of urinary system stones were found to range between 11.1% and 14.8%, and they were seen 1.5 times more frequently in males than in females [18,19]. The lowest, and the highest prevalence rates were observed in The Black Sea (9.5%), and Aegean Regions (12.6%), respectively. In the Marmara Region, its prevalence was found to be 11.4 percent [19]. In our study, the prevalence of stone disease was found to be 3.8%, and almost all these patients were male (89.1%). The reason for the lower incidence of stone disease compared to the literature is that our patient population was mostly asymptomatic, and they applied to the hospital usually for other indications. This fact may explain the low rate of definitive treatment applications (10.9%). In addition, the stone disease was most commonly seen (3.9%) in patients not evaluated in the disability detection group.

It should be noted that one-tenth of these patients who applied for completely different reasons were directed to further treatment with the diagnosis of incidental urinary system stone disease, and surgery was planned for 7.3% of the whole group. This shows us that the health board can also work with a focus on treatment.

The third disease group comprised patients with neurological causes of incontinence, and the majority (71.4%) of this group consisted of patients with a diagnosis of neurogenic bladder. Neurogenic bladder is a lower urinary system disorder secondary to nervous system damage or diseases. Multiple sclerosis, Parkinson's disease, spina bfida, and diabetic neuropathy, and spinal cord injury play a role in its etiopathogenesis [20]. In a study conducted with people with locomotor system disabilities in our country, one of the most common additional pathologies was found to be neurogenic bladder [21]. In our study, the most important etiologic factor was determined as trauma such as falling from a height or traffic accident. Approximately 12,000 new cases are recorded each year in the United States (US) [22]. Some degree of impairment of bladder function has been reported within one year after a traumatic incident in approximately 81% of these patients [23].

BPH is the most important cause of lower urinary tract symptoms (LUTS) in men. It is the most common benign neoplasia in aging men, with a frequency of 8% in the fourth and 90% in the ninth decade of life [24]. In our country, although there is no direct study to determine the prevalence of BPH, in the study of Uluocak et al., its prevalence rates varied between 4.1% and 34.9% according to different diagnostic criteria of benign prostatic obstruction [25]. In the study of Akı et al., only 14.8% of the cases in all age groups had not LUTS [26]. Although BPH and LUTS do not exactly overlap, they almost always coexist, and it has been reported in previous publications that it may provide insight into the prevalence of BPH [27]. In our study, the prevalence of BPH was 0.89% in the general group, while it was 5.9% in the disability detection group consisting of older patients. These numbers fall far behind the literature data. The biggest reason for this is that BPH is not seen as a disability and is not a remarkable diagnosis in terms of the health board criteria, so it is not recorded and/or questioned.

Another urological diagnosis observed in our study was varicocele (0.68%). Varicocele is the most important, and known cause of male infertility. It is seen in 15-20% of the otherwise healthy male population, and in 25% of men with defective spermatogenesis. This rate rises to 35-40% in men under investigation for infertility [28]. In our study, the diagnosis of varicocele was seen at a low rate not comparable with the literature data. Because the diagnosis of varicocele, just like BPH, is not an important issue in the decision-making in patients applied to the health board.

Half of the patients (46.9%) we examined under the heading of the other group consisted of patients with solitary/single-functioning kidneys, and the percentage of patients nephrectomized due to kidney tumors was not included in this estimation. The causes of the solitary kidney are usually unilateral renal agenesis, congenital hypoplasia/dysgenesis and surgeries. The prevalence of renal agenesis is 3.3 per 10,000 live births [29]. In our patient group, renal agenesis seems to be the most important cause of solitary kidney with 39.1 percent. However, when patients nephrectomized due to kidney tumors were added to this group, surgery seemed to be the most important etiologic factor.

The most important limitation of our study is that due to the diagnostic selectivity of the health board, some diagnoses were identified less than they actually are. For example, urological pathologies such as varicocele, BPH or kidney cyst, which are frequently seen in the community, are not important in the assessments of the health board, do not constitute a disability or defect, therefore they are not questioned and recorded.

Conclusion

Urogenital system malignancies and urinary system stones have been identified as the most common pathologies in patients applied to the health board. Although our patient population does not directly reflect the condition in Turkey in general, it may be a benchmark for larger-scale studies.

In addition, the fact that some diseases, especially urolithiasis which were diagnosed incidentally in the examinations made

for the determination of health status, with further examination and treatment shows the contribution of the health board examinations to the treatment as well as determination of the health status.

Ethics Committee Approval: The study was approved by University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital Ethical Committee, Bakirkoy, Istanbul, Turkey (Approval No: 2021/187).
Informed Consent: An informed consent was obtained from all the patients for research.
Publication: The results of the study were not published in full or in part in form of abstracts.
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Original Article – Urolithiasis

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The Impact of Ureterenoscopic Stone Removal Timing on Kidney Functions: A Retrospective Analysis of 137 patients in a Single Center

Üreterenoskopik Taş Cerrahisi Zamanlamasının Böbrek Fonksiyonlarına Etkisi: Tek Merkezde 137 Hastanın Retrospektif Analizi

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Abstract

Objective: To investigate the effect of ureterorenoscopic stone removal timing on kidney function in unilateral ureteral stones.
Materials and Methods: Hundred and eighty-seven patients included in the study were divided into two groups: 98 patients who underwent surgery ≤14 days after the stone diagnosis constituted the Early Surgery Group and 39 patients who were operated >14 days after the stone diagnosis comprised the Late Surgery Group. Preoperative serum levels of creatinine, blood urea nitrogen (BUN), and glomerular filtration rates (GFR) were recorded for the patients in both groups. In the postoperative first month, serum creatinine, BUN, and GFR were again recorded and compared with the preoperative values.
Results: The mean preoperative serum creatinine, GFR, and BUN levels in the Early Surgery Group were 1.25 ± 0.65µmol/L, 80.04 ± 33.6ml/min/1.73m2, and 50 ± 16.6mmol/L, respectively. A decrease was observed in serum creatinine (0.82 ± 0.22µmol/L, p< 0.001) and BUN (14.08 ± 7.25mmol/L, p< 0.001) levels one month after surgery, whereas GFR increased (105.33 ± 21.6ml/min/1.73m2, p< 0.001). In the Late Surgery Group, postoperative levels of serum creatinine (0.94 ± 0.33 vs. 0.95 ± 0.30µmol/L, p= 0.102), and BUN (17.38 ± 9 vs. 17.92 ± 8.8mmol/L, p= 0.283), increased minimally, also a minimal decrease was observed in GFR (95.15 ± 27.3 vs. 93.77 ± 24.3ml/min/1.73m2, p= 0.338) without any statistically significant difference.
Conclusion: We believe that surgical treatment should be planned within two weeks at the latest, as prolonged obstruction may result in kidney damage.

Keywords: ureterorenoscopic stone removal, ureteroscopy, ureter stone, kidney function, medical expulsive therapy

Öz

Amaç: Üreterorenoskopik taş çıkarma cerrahisi zamanlamasının böbrek fonksiyonları üzerine etkisinin incelenmesi.
Gereçler ve Yöntemler: Çalışmaya dahil edilen 137 hasta iki gruba ayrıldı. 98 hastaya taş tanısından sonra 14 gün veya daha kısa sürede cerrahi uygulanırken (Erken Cerrahi Grubu), 39 hastaya (Geç Cerrahi Grubu) ise taş tanısını takiben 14 günden daha uzun sürede cerrahi uygulanmıştı. Preoperatif serum kreatinin, kan üre nitrojeni (BUN), tahmini glomerüler filtrasyon hızı (GFR) her hasta için kayıt edildi. Postoperatif birinci ayda serum kreatinin, BUN ve GFR değerleri, ilk ölçümlerle karşılaştırıldı.
Bulgular: Erken cerrahi grubunda ortalama serum kreatinin, GFR ve BUN seviyeleri sırasıyla 1,25 ± 0,65µmol/L, 80,04 ± 33,6ml/dk/1.73m2, 50 ± 16,6mmol/L idi. Operasyon sonrası birinci aydaki serum kreatinin (0,82 ± 0,22µmol/L, p< 0,001) ve BUN (14,08 ± 7,25mmol/L, p< 0,001) seviyelerinde düşüş izlenirken, GFR'de (105,33 ± 21,6ml/min/1.73m2, p< 0,001) artış tespit edildi. Geç cerrahi grubunda serum kreatinin (0.94 ± 0,33'e karşı 0,95 ± 0,30µmol/L, p = 0,102) ve BUN (17,38 ± 9'e karşı 17,92 ± 8,8mmol/L, p= 0,283) seviyesinde minimal artış ve GFR ölçümlerinde (95,15 ± 27,3'e karşı 93,77 ± 24,3ml/dk/1,73m2, p= 0,338) minimal ve istatistiksel açıdan anlamlı olmayan azalma izlenmiştir..
Sonuç: Üreter taşlarında cerrahi tedavinin en geç iki hafta içinde planlanması gerektiğini düşünüyoruz. Cerrahi tedavinin geciktirilmesi böbreklerin hasarlanmasına neden olabilir.

Anahtar kelimeler: üreterorenoskopik taş çıkarma, üreteroskopi, üreter taşı, böbrek fonksiyonu, medikal ekspulsif terapi

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Introduction

Worldwide, the prevalence of urinary system stone disease has been reported to vary between 1% and 20% [1]. Urinary system stones are treated according to their size, their anatomical location, and the complications they cause. Treatment options for ureteral stones include observation, medical expulsive therapy (MET), extracorporeal shock wave lithotripsy (ESWL), percutaneous antegrade ureteroscopy, retrograde ureteroscopy, and open or laparoscopic ureterolithotomy [2]. The treatment alternative chosen will depend on the location and size of the stone, the available technology, the treatment costs, the surgeon's experience and the patient's preference [3].

A meta-analysis has revealed that 68% of stones smaller than 5mm can pass spontaneously. This rate decreases to 47% for stones 5–10 mm in size [4]. The location of the stone is also an important factor in the possibility of spontaneous passage; 48% of proximal ureteral stones, 60% of middle ureteral stones, and 75% of distal ureteral stones may pass spontaneously [5]. For small ureteral stones, when there is no sign of infection and when the symptoms can be controlled, waiting for the stone to pass spontaneously is a good option. This approach also protects the patient from invasive surgical procedures and unnecessary costs. MET is an effective treatment approach for this patient group [6]. The MET method should not be used for stones larger than 10 mm [7].

It is still unclear exactly how long the waiting period will be between observation or MET and spontaneous stone passage. According to various studies, this period usually ranges from two to six weeks [8,9]. In patients with complete renal obstruction, urinary diversions may save kidney functions within a week, but, even if the obstruction is resolved, kidney functions may not recover for longer periods [10].

In this study, we aimed to evaluate the effects of ureteorenoscopic stone removal on kidney function in unilateral ureteral stones.

Materials and Methods

Patient Selection

Local ethics committee approval was obtained prior to study (approval number: 2021/385). This retrospective study analyzed data from 259 patients, who underwent URS for unilateral ureteral stones at Kayseri City Hospital between June 2017 and December 2020. Patients were excluded from the study if their serum creatinine values, and glomerular filtration rate (GFR) were unknown during the postoperative period, if computed tomography had not been used to diagnose their unilateral ureteral stones, if their GFR measures were ≤ 60, or if their stone sizes were > 10mm. The patients for whom the location and size of the stone could not be determined on preoperative radiological imaging (n:44), patients with stones larger than 10 mm (n:30), cases with GFR below 60 ml/min/1.73 m2 (n:27) and 21 patients with missing data were excluded from the study. In total, 137 patients were included in the study.

Study Design

The sampled patients were divided into two groups: those who underwent surgical intervention at ≤14 days (Early Surgery Group) and at >14 days after stone diagnosis (Late Surgery Group). Although there are studies stating the duration of observation and MET treatments between two and six weeks [8,9], we determined 14 days as the cut- off value in our study. Preoperative levels of serum creatinine, blood urea nitrogen (BUN), and glomerular filtration rate (GFR), location of stones in the ureters, the degree of hydronephrosis, age, gender of the patients, and time of diagnosis were recorded. The GFR was calculated for each patient based on the modification of Diet in Renal Diseases Study Formula (GFR=186 * [serum creatinin] -1.154 X [age] – 0.203 [if female] * 0.742 [if African American] * 1.212). The severity of hydronephrosis was graded according to the anteroposterior diameter of the renal pelvis as follows: Grade 1 (5-10 mm), Grade 2 (10-15 mm), Grade 3 (15-20 mm), and Grade 4 (>20 mm). In the postoperative first month, serum creatinine, BUN, and GFR were again recorded and compared with the preoperative values.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 25.0 (IBM SPSS, Armonk, NY, USA). Normal distribution of the continuous variables was analyzed using the Shapiro–Wilk test and histograms. Continuous variables with normal distribution were expressed as mean ± standard deviation (SD). In independent groups, the continuous variables with normal distribution were compared using Student's t test. Identification rates were also compared using Pearson's chi-squared test. A p-value of <0.05 was considered significant.

Results

In total, 137 (98 in the Early Surgery Group and 39 in the Late Surgery Group) patients were sampled. The mean age of the 96 patients in the Early Surgery Group was 43.62 ± 13.9 years including 38 (39.6%) female, and 58 (60.4%) male patients. The mean age of the 39 patients in the Late Surgery Group was 46.46 ± 13.7 years; including 12 (30.8%) female, and 27 (69.2%) male patients. In the Early, and Late Surgery Groups mean time intervals between the stone diagnosis and surgery were 5.4 ± 3.11, and 27.79 ± 15.35 days, respectively (p< 0.000). **Table 1** presents the participants' demographic and clinical data. A decrease was observed in serum creatinine (0.82 ± 0.22µmol/L, p< 0.001) and BUN (14.08 ± 7.25mmol/L, p< 0.001) levels one month after surgery and the GFR increased (105.33 ± 21.6ml/min/1.73m2, p< 0.001) in the Early Surgery Group. **Table 2** presents the pre- and postoperative parameters for the Early Surgery Group. In the Late Surgery Group, postoperative serum creatinine levels increased minimally (0.94 ± 0.33 vs. 0.95 ± 0.30µmol/L, p= 0.102), but GFR decreased (95.15 ± 27.3 vs. 93.77 ± 24.3ml/min/1.73m2, p= 0.338). Although there was an increase in BUN (17.38 ± 9 vs. 17.92 ± 8.8mmol/L, p= 0.283) values, the intergroup different was not statistically significant. **Table 3** depicts the pre- and post-operative parameters for the Late Surgery Group.

Table 1. Demographic and clinical characteristics of the patients

		Early Surgery Group		Late Surgery Group		
		Mean	**n (%)**	**Mean**	**n (%)**	**P-value**
Age (years)		43.62 (±13.9)		46.46 (±13.7)		0.285
Gender	Female		38 (39.6)		12 (30.8)	0.336
	Male		58 (60.4)		27 (69.2)	
Hydronephrosis	Grade 1-2		54 (56.3)		23 (59.0)	0.599
	Grade 3-4		42 (43.8)		16 (41.0)	
Localization of ureteral stones	Proximal		20 (20.8)		8 (20.5)	0.917
	Middle		28 (29.2)		11 (28.2)	
	Distal		48 (50.0)		20 (51.3)	
Preoperative serum creatinine (µmol/L)		1.25 (±0.65)		0.94 (±0.33)		**0.006**
Preoperative glomeruler filtration rate (ml/min/1.73m^2)		80.04 (±33.6)		95.15 (±27.3)		**0.014**
Preoperative blood urea nitrogen (mmol/L)		19.50 (± 16.6)		17.38 (±9.1)		0.455
Time to surgery (days)		5.45 (± 3.11)		27.79 (±15.35)		**0.000**

Table 2. Pre- and postoperative serum levels and glomerular filtration rates of the patients in the Early Surgery Group

	Preoperative	**Postoperative**	**P-value**
Serum creatinine (µmol/L)	1.25 (± 0.65)	0.82 (± 0.22)	**<0.001**
Glomeruler filtration rate (ml/min/1.73m2)	80.04 (± 33.6)	105.33 (± 21.6)	**<0.001**
Blood urea nitrogen (mmol/L)	19.50 (± 16.6)	14.08 (± 7.25)	**<0.001**

Table 3. Pre- and postoperative serum creatinine levels and glomerular filtration rates of the patients in the Late Surgery Group

	Preoperative	**Postoperative**	**P-value**
Serum creatinine (µmol/L)	0.94 (± 0.33)	0.95 (± 0.30)	0.102
Glomeruler filtration rate (ml/min/1.73m^2)	95.15 (± 27.3)	93.77 (± 24.3)	0.338
Blood urea nitrogen (mmol/L)	17.38 (± 9.0)	17.92 (± 8.8)	0.283

Discussion

Urinary stone disease is an important public health problem in both adults and children. Recurrence is seen in one out of every three patients with urinary stone [11]. Urinary system stones may cause damage to the nephrons. Recurrent stones may lead to the development of a non-functioning kidney as an end-stage complication [12]. As a subgroup of urinary systems stones, ureteral stones can ensue in renal damage by causing ureteral obstruction [13]. Application of diversion in the first week after complete ureteral obstruction provides almost complete recovery of renal functions. While partial improvement was observed in renal functions in the diversions performed until the 12th week, the renal functions did not recover after urinary diversions performed after the 12th week [10]. In a study conducted in rabbits, blood perfusion had decreased in the first period in the obstructed kidney, there was a sharp rebound after a few days and then decreased again. The average rebound time in blood flow was 7.2 days [14]. Normally, it is accepted that a single morphologically and physiologically normal kidney is sufficient to perform all renal functions [15]. Therefore, unilateral ureteral obstructions do not usually cause renal dysfunction in healthy individuals. However, many patients may have abnormal renal function test results with normal contralateral kidney due to unilateral obstruction [16]. Similarly, although the contralateral kidneys of the patients were morphologically normal in our study, improvement in renal function tests was observed in patients in the Early Surgery Group.

Patients with unilateral obstruction and normal functioning contralateral kidneys demonstrate more frequently urinary dysfunction than patients with a single kidney [17]. In a prospective observational study on 152 patients; acute renal damage has been reported in 37 (29%) of 126 patients with unilateral ureteral stones. Renal recovery has been reported in

72% -100% of the cases after ureteral stone surgery. It has been shown that early intervention is associated with higher recovery rates [18]. Likewise, improvement in renal functions was observed in our Early Surgery Group, whereas renal recovery was not observed in the Late Surgery Group.

Although noninvasive treatments such as observation and medical expulsive therapy (MET) are being used in the treatment of ureteral stones, there is no consensus on duration of these treatments, and selection of eligible patients. In the studies in the literature, MET was generally performed between 2 and 6 weeks prior to surgery. MET has been accepted to have unsuccessful outcomes for varying periods of time depending on the center administering the treatment [9]. Lack of a consensus on appropriate timing for uterorenoscopy or urinary diversion has led to different approaches. In our study, a serious improvement was observed in kidney functions in the group of patients who were selected for early surgical treatment, while any change in renal functions was not detected in the Late Surgery Group. Delaying surgical management of an ureteral stone for MET or any other reason may result in renal damage. This important issue should be taken into consideration when treating patients using alternatives other than urinary diversion.

The weaknesses of our study can be listed as its retrospective design, insufficient number of patients, and the inability to standardize the groups in terms of their renal functions. Although prospective randomized studies on this issue are required, delaying surgical treatment may cause ethical problems. Application of different treatment approaches to standard groups under the same conditions is not accepted by the local ethics committee. For this reason, our study was designed retrospectively. Although the groups in our study were similar in terms of age, gender, stone location, degree of hydronephrosis, blood urea level, a significant intergroup difference was found between them in terms of preoperative serum creatinine levels and glomerular filtration rates. It was thought that as the renal dysfunction worsened, clinicians might have drifted away from observation and medical treatment which explains why the groups could not be standardized in this respect. There are not enough studies in the literature regarding the timing of surgery in ureteral stones. Therefore, multicenter studies in larger patient groups are required.

Conclusion

Treatment methods such as observation and MET applied to patients in order to reduce the morbidity caused by surgery do not eliminate obstruction. In addition, there is no consensus yet on how long these treatments will be applied. We believe that surgical treatment should be planned within two weeks at the latest, as prolonged obstruction may result in kidney damage.

Ethics Committee Approval: The study was approved by the Ethics Committee of Kayseri City Education and Research Hospital (Approval Date, and Registration Number: 04.29. 2021/385).
Informed Consent: An informed consent was obtained from all the patients.
Publication: The results of the study were not published in full or in part in form of abstracts.
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Complication Rates and Postoperative Renal Function in Partial Nephrectomy- Which Factors Should be Considered?

Parsiyel Nefrektomide Komplikasyon Oranları ve Ameliyat Sonrası Böbrek Fonksiyonu- Hangi Faktörler Dikkate Alınmalıdır?

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Abstract

Objective: To specify the prognostic factors predicting complication rates and postoperative renal function in patients operated with partial nephrectomy.
Materials and Methods: Our health center's archive system was scanned retrospectively for the time interval between January 2006- January 2021 for patients operated with partial nephrectomy for renal mass. History, comorbidities and laboratory results, operational information, tumor morphologies in radiographic images and its specified scores (R.E.N.A.L. score, PADUA score, C-index), peroperative and postoperative complications and pathology results of 148 regularly followed-up patients were analyzed.
Results: Mean age of the patients was 55.04±10.91 years, ratio of male to female was 1.27 and mean tumor size was 3.56 cm. Mean follow-up period was 55.53±42.26 months. Postoperative creatinine value in the 6th month showed an increase of 0.18 mg/dl compared to preoperative value. Estimated glomerular filtration rate (eGFR) also decreased by an average of 18.3%. Operation of grade 4 tumors significantly affected the postoperative renal function. PADUA score (p=0.023) had a significant effect on postoperative GFRs and duration of ischemia. Also, difference in pre-and postoperative GFRs and its percentage change were significantly affected by C-index (p=0.035, p=0.042). Pathological size (p=0.038), R.E.N.A.L. score (p=0.001), PADUA score (p<0.001), duration of ischemia (p=0.045) had a positively and C-index (p=0.001) had a negatively significant correlation with Modified Clavien-Dindo Complication Scoring System.
Conclusion: All nephrometry scores, duration of ischemia and tumor size were associated with the complication rates according to Clavien classification. Tumor grade, PADUA score and C-index are valuable parameters for predicting renal dysfunction after partial nephrectomy.

Keywords: nephrometry score, R.E.N.A.L. score, PADUA score, C-index, nephrectomy, renal function

Öz

Amaç: Parsiyel nefrektomi yapılan hastalarda komplikasyon oranlarını ve postoperatif böbrek fonksiyonunu öngören prognostik faktörleri belirlemek.
Gereçler ve Yöntemler: Ocak 2006-Ocak 2021 tarihleri arasında renal kitle nedeniyle parsiyel nefrektomi yapılan hastaların verileri hastane arşiv sisteminden retrospektif olarak tarandı. Düzenli takip edilen 148 hastanın öyküsü, komorbiditeleri ve laboratuvar sonuçları, operasyon bilgileri, radyografik görüntülerdeki tümör morfolojileri ve belirtilen skorları (R.E.N.A.L. skor, PADUA skoru, C-indeks), peroperatif ve postoperatif komplikasyonlar ve patoloji sonuçları analiz edildi.
Bulgular: Hastaların ortalama yaşı 55,04±10,91 yıl, erkek/kadın oranı 1,27 ve ortalama tümör boyutu 3,56 cm idi. Ortalama takip süresi 55,53±42,26 aydı. Ameliyat sonrası kreatinin değeri 6. ayda ameliyat öncesi değere göre 0,18 mg/dl artış gösterdi. Tahmini glomerüler filtrasyon hızı (eGFR) da ortalama %18,3 oranında azaldı. Grade 4 tümörlerin operasyonu, postoperatif böbrek fonksiyonunu önemli ölçüde etkiledi. PADUA skoru (p=0,023) postoperatif GFR'ler ve iskemi süreleri üzerinde anlamlı bir etkiye sahipti. Ayrıca ameliyat öncesi ve sonrası GFR farkları ve yüzde değişimi C-indeksinden anlamlı olarak etkilenmiştir (p=0.035, p=0.042). Modifiye Clavien-Dindo Komplikasyon Skorlama Sistemi ile patolojik boyut (p=0,038), R.E.N.A.L. skor (p=0,001), PADUA skoru (p<0,001), iskemi süresi (p=0,045) pozitif ve C-indeks ile (p=0,001) negatif anlamlı ilişkiye sahipti.
Sonuç: Clavien sınıflamasına göre komplikasyon oranları, tüm nefrometri skorları, iskemi süresi ve tümör boyutu ile ilişkilidir. Parsiyel nefrektomi sonrası böbrek fonksiyon bozukluğunu öngörmede ise, tümör derecesi, PADUA skoru ve C-indeks değerli parametrelerdir.

Anahtar kelimeler: nefrometri skoru, R.E.N.A.L skor, PADUA skoru, C-indeks, nefrektomi, böbrek fonksiyonu

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Introduction

In recent years, majority of renal masses are incidentally diagnosed with the increase of advanced imaging techniques [1]. Having similar outcomes as radical nephrectomy (RN), partial nephrectomy (PN) has been the gold standard for <4 cm renal masses [2]. As expected, the most important outcomes of PN are reduced risk of chronic kidney disease (CKD), cardiovascular disease and increased overall survival [3]. Limited indications for PN have been extended in time with observing the perioperative and oncological results and long-term overall and disease-free survival rates both in T1a (<4cm) and T1b (4-7cm) tumors [4].

Renal functions may be affected at various levels in patients undergoing PN due to morphological features of the tumor and operational techniques [5,6]. Nephrometry scores (R.E.N.A.L. score, PADUA score and C-index) announced by various centers are frequently used as predictors of outcomes after PN. Lately, studies about this subject are drawing attention and in the current study, our aim is to evaluate and sum up the factors affecting complications and renal function loss during and after PN.

Materials and Methods

Hundred and forty-eight patients that underwent open/laparoscopic PN between January 2006- January 2021 in our high load, experienced urology clinic of a tertiary training and research hospital were evaluated in this study, and patients with missing data were excluded. The study was approved by the Ethics Committee of University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital (Approval number: 07.07.2020/2888). A written informed consent form has been acquired from all patients included in the study indicating that their data may be used for scientific purposes. The study was performed in accordance with ethical principles of the Declaration of Helsinki and its later amendments.

Demographics, habits, comorbidities, clinical and laboratory results, tumor morphology in radiologic images (computerized tomography or magnetic-resonance imaging), surgical information (type of operation, duration of ischemia, and amount of bleeding), tumor pathology and follow-up data were recorded. Creatinine values of patients were evaluated preoperatively and postoperatively at the 6th month. Estimated glomerular filtration rate (eGFR) values were calculated with the Cockcroft-Gault formula. Peri-/post-operative complications were evaluated via the Modified Clavien-Dindo Complication Scoring System [7].

Patients without any symptoms were noted as incidental cases. Hematuria and flank pain were the mostly encountered localized symptoms. Most common systemic symptoms were fever, weight-loss and fatigue. All patients were evaluated with contrast-enhanced abdominal computerized tomography (CT) or magnetic resonance imaging (MRI) prior to surgery. Thorax CT was used for thoracic evaluation. For pathological classification, TNM (tumor-node-metastasis) 2017 criteria were used [8]. Largest size, stage and Furhman grades of the tumor were noted postoperatively. European Association of Urology (EAU) 2020 guidelines were taken into consideration to follow-up the patients according to their tumor stage [2].

Surgical Method

All surgeries (both open and laparoscopic) were performed by a highly experienced urology team with specialized assistants and nurses. During open PN, subcostal/transcostal flank incision was done with the patient in lateral decubitis position. All adipose tissues excepting those around the tumor were dissected. Zero-ischemia was used for small tumors with convenient localization. Renal artery clamping with mannitol infusion and renal cooling with ice-slush was used to excise bigger tumors in unsuitable locations. Masses were wedge-resected with leaving at least 0.5cm safe surgical margin. Bleeding vessels were ligated with 4/0 polyglactin sutures and hemostatic agents (Surgicel and Spongostan, Ethicon® Inc., Somerville, NJ, USA) placed between U sutures was used for the closure of the renal parenchymal defect. All procedures were done retroperitoneally, primary repair of peritoneum was performed if peritoneal defects were encountered.

During laparoscopic PN, three or four ports were placed transperitoneally. Tumors were resected using similar techniques as in open PN, with zero-ischemia or clamping renal artery depending on the size and localization of the tumor. Defect in the renal parenchyma was repaired with V-Loc (Covidien™, Ireland) sutures.

Radiological Evaluation and Nephrometry Scoring Systems

Patients with accessible pre-operative contrast enhanced (CT/MRI) images were included in the study. These images were evaluated by two urologists from the study team in terms of the complexity of renal anatomy and nephrometry scores (R.E.N.A.L. score, PADUA score and C-index).

R.E.N.A.L. scoring system: First defined by Kutikov and Uzzo in 2009, and five characteristic features of the tumor are evaluated.

(R) Radius: Maximum tumor diameter (cm), 1 point is given if the tumor is ≤4 cm, 2 points if between 4.1-7 cm and 3 points if >7cm.

(E) Exophytic/endophytic localization: 1 point if the tumor is ≥50% exophytic, 2 points if ≤50% exophytic, 3 points if completely endophytic.

(N) Nearness: Proximity of the tumor to the collecting system or renal sinus (mm), 1 point if ≥7mm, 2 points if 4.1-6.9 mm, 3 points if ≤4mm.

(A) Anterior/posterior: No scoring is made for this. Only letters of a&p are given to the total score.

(L) Localization: 1 point if the tumor is completely above or below the polar line, 2 points if the tumor crosses the polar line, 3 points if 50% of the tumor crosses the polar line or completely

fills the middle of the polar line.

According to this scoring, those with a total score between 4-6 are grouped as low, those between 7-9 as medium, and those between 10-12 as high risk group [9].

PADUA scoring system: Defined by Ficarra et al. at the same year as the R.E.N.A.L. score. It takes its name from the initials of Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification of renal tumors, adapted to the city of Padua/Italy. While all other parameters are similar to the R.E.N.A.L. score, there are two differences. One is the use of the axial polar line to evaluate polar localization. The other is to evaluate laterality and renal sinus involvement with respect to the renal edge. According to this classification, kidney tumors score between 6 and 14. Depending on their anatomical localization, and 6-7 points are considered low, 8-9 points medium, and >10 points high-risk group [10].

C-index: Simmons et al. defined this index in 2010, one year after other scoring systems were introduced. The aim is to determine the difficulty level of the tumor resection. It measures the tumor size and the distance from the outer margin of the tumor to the center in sagittal section. The center of the kidney is calculated by taking the exact midpoint of the section where the kidney was first and last seen (distance x). With the same method, the exact midpoint of the tumor is also calculated (distance y). When these points are combined to form a right triangle, the "C-index" is calculated by dividing the length of the hypotenuse (found according to the Pythagorean theorem) by the radius (r) of the tumor. According to this formula, as the C-index value decreases, tumor resection becomes more challenging. A cut-off value of 2.5 was determined by authors, and the surgery was considered easier at a value of >2.5, while it was stated that a more difficult and complex surgery was required when C-index <2.5 [11].

Calculation methods of R.E.N.A.L. and PADUA scoring systems, and C-index are shown in **Figure 1**.

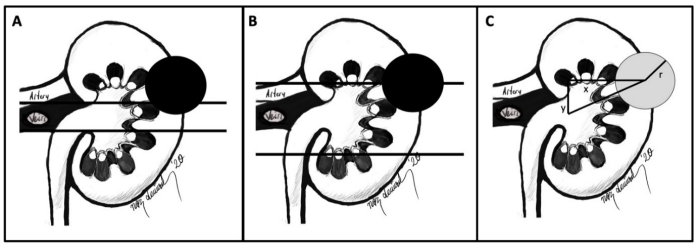

Figure 1. Calculations of nephrometry scores A) R.E.N.A.L. Score B) PADUA Score C) C-Index

Statistical Method

According to the distribution of variables, differences between two groups were analyzed using Student-T test and Mann- Whitney U test. For more than two groups, One-Way ANOVA and Kruskal- Wallis test was used. Bonferroni correction was used for evaluating multiple nonparametric subgroups. The values presented as ratios were analyzed by chi-square test. Correlations between parameters were evaluated with Spearman's rho correlation analysis. $p<0.05$ level was considered statistically significant. For all statistical analysis, SPSS 17.0 (IBM SPSS Statistics Corp., Armonk, NY, USA) software was used.

Results

Mean age of the patients was 55.04±10.91 years. Sixty-five (43.9%) patients were female and 83 (56.1%) were male. Mean follow-up period was 55.53 ±42.26 months. Eighty-four (56.8%) patients had incidental renal tumors, 62 (41.9%) had local, and only 2 (1.3%) cases had systemic symptoms. Sixty-four (43.2%) patients were smokers. Mean cigarette consumption rate was 12.6±23.6 packages/year. Patients had flank pain (n=54: 36.5%), hematuria (n=8: 5.4%), fever of unknown origin (n=1: 0.7%), hypertension (n=59: 39.8%), diabetes mellitus (n=25: 16.9%), and chronic obstructive pulmonary disease (n=9: 6.1%). Mean R.E.N.A.L, PADUA scores, and C-indexes were 6.45±1.60, 8.31±1.34, and 2.68±1.24, respectively.

Hundred and seventeen patients had open PN and 31 had laparoscopic PN. Mean ischemia time of all operations was 13.23±11.59 minutes. There were no statistically significant difference between surgical methods in terms of R.E.N.A.L. scores, C-Indices, operative time, timing of surgery (mandatory/elective), comorbidity rate or age of the patients. Duration of ischemia ($p=0.003$) was significantly shorter in open surgery compared to laparoscopic procedures. In three cases, operation was converted from laparoscopic to open surgery. One of these patients had ureteral injury, the tumor of the second patient was suspected to be of splenic origin and in the third case surgical margin was violated.

Postoperatively, Clavien grade I-II-IIIA, IIIB, and IVA complications were observed in 55, 17, 3, 7, 1 patients, respectively. Embolization was performed in two patients with Clavien IIIA complications, and perioperatively-placed double J (JJ) stent in one patient was removed. Four patients with grade IIIB complications underwent JJ stenting under general anesthesia due to discharge coming from the wound or drain site in postoperative period. One patient had persistent urinary leakage from the drain and inserted JJ stent could not solve the problem so the patient was explored. One patient was converted to open surgery because of ureteral injury during laparoscopic PN. One patient with grade IVA complications had renal loss because of postoperative renal vein thrombosis. Clavien classification was positively associated with pathological size ($p=0.038$), R.E.N.A.L. score ($p=0.001$), PADUA score ($p<0.001$), duration of ischemia ($p=0.045$) and negatively associated with C-index ($p=0.001$) **(Table 1)**.

Postoperative GFR changes and creatinine levels are shown in **Table 2**. In Grade 4 tumors, postoperative creatinine levels were significantly higher than other tumor grades **(Table 3)**. Correlations between nephrometry scores and renal functions are given in **Table 4**. Postoperative GFRs were significantly affected

Table 1. Comparison of complications with nephrometry scores, tumor size and ischemia times

Clavien grade	Pathological size	R.E.N.A.L. score*	PADUA score*	Ischemia duration	C-index*
I (n=55)	p=0.038	p=0.001	p<0.001	p=0.045	p=0.001
II (n=17)					
IIIA (n=3)					
IIIB (n=7)					
IVA (n=1)					

* P values were obtained by comparing subgroups of nephrometry scores (low-moderate-high) according to complications

Table 2. Renal functions of the patients who underwent partial nephrectomy and factors affecting postoperative renal function

	Mean±SD /Min-Max
Preoperative GFR (ml/min/1.73m²)	90.3±27.4 / 11.1-173.0
Postoperative GFR (ml/min/1.73m²)	79.6±26.8 / 4.9-148.6
GFR decrease (ml/min/1.73m²)	16.1±13.6 / 0-64.7
GFR decrease rate (%)	18.3±16.2 / 0-109.8
Preoperative creatinine (mg/dl)	0.94±0.49 / 0.4-5.72
Postoperative creatinine (mg/dl)	1.12±0.96 / 0.49-11.6

Mean±SD		Postoperative GFR (ml/min/1.73m²)		Postoperative creatinine (mg/dl)		GFR % change		GFR difference (ml/min/1.73m²)	
		Mean±SD	P-values	Mean±SD	P-values	Mean±SD	P-values	Mean±SD	P-values
Tumor grade	**Grade 1**	80.3±22.2	**0.001***	0.93±0.26	**0.001***	18.7±11.1	**0.012***	18.5±13	0.099
	Grade 2	79.9±27.9		1.06±0.37		16.5±11.7		15.5±13	
	Grade 3	74.1±25.0		1.15±0.46		15.7±12		13.4±13.2	
	Grade 4	39.5±21.4		3.12±3.48		53.1±35.4		30.5±20.9	
HT	**No**	82.4±25.2	0.167	1.15±1.23	0.719	17.1±15.6	0.167	16.2±14.5	0.606
	Yes	76.3±28.3		1.09±0.49		19.8±16.8		16.2±12.4	
DM	**No**	80±25.5	0.738	1.13±1.06	0.704	17.6±17	0.05	15.9±14.3	0.148
	Yes	78.2±31.3		1.1±0.48		20.8±12.7		17.1±10.6	
Operation type	**Open**	78.1±27.3	0.199	1.17±1.06	0.066	19.1±17.5	0.812	16.6±14.5	0.886
	Lap	85.5±23.5		0.92±0.29		16.1±9.7		15.2±9.8	

Table 3. Comparison of tumor grade groups according to postoperative creatinine levels

		Postoperative creatinine	GFR % change
		P-values	P-values
Grade 1	**Grade 2**	>0.99	>0.99
	Grade 3	>0.99	>0.99
	Grade 4	**0.001***	0.256
Grade 2	**Grade 3**	>0.99	>0.99
	Grade 4	**0.002***	**0.011***
Grade 3	**Grade 4**	**0.012***	**0.010***

SD: standard deviation; GFR: glomerular filtration rate; *statistically significant p value (p<0.05)

Table 4. Relationship between renal functions and nephrometry scores

	R.E.N.A.L. score				PADUA score			C-index		
	4-6 (n=80)	7-9 (n=62)	10-12 (n=6)**		6-9 (n=116)	10-12 (n=32)		<2.5 (n=72)	≥2.5 (n=76)	
	Mean±SD	Mean±SD	Mean±SD	P	Mean±SD	Mean±SD	P	Mean±SD	Mean±SD	P-values
Preop creatinine (mg/dl)	0.95±0.59	0.94±0.34	0.83±0.31	0.816	0.94±0.53	0.96±0.32	0.417	0.91±0.27	0.97±0.63	0.740
Postop creatinine (mg/dl)	1.03±0.41	1.25±1.4	1.03±0.47	0.404	1.02±0.39	1.5±1.9	0.096	1.23±1.31	1.02±0.42	0.241
Preop GFR (mL/min/1.73m2)	89.7±26.2	90.1±28	100.7±38.5	0.941	91.3±26.9	86.9±30.1	0.149	89.4±25.5	91.1±29.2	0.710
Postop GFR (mL/min/1.73m2)	80.6±24.3	78.2±29.8	80.8±30	0.610	82.0±25.3	69.8±30.1	**0.023***	76.9±28.2	82.1±25.3	0.237
GFR difference (ml/min/1.73m2)	15.8±12.5	15.7±14.8	24.4±13.9	0.562	15.0±11.5	19.6±16.7	0.225	18.3±14.1	14.1±12.8	**0.035***
GFR percentage change (%)	18.1±15.9	18.0±17.1	24.0±9.2	0.516	16.9±14.8	23.1±20.1	0.127	20.8±16.6	16.0±15.5	**0.042***
Duration of operation (minutes)	172.1±35.8	170.5±37.6	165.0±37.8	0.805	170.9±36.1	171.7±38.0	0.916	172.4±35.1	169.9±37.7	0.673
Duration of ischemia (minutes)	11.0±12.8	12.9±11.0	13.8±10.1	0.201	10.6±11.7	16.1±10.6	**0.008***	11.8±10.8	12.0±12.4	0.822

*Significant p value; ** It was not included in the analysis because of small number of patients; Preop: preoperative; Postop: postoperative; SD: standard deviation; GFR: glomerular filtration rate

Table 5. Relationship between ischemia times and renal functions

	Duration of ischemia (minutes)			
	0 (n=60)	0-20 (n=55)	>20 (n=33)	
	Mean±SD	Mean±SD	Mean±SD	P-values
Postoperative creatinine (mg/dl)	1.09±0.37	1.18±1.48	1.10±0.51	0.206
Postoperative GFR (ml/min/1.73m²)	77.8±23.8	81.5±25.3	79.7±34.1	0.610
GFR difference (ml/min/1.73m²)	15.0±13.4	16.4±13.7	17.8±13.9	0.556
GFR percentage change (%)	16.1±11.9	19.8±20.2	19.9±15.4	0.650
Transfusion, n (%)	11 (18.3)	15 (27.3)	8 (24.2)	0.539

SD: standard deviation; GFR: glomerular filtration rate

by PADUA scores (p=0.023). Additionally, PADUA scores over 10 significantly altered the duration of ischemia (p=0.008). Also, difference between pre-and post-operative average GFR values, and its percentage change were significantly affected by C-index (p=0.035, p=0.042).

Although the results of postoperative GFR, difference between pre-, and post-operative GFR values, and decrease rates in postoperative GFR were relatively more physiologic in zero-ischemia group than 0-20 min-, and >20 min- ischemia groups without any statistically significant intergroup differences **(Table 5)**.

Discussion

In recent years, management of renal masses rapidly changed from RN to nephron-sparing techniques to preserve kidney function and reduce associated comorbidities [3,12]. Initially, PN was only performed in mandatory indications (solitary kidney, bilateral tumors, impaired renal function etc.), but nowadays it is performed safely in patients with healthy kidneys with similar long-term oncological results as RN [4,13].

PN instead of RN in T1 tumors has been shown to

prevent the development of long-term renal injury in the postoperative period and consequently reduce mortality rates from cardiovascular disease [3]. Since there is a significant relationship between duration of ischemia and postoperative renal injury, ischemia times should not exceed 20-25 minutes. Thompson et al. stated each minute over 25 minutes increases the risk of acute renal injury and subsequent development of chronic renal injury by 5-6% [14]. In a multi-institutional study by the same author concerning ischemia times during PN performed in patients with solitary kidneys, warm ischemia times over 20 minutes was associated with an increased risk of chronic renal failure and permanent requirement for dialysis [15]. Simmons et al. evaluated parenchymal atrophy measuring pre-, and post-operative parenchymal thickness, and reported development of severe parenchymal atrophy when duration of ischemia exceeded 40 minutes [16]. In a review in 2016 by Rod et al. [17] which evaluated postoperative renal functions according to duration of ischemia, zero ischemia was not superior to ischemia lasting less than 25 minutes. Gupta et al. indicated also age, comorbidity, preoperative GFR, tumor complexity, type and duration of ischemia as independent parameters affecting postoperative GFR [18]. Diversely, Çömez et al. reported no significant difference between pre-and post-operative eGFRs [19]. In our study, as the duration of ischemia increased, renal functions started to deteriorate but there were no statistically significant difference between ischemia times and postoperative GFRs, pre-, and post-operative GFRs, decreasing rates in postoperative GFRs and amount of transfused blood and/or solutions. These results we obtained in our study may be associated with very limited number of our patients had ischemia times over 25 minutes.

Nephrometry scores have been put forward to predict postoperative renal function in patients undergoing PN. C-index is associated with glomerular filtration rate and its decrease percentage. In cases with a C-index of 2.5 or less, the risk of 30% functional loss increased 2.2-fold [20]. In our study, postoperatively GFR decreasing rates were found to be significantly different between C-index (<2.5 vs ≥2.5) and between PADUA score subgroups (6-9 vs 10-12). This significance was detected in difference in GFRs and GFR percentage change for C-index and only postoperative GFR for PADUA scores. Even though there still is a higher numerical GFR difference and percentage change in PADUA 10-12 subgroup, this insignificance may caused by the asymmetrical distribution of the subgroups regarding PADUA scores (116 vs. 32). Additionally, no significant difference was detected between R.E.N.A.L. score subgroups.

Tatsugami et al. found no significant difference in postoperative renal functions between patients undergoing open/laparoscopic PN [21]. In our study, although there was a statistically significant difference between the duration of ischemia depending on the type of operation; there was no statistically significant difference between type of surgery and postoperative creatinine, pre-, and post-operative GFR values, GFR decrease and GFR decrease rates similar to the literature. Toosy et al. showed pneumoperitoneum created during laparoscopy protects the kidney from ischemia and reperfusion injury in rats [22]. Although the duration of ischemia in the laparoscopic group is increased, pneumoperitoneum created during LPN may explain the fact that ischemia time has no impact on postoperative GFR. Also, clinical studies have shown that at postoperative 6th month, renal function is not affected up to 55 minutes of ischemia times in laparoscopic cases [23]. Adamy et al. evaluated 987 patients operated by open/laparoscopic methods, stating that the average duration of ischemia was 40 min for open and 35 min for laparoscopic surgeries [24]. They also reported that the postoperative eGFR value of laparoscopically-treated patients was significantly higher compared to open surgery.

Complications such as hemorrhage, renal injury and urinary fistula may occur after PN. R.E.N.A.L., PADUA, and C-index scores may predict complications after PN. Ficarra et al. who first mentioned the concept of PADUA scoring, demonstrated that those with PADUA scores of 6-7 had 14 times lower risk of complications than those with 8-9 and risk increased by 30 times in those with >10 [10]. In recent years, Draeger et al. reported that PADUA scores were more related to complication severity rather than complication rates [25]. Rosevear et al. reported that patients who developed complications after PN had higher R.E.N.A.L. scores [26]. Similarly, in our study, a statistically significantly positive correlation was found between PADUA and R.E.N.A.L. scores and severity of complications. We also found a negative association between C-index and severity of complications.

Gill et al. reported that complications of 1800 patients undergoing open/laparoscopic PN were comparable [27]. In our study, no association was found between open/laparoscopic surgery and Clavien classification. As Patard et al. suggested, tumor size had no effect on surgical and medical complications, but they found that the blood transfusion rate was significantly higher in the group with larger tumors [28]. The reason for this discrepancy is that they had not considered blood transfusion as a complication (normally counted as Clavien II complication). We also found a statistically significant association between Clavien classification and tumor size. The main reason for this relationship is the greater amount of blood loss in large tumors. We believe excessive bleeding may be due to increased angiogenesis in large tumors.

In literature, multivariate analysis of various factors has been investigated as prognostic factors in nephron-sparing surgeries. However, to determine the values that can predict the outcomes, number of cases and regularly followed-up patients should be also considered. Even though this study has one of the longest follow-up span in the literature, low number of cases can be asserted as the main limitation of this study. This study also has the feature of being supplementary to our recent study about

the prognostic factors indicating surgical margin status and recurrence in partial nephrectomy patients [29]. The number of patients have increased throughout the years, enriching this study. Our clinic is an experienced, high-load center but unreachable data of especially patients included earlier in the study, and the change of achiving systems are responsible for inadequate sample size. Also, our results are mostly descriptive and bivariate as the study was planned. These comparative results has the potential to be coincidental and multivariate logistic regression analysis of these findings will give more comprehensive outcomes. In recent years, performance scoring, such as Eastern Cooperative Oncology Group (ECOG), has an important role in evaluation of candidates for PN. Due to the retrospective design of the study, lack of performance scores is another limitation.

Conclusions

According to our study, R.E.N.A.L. score, PADUA score and C-index are effective in predicting complications that may occur in patients undergoing PN. Additionally, complication rates increase in direct proportion to tumor size. According to PADUA scoring system and C-index high-risk renal tumors cause greater renal function loss after PN compared to low risk tumors. Although the duration of ischemia did not cause a significant difference in renal function loss, tumor grade has been shown to be a direct predictor for postoperative renal functions. Nevertheless, meta-analyzes and prospective trials with higher volumes are mandatory to reach a definitive conclusion.

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital (Approval date, and Registration number: 07.07. 2020/2888).

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

Publication: The results of the study were not published elsewhere in full or in part in form of abstracts.

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Original Article – Renal Transplantation

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Coronavirus Disease 2019 in Kidney Transplant Recipients: Our Single Center Experiences

Böbrek Nakli Alıcılarında Koronavirüs 2019 Hastalığı: Tek Merkez Deneyimlerimiz

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Abstract

Objective: To investigate whether tacrolimus (Tac), mycophenolate mofetil (MMF), mycophenolic acid (MPA), prednisolone (Pred) and methylprednisolone (MP) are affect the COVID-19 pathogenesis and on its progression in kidney transplantation recipients diagnosed with COVID-19 patients.
Materials and Methods: Among patients hospitalized due to COVID-19, patients who had kidney transplantation were retrospectively detected on the online database of our center. Referral complaints, laboratory and radiological data at referral, applied treatment protocols, and ultimate conditions of the patients were documented.
Results: Among the total of 11 patients, 73% (8) were male and 27% (3) were female. The mean age was 49.63 (27-71). Hypertension and diabetes mellitus were the most common comorbid diseases. The most common symptoms were coughing, fever and exhaustion-fatigue. High serum reactive protein and lymphopenia were detected in almost all patients. Acute renal failure was observed in seven patients (73%). While all patients were using Tac and Pred, nine patients (82%) were using MMF and two patients (18%) were using MPA. Hydroxychloroquine, favipiravir, and azithromycin were treatments for COVID-19. RT-PCR results of 11 patients were positive in 7 and negative in 4 patients. The mean hospital stay of the discharged patients was 8.8 days. Eight patients recovered and were discharged, treatment of two intubated patients continues in intensive care unit and one patient died.
Conclusion: Clinical characteristics of COVID-19 in kidney transplanted patients are similar to the general population and it should be kept in mind that the disease occurs with moderate-severe pneumonia in this patient group. Disease progress can be stopped through early treatment.

Keywords: COVID-19, kidney transplantation, kidney recipients, kidney, immunosuppressive treatment

Öz

Amaç: COVID-19 tanılı böbrek nakli alıcılarında takrolimus (Tac), mikofenolat mofetil (MMF), mikofenolik asit (MPA), prednizolon (Pred) ve metilprednizolonun (MP) COVID-19 patogenezine ve progresyonuna etkisi olup olmadığını araştırmak.
Gereçler ve Yöntemler: Merkezimizin online veri tabanında geriye dönük olarak tarama yapıldı ve COVID-19 nedeniyle hastaneye yatırılan hastalardan böbrek nakilli hastalar tespit edildi. Şikayetleri, laboratuvar ve radyolojik veriler, uygulanan tedavi protokolleri ve hastaların son durumları ortaya koyuldu.
Bulgular: Toplam 11 hastanın %73'ü (8) erkek, %27'si (3) kadındı. Yaş ortalaması 49.63 (27-71) idi. Hipertansiyon ve diabetes mellitus en sık eşlik eden hastalıklardı. En sık görülen semptomlar öksürük, ateş ve halsizlik-yorgunluktu. Hemen hemen tüm hastalarda yüksek serum reaktif protein ve lenfopeni saptandı. Yedi hastada (%73) akut böbrek yetmezliği oluşumu gözlendi. Tüm hastalar Tac ve Pred kullanırken, dokuz hasta (%82) MMF ve iki hasta (%18) MPA kullanıyordu. Hidroksiklorokin, favipiravir ve azitromisin, COVID-19 için uygulanan tedavilerdi. 11 hastanın RT-PCR sonucu 7'sinde pozitif, 4'ünde negatif bulundu. Taburcu edilen hastaların ortalama hastanede kalış süresi 8,8 gün olarak tespit edildi. Sekiz hasta iyileşerek taburcu edildi, entübe edilen iki hastanın tedavisi yoğun bakımda devam ederken bir hasta hayatını kaybetti.
Sonuç: Böbrek nakli yapılan hastalarda COVID-19'un klinik özellikleri genel popülasyonla benzerlik göstermektedir ve bu hasta grubunda hastalığın orta-şiddetli pnömoni ile ortaya çıktığı akılda tutulmalıdır. Erken aktif tedavi ile hastalığın ilerlemesi durdurulabilir.

Anahtar kelimeler: COVID-19, böbrek nakli, böbrek alıcısı, böbrek, immünsupresif tedavi

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Introduction

A novel type of coronavirus disease emerged in December 2019 in Wuhan, the largest (and capital) city of Hubei Province in China [1]. Its rapid spread across the world led to it being declared a pandemic by the World Health Organization (WHO) [2]. The disease was named COVID-19 and the effective virus was named SARS-CoV-2 [3]. Although the disease generally affects the respiratory system, it also presents with different symptoms ranging from a mild cold to severe respiratory syndrome and can also affect kidneys, heart, skin, respiratory, and nervous systems [4,5]. Advanced age and presence of hypertension (HT), smoking, chronic obstructive pulmonary disease (COPD), and diabetes mellitus (DM) increase the risk and the extent of the effect of the disease [6–8]. Since immunosuppression is the most significant characteristic of COVID-19, patients with a suppressed immune system or those using immune system suppressing drugs constitute a particular population whose needs should be considered separately.

Kidney transplant patients would usually take immunosuppressive treatment, such as tacrolimus (Tac, calcineurin inhibitors), mycophenolate mofetil (MMF), mycophenolic acid (MPA), and steroids (Pred) or methylprednisolone (MP) [9]. There is no suitable, efficient, and clear treatment protocol is currently available for how these treatments should be applied for a patient with COVID-19 disease now.

Our aim in this study is to examine whether the continuous use of immunosuppressive drugs in kidney transplant patients is effective in the pathogenesis of COVID-19 and its effects on the progression of the disease. In addition, it is to examine the diagnosis, treatment and follow-up protocols applied in our center in the light of current COVID-19 literature and to determine a treatment specific to both COVID-19 and immunosuppression.

Materials and Methods

In this study, patients who were hospitalized and treated for COVID-19 in our center since 11 March 2020 (when the first COVID-19 patient was detected in our country) were evaluated retrospectively through the hospital's online database. Consent for the study was obtained from the Ethics Committee of University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital (Ethics committee approval no: 2020/183).

Patients were identified who had been treated for COVID-19 and had also received a kidney transplant. Key parameters for these patients were examined as follows: demographic characteristics; complaints and symptoms at the time of first admittance; vital findings; thorax computed tomography (Tx-CT) findings; lowest-highest values for white blood cells (WBC), thrombocyte (Plt), lymphocyte (Lym), fibrinogen (Fib) creatinine (Cr), C-reactive protein (CRP), procalcitonin (Proc), D-dimer (DD), and ferritin (Fer); real-time polymerase chain reaction (RT-PCR) results; and drugs used before, for induction during, and after transplantation (anti-thymocyte globulin, ATG) plasmapheresis, rituximab, calcineurin inhibitor (Tac), antimetabolite (MMF/MPA), steroids (Pred/MP). In addition, further details were noted as follows: regulation of drugs during COVID-19 treatment (changing, discontinuing, and continuing dose adjustment); treatments specific for COVID-19 (hydroxychloroquine, HQ), azithromycin, oseltamivir, interleukin-6 blocker/tocilizumab, Favipiravir (Fav) and intravenous immunoglobulin (IVIG); antibacterial treatments; anticoagulant-antiaggregant treatments; vitamin-C use; intensive care unit (ICU) and intubation requirements; total hospitalization duration; and final condition (discharged, deceased, or continuing treatment).

Patients included in the study were those with kidney transplantation, with or without RT-PCR positive, and considered COVID-19 clinically and/or radiologically. Patients who were not considered COVID-19 clinically and radiologically during the follow-up and had a negative RT-PCR result were excluded from the study.

Results

Based on the examination, 11 patients met the inclusion criteria. Of these, 73% (n=8) of these patients were male and 27% (n=3) were female. The mean age was 49,63 (27-71) years. Live donor transplantation had been performed with six patients, deceased donor transplantation had been performed with four patients, and donor-type data could not be acquired for one patient **(Table 1)**. Considering the mean time between kidney transplantation and infection was 24,4 (3-52) months. Comorbid diseases were HT for eight (73%) patients, DM for three (27%) patients, congestive heart failure (CHF) and COPD for one (9%) patient, and three (27%) patients had no comorbid diseases.

Although coughing (45%), fever (45%), weakness-exhaustion (45%) and dyspnea (36%) were observed most commonly, headache, diarrhea, myalgia, chills, nausea, and vomiting were also present among causes for admittance. Bilateral ground-glass appearance was observed in 9 patients (81%), pleural effusion in three patients, and one-sided involvement in one patient (using Tx-CT). No significant pulmonary involvement was detected in just one patient.

Fever above 38°C was detected in two patients. While oxygen saturation was nearly 60% at room air in only one patient, it was over 93% for other patients and the mean value was 96.3%. Apart from one patient, recorded blood pressures of all patients were within the normal range. The mean values for lowest-highest values were as follows: for complete WBC count 4.5-9.95 (10e3/uL); for Plt 144000-228000 (10e3/Ul); for Lym 0.5-1.14 (10e3/Ul) and for Fib 393-498 (mg/dL) respectively. Acute kidney injury (AKI) was observed in eight (73%) of the patients with a mean basal Cr of 1.52 mg/dL (1.8-1.0) **(Figure 1)**. Mean values for lowest and highest were detected for CRP 29-70 mg/L, Proc 0.19-5.9 ng/mL, Fer 468-673 µg/L and DD 0.56-1.06 µg FEU/mL respectively.

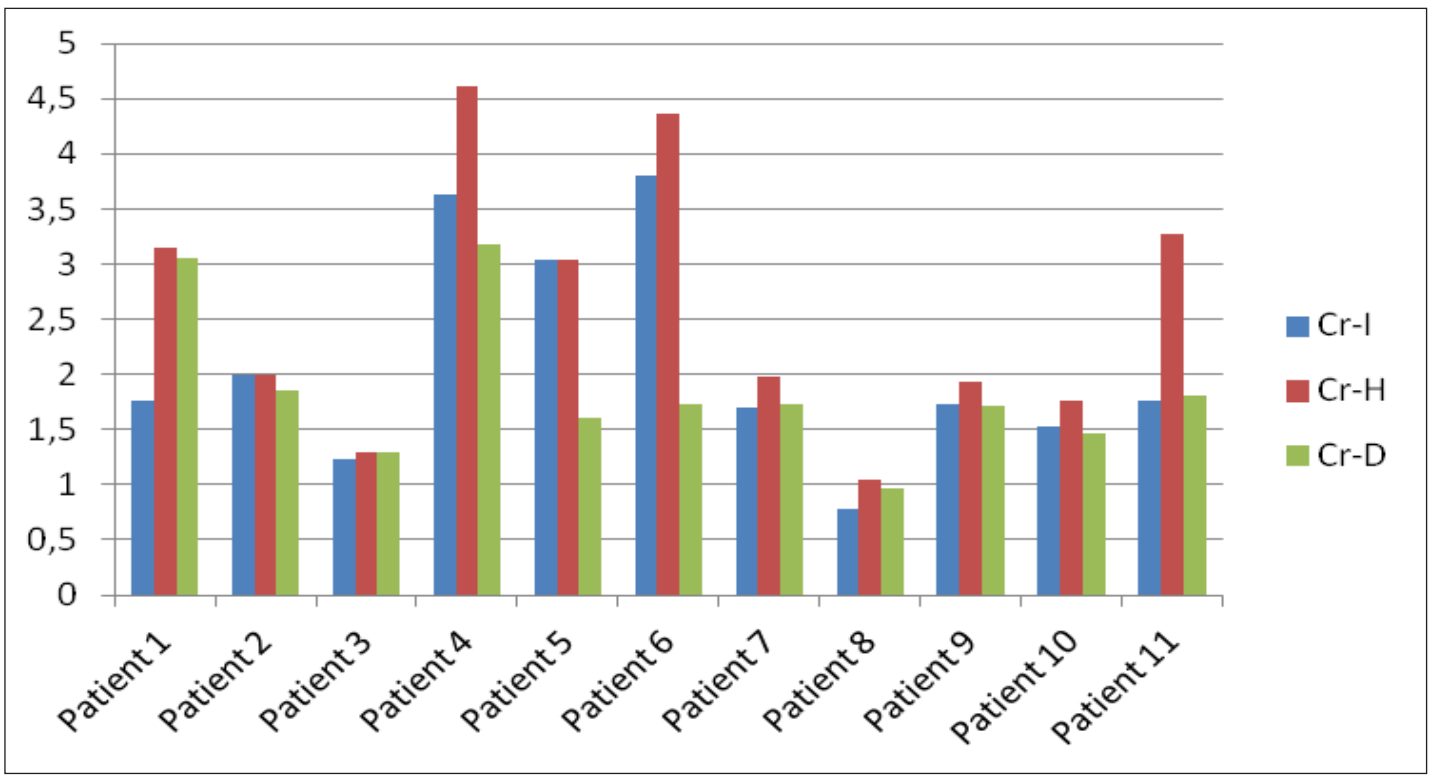
It was observed that ATG was used for seven patients and pulse steroid was used for two patients for induction, whilst no

Table 1. Patients demographics and outcomes

Pt	Sex	Age	Donor type	Time from transplant to infection (months)	ICU	INT	RT-PCR	Hospital stay (days)	Outcome
1	M	62	LDRT	44	Yes	Yes	Positive	11	Death
2	M	44	LDRT	13	No	No	Positive	6	Recovered
3	F	46	DDRT	19	No	No	Positive	11	Recovered
4	M	71	DDRT	34	Yes	Yes	Positive	**Continues**	-
5	M	60	DDRT	3	No	No	Negative	9	Recovered
6	F	36	LDRT	9	No	No	Negative	13	Recovered
7	M	37	Unknown	52	No	No	Positive	8	Recovered
8	M	57	LDRT	45	No	No	Positive	7	Recovered
9	M	50	DDRT	12	No	No	Positive	8	Recovered
10	M	27	LDRT	18	No	No	Negative	7	Recovered
11	F	56	LDRT	20	Yes	Yes	Negative	**Continues**	-

DDRT: deceades donor received transplantation; F: female; ICU: intensive care unit; INT: intubation; LDRT: living donor received transplantation; M: male; Pt: patient; RT-PCR: real-time polymerase chain reaction

Figure 1. Levels of creatinine (mg/dL)



Cr-I: initial creatinine; Cr-H: highest creatinine; Cr-D: discharge creatinine

induction treatment was given for one patient due to a low risk in terms of immunity. For the purpose of desensitisation before transplantation, rituximab and plasmapheresis were applied. While all patients used Tac and Pred after transplantation, 9 patients (82%) used MMF and two patients (18%) used MPA as an antimetabolite. Antimetabolite treatment was discontinued for 10 patients, Tac was continued by either adjusting or decreasing dosages for 7 patients, and MP (20 mg/day dosage) was given to all patients **(Table 2)**.

As suggested by the World Health Organization (WHO), all patients received hydroxychloroquine (HQ) for 5–10 days (first day 2×400 mg loading, then 2×100 mg maintenance)

Table 2. Transplant characteristics and outcomes

Pt	Donor	Releated	Degre of relationship	Induction	Plasmapheresis	Rituximab	CNI	CNI-IL	Antimetabolite	Steroids	IR
1	LDRT	Yes	Wife	ATG	No	No	Tac	2,47	MMF	Pred	Only MP
2	LDRT	Yes	Mother	P.Steroid	No	No	Tac	5,34	MMF	Pred	No Change
3	DDRT	-	-	ATG	No	No	Tac	9,58	MPA	Pred	Only MP
4	DDRT	-	-	ATG	Yes	No	Tac	17	MMF	Pred	Only MP
5	DDRT	-	-	ATG	No	No	Tac	15,4	MMF	Pred	Tac+ MP
6	LDRT	Yes	Mother	ATG	Yes	Yes	Tac	11,4	MMF	Pred	Tac+ MP
7	Unknown	-	-	Unknown	Unknown	Unknown	Tac	8,03	MMF	Pred	Tac+ MP
8	LDRT	Yes	Wife	No	No	No	Tac	13,13	MMF	Pred	Tac+ MP
9	DDRT	-	-	ATG	Yes	Yes	Tac	19,05	MMF	Pred	Tac+ MP
10	LDRT	Yes	Brother	P.Steroid	No	No	Tac	5,16	MMF	Pred	Tac+ MP
11	LDRT	Yes	Sister	ATG	Yes	Yes	Tac	2,59	MPA	Pred	Tac+ MP

ATG: antithymocyte globulin; CNI: calcineurin inhibitor; DDRT: deceades donor received transplantation; IL: initial level; IR: immune regulation; LDRT: living donor received transplantation; MMF: mycophenolate mofetil; MP: methylprednisolone; MPA: mycophenolic acid; P: pulse; Pt: patient; Pred: prednisolone; Tac: Tacrolimus

Table 3. COVID-19 specific treatment

Pt	HQ	Os	Az	Tos	Fav	IVIG	Antimicrobial treatments	Thromboprophylaxis	Asc. A
1	Yes	Yes	Yes	No	Yes	No	Piperacillin-Tazobactam	LMWH	No
2	Yes	Yes	No	No	No	No	No	No	No
3	Yes	Yes	Yes	No	No	No	No	LMWH	No
4	Yes	Yes	Yes	No	Yes	No	Ertapenem	LMWH	Yes
5	Yes	No	No	No	No	No	Ceftriaxone	LMWH	No
6	Yes	No	No	No	No	No	Ceftriaxone	LMWH	No
7	Yes	No	Yes	No	No	No	No	LMWH	No
8	Yes	No	No	No	No	No	No	ASA	No
9	Yes	No	Yes	No	No	No	No	LMWH	No
10	Yes	No	No	No	No	No	Ceftriaxone	LMWH	No
11	Yes	No	No	No	Yes	No	Ertapenem+Vancomycin+Meropenem	LMWH+ASA	Yes

ASA: acetylsalicylic acid; Asc. A: ascorbic acid; Az: azithromycin; Fav: favipiravir; HQ: hydroxychloroquine; IVIG: intravenous immunoglobulin; LMWH: low molecular weight heparin; Os: oseltamivir; Pt: patient

and six patients received azithromycin for 5 days (1×500 mg on first day, then 1×250 mg) in line with COVID-19 Treatment Guidelines prepared by the Science Board formed within the Ministry of Health in our country [10]. In addition to the treatments mentioned here, 4 patients were also given oseltamivir (2×75 mg/day for 5 days) in the early period of the pandemic. All patients were given an electrocardiogram before starting these treatments and QT distances were calculated and detected within normal ranges for all patients. According to our Ministry of Health's COVID-19 guidelines, 3 patients received a 5-day treatment regimen of Fav (2×1600 mg/day loading, 2×600 mg/day maintenance). Neither tocilizumab not IVIG treatment were used for any of the patients. Ceftriaxone, ertapenem, vancomycin, and piperacillin-tazobactam were used for six patients requiring antimicrobial treatment. Low molecular weight heparin (LMWH) enoxaparin sodium (4000 IU/0.4 ml or 6000 IU/0.6 ml) and 100 mg/day acetylsalicylic acid alone or in combination were used for thromboprophylaxis **(Table 3)**.

While COVID-19 was confirmed through RT-PCR in 7 of 11 patients (63.6%) from laboratory diagnosis, 4 patients were RT-PCR negative **(Table 1)**. COVID-19 was diagnosed through clinical, laboratory, and pulmonary tomography findings in our RT-PCR negative cases. Eight patients recovered and were discharged (72.7%); two intubated patients remain under treatment in the

ICU (18.2%) (during the writing process of this manuscript), and one patient died (9.1%). The mean hospitalization duration for discharged patients was 8.8 days **(Table 1)**.

Discussion

In terms of gender, parallel to general population data reporting that COVID-19 is more commonly presented in males, 73% of our patients were male [11]. Interestingly, the mean age was lower (49,63 years) compared to the general population. Considering our youngest patient was 27 years old, it should be recognised that all age groups are at risk of this disease. Since the deceased–live donor rate in our country is approximately 30%-70%, a similarity was observed in kidney transplanted COVID-19 patients in terms of the deceased–live donor rate.

Published studies have shown that comorbid diseases play a significant part in the overall effects of COVID-19 [12]. Similar to the literature, our study shows that HT, DM, COPD and CHF are among the leading causes of increased risk. It should be recognised that a comorbid disease increases the risk; however, it is equally important to keep in mind that COVID-19 can also affect otherwise healthy individuals. Because our study showed that our two patients had no comorbidity.

Considering the reports in terms of the time passing between transplantation and infection formation, patient groups within a time range expressed as day, month, or year are also present [11]. Intensive use of immunosuppression can worsen the course of the disease. On the other hand, reducing the dose may cause deterioration of the graft function and thus the emergence of AKI and worsening of the situation [13].

The WHO have separated COVID-19-related symptoms into three groups: common, less common, and severe. While fever, dry cough, and fatigue are common, symptoms such as pain and aches, sore throat, diarrhea, conjunctivitis, headache, inability to taste or smell, skin rash, or colour change in fingers or toes were stated as fewer common symptoms. Severe symptoms include breathing difficulty or dyspnea, chest pain or tightness, and loss of speaking or movement [14]. Although these symptoms are applied to the general population, the symptoms among our patient group were parallel to the general population.

While mild-to-moderate symptoms we mostly detected among the general population in radiological terms, moderate-to-severe pulmonary symptoms were detected at a rate of 90% among our patient group. Only one patient had no remarkable pulmonary effects. Accordingly, we consider pulmonary involvement to be more common among patients with kidney transplantation, and it would therefore be accurate to predict that pneumonia might have a more severe course.

Lymphopenia was reported as the most characteristic aspect of COVID-19 in terms of laboratory variables. Authors emphasise that, together with lymphopenia, CRP, Fer, and DD increases, Proc may also increase in the case of bacterial co-infection [15]. It was also reported that Plt and Fib increased in mild-to-moderate cases based on the disease condition, but may decrease in severe cases. Among our sample, high CRP and Fer were observed together with lymphopenia in all patients (100%), Fib increase was observed in 82%, and DD increase was observed in 54% of patients. Three patients had high procalcitonin and the fact that one of these patients died and the other two were intubated in ICU (during the writing process of this manuscript) shows that high Proc likely increases mortality risk and can be a predictive factor. As in the general population, we recommend the use of lymphopenia and high CRP, Fer, Fib, and DD for COVID-19 diagnosis among patients who have had kidney transplantation.

Many different approaches were identified among the immunosuppressive treatments presented in this study. The application of many different protocols were reported, such as the continuation of present treatments, completely ceasing treatment, increase treatment dosage, only cutting antimetabolites, continuing only with Pred or MP, or use of Tac and MP [16–18]. With so many different options being used, the novel character of COVID-19 and a lack of adequate information infrastructure is resulting in a lack of an efficient, reliable, and suitable treatment protocol. Treatments may differ as different types and doses of immunosuppressives used for each patient is a factor affecting each patient clinic. We think that treatment should be evaluated based on each patient and regulated depending on the mild-moderate-severe character of the disease. In the case of mild disease, the dose of Tac should be adjusted (drug interactions with lopinavir/ritonavir, HQ etc.), closely followed-up, and decreased if necessary, whilst antimetabolites can be used very carefully to preserve graft function in the patient group without any severe change in laboratory parameters. However, since most patients have lymphopenia, the correct approach would be to commence antimetabolites after the laboratory parameters return to normal. Only low dose Tac should be given in moderate cases of the disease, and Tac should be discontinued in severe disease presentations, such as in ICU and intubation. Furthermore, we suggest that MP should be administered at 20 mg/day MP in all disease groups.

Although there is no specific and efficient treatment for COVID-19 as yet, HQ, lopinavir+ritonavir, remdesivir, Fav, convalescent plasma, and Interleukin-6 (IL-6) blockers are the drugs currently being used [19]. On the other hand, promising vaccination studies on COVID-19 continue rapidly all over the world. Most of the mRNA vaccines which are a new technological product and inactive coronavirus vaccines, announced the phase 3 results, and many countries in the world, including our country, are gradually carrying out vaccination studies. Azithromycin and oseltamivir have also been used in the early periods of the pandemic, they are not suggested as treatment since the studies demonstrated that they have no efficiency. The drugs most commonly used are HQ and lopinavir+ritonavir, which are suggested for all mild-moderate and severe patient groups [20–22]. Conversely, remdesivir, convalescent plasma and Fav are used in the advanced stage of the disease [23–25]. It was reported that IL-6 blocker-tocilizumab was given in cases of cytokine storm and IVIG was given in cases of severe disease [26,27]. It is

recommended that the ECG should be checked at intervals before commencing the treatment and at intervals during the treatment, as HQ and azithromycin may lengthen the QT range and cause lethal arrhythmias. No negative condition was detected in terms of arrhythmia among our patient group.

Among antiviral drugs, Fav is more commonly used in our country [10]. Again, while Fav was used in cases of severe disease in the early periods of the pandemic, we observed that Fav would be more effective when started in patients with lowered oxygen saturation in the early periods of the disease and would reduce the need for ICU and intubation. When we examined why the treatment was not effective for three patients given Fav treatment, it was evident that for these patients at the time of admission to the hospital, one was intubated (deceased patient) and the other two patients were at an advanced stage (intubated at follow-up) of the disease. This result has shown that the initiation of Fav therapy in the early stages of the disease supports our view, as already emphasised. We will be able to reach objective conclusions from the data when the clinical study in our center is completed.

Considering that bacterial co-infection may be present when the disease has a slow course and clinical and laboratory recovery is not observed, a wide spectrum antibiotic should be added to the treatment regime. In our patients with resistant high fever and persistent or increasing highly acute phase, ceftriaxone, piperacillin-tazobactam, ertapenem, meropenem, and vancomycin were added as antibacterial treatment.

Many clinical and postmortem studies have reported that COVID-19 creates a tendency toward thrombosis and the thrombotic incidence accordingly causes systemic symptoms [5,28,29]. Thus, it is suggested that prophylaxis is given or treatment to prevent a thromboembolic event is provided to patients [30]. Except one patient all of them were given 4000IU/LMWH prophylaxis. Patients for whom thrombosis-related symptoms (tachypnea) or examination findings were detected the dose was adjusted according to the weight and LMWH was switched to the treatment dose (×2).

Our study has some limitations. Including a small number of patients, retrospective and observational study nature, and a lack of information on outpatients were all factors considered among these limitations.

Conclusion

From our study, it should be considered that although the clinical characteristics of COVID-19 among kidney transplant patients are similar to the general population, the disease occurs with moderate-severe pneumonia among this patient group. Furthermore, it should be considered that commencing active treatment early would positively affect the progression of the disease which would also be overcome with less harm to patients. Although prospective and randomised controlled studies with a higher number of patients are needed, we think that our study can contribute to related literature.

Ethics Committee Approval: The study was approved by University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital Ethical Committee, Bakirkoy, Istanbul, Turkey (Approval number, and registration number: 04.05.2020/183).

Informed Consent: An informed consent was obtained from all the patients for research.

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Original Article – Andrology

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Is There Any Association Between Uric Acid to High-density Lipoprotein Cholesterol Ratio and Erectile Dysfunction?

Ürik Asitin Yüksek Yoğunluklu Lipoprotein Kolesterole Oranı ile Erektil Disfonksiyon Arasında Bir İlişki Var mı?

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Abstract

Objective: Elevated uric acid (UA) and low levels of high-density lipoprotein (HDL) cholesterol are associated with cardiovascular events and mortality. Erectile dysfunction (ED) has been considered an early marker of cardiovascular disease (CVD). Therefore, this study aimed to investigate the uric acid/ HDL ratio (UHR) as a nowel marker in patients with ED.
Materials and Methods: The study included 147 patients with a mean age of 50 years (range 32-76 years). Retrospective analyses were performed on the patients who were admitted to urology outpatient clinics. The laboratory parameter results were retrieved from the hospital medical records, and the UHR value was calculated. Patients were categorized into three groups according to the International Index of Erectile Function (IIEF) score. UHR was compared between groups, and its predictive value was evaluated using regression analysis and ROC curve analysis.
Results: Age was found to be significantly different in all three groups (Groups 1-2, p=0.001; Groups 1-3, p=0.000; Groups 2-3, p=0.001). It was observed that the degree of ED increased with age. The values of UA and HDL were similar in all groups (p>0.05). In contrast, the UHR value was statistically significantly higher 0.15 (0.083-0.288, p =0.047) in the moderate-severe ED (Group 3). ROC curve analyses revealed that UHR predicted severe ED (IIEF 5-11) with 42.9% sensitivity and 87.3% specificity (AUC:0.66, CI 95% 0.538-0.781, p=0.019).
Conclusion: UHR may serve as a severe ED indicator in patients admitted to the cardiology outpatient clinic since it has a significant association with a low IIEF score.

Keywords: erectile dysfunction, uric acid, high-density lipoprotein, uric acid/ HDL ratio

Öz

Amaç: Yüksek ürik asit (UA) ve düşük yüksek yoğunluklu lipoprotein (HDL) kolesterol seviyeleri kardiyovasküler olaylar ve mortalite ile ilişkilidir. Erektil disfonksiyon (ED), kardiyovasküler hastalığın erken bir belirteci olarak kabul edilmiştir. Bu nedenle, bu çalışmada ED'li hastalarda bir yeni belirteç olarak ürik asit/HDL oranını (UHR) araştırmayı amaçladık.
Gereçler ve Yöntemler: Çalışmaya yaş ortalaması 50 (32-76 yaş aralığında) olan 147 hasta dahil edildi. Üroloji polikliniğine başvuran hastaların retrospektif analizleri yapıldı. Hastaların laboratuvar parametreleri hastane tıbbi kayıtlarından alındı ve UHR değerleri hesaplandı. Hastalar Uluslararası Erektil Fonksiyon İndeksi (IIEF) skoruna göre üç gruba ayrıldı. UHR gruplar arasında karşılaştırıldı; prediktif değeri regresyon analizi ve ROC eğrisi analizi ile değerlendirildi.
Bulgular: Her üç grupta da yaş anlamlı olarak farklı bulundu (Grup 1-2, p=0,001; Grup 1-3, p=0,000; Grup 2-3, p=0,001). ED derecesinin yaşla birlikte arttığı gözlendi. Ürik asit ve HDL değerleri üç grup arasında anlamlı farklılık göstermedi (p>0.05). Buna karşılık, orta-şiddetli ED'de (Grup 3) UHR değeri istatistiksel olarak anlamlı derecede yüksekti 0.15 (0.083-0.288, p=0.047). ROC eğrisi analizi, UHR'nin % 42.9 duyarlılık ve % 87.3 özgüllükle (AUC: 0.66, CI %95 0.538-0.781, p=0.019) şiddetli ED'yi (IIEF 5-11) öngördüğünü ortaya koydu.
Sonuç: UHR, düşük IIEF skoru ile anlamlı bir ilişkisi olduğu için kardiyoloji polikliniğine başvuran hastalarda ciddi bir ED göstergesi olarak kullanılabilir.

Anahtar kelimeler: erektil disfonksiyon, ürik asit, yüksek yoğunluklu lipoprotein, ürik asit/HDL oranı

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Introduction

Sexual health is one of the essential components of global health and good life of quality. Atherosclerotic cardiovascular disease (ASCVD) and vascular sexual dysfunction have similar pathogenesis [1]. Erectile dysfunction (ED) is defined as the inability of erection to last long enough to start and maintain sexual intercourse. About 1/4 to 1/3 of adult men experience this problem [2,3]. ED may develop due to many reasons such as genetic, organic, anatomical disorders, systemic diseases, lifestyle, and environmental factors. Usually, the underlying cause is not single but a combination of several factors [4].

Vascular damage due to endothelial dysfunction prevents adequate vasodilation of the penile vessels in response to sexual stimulation and causes ED. Therefore, vascular ED may be an early manifestation of CVD and is associated with vascular risk factors such as hipertension (HT), diabetes mellitus (DM), dyslipidemia and, smoking [5].

The enzyme xanthine oxidase synthesizes uric acid [6]. Uric acid (UA) to high-density lipoprotein (HDL)-cholesterol ratio (UHR) is a new parameter, which has been investigated in patients with type 2 diabetes mellitus with metabolic syndrome [7]. HDL cholesterol levels are negatively correlated with oxidative stress and the degree of inflammation in chronic diseases [8]. Several epidemiological studies showed significant relationship between serum UA levels and various cardiovascular conditions such as HT, metabolic syndrome, coronary artery disease (CAD), cerebrovascular (CV) disease, and dementia. [9-12].

Studies concluded that there is a significant relationship between uric acid and inflammation. It has been claimed that the effects of uric acid on mortality and poor prognosis occur through its pro-inflammatory mechanism [13]. High uric acid and low HDL lead to poor cardiovascular outcomes by increasing endothelial dysfunction and oxidative stress. Studies have shown that the combined effect of the two causes more damage [14,15]. The related literature shows that, there is limited knowledge about the relationship between UHR and ED. Considering the strong relationship between erectile dysfunction and cardiac diseases, it was hypothesized that the uric acid to HDL ratio, associated with cardiovascular mortality, could predict erectile dysfunction.

Material and Method

This single-center study was conducted on a total of 147 patients with a mean age of 50 years (range 32-76 years). Retrospective analyses were performed on the patients who have been admitted to urology outpatient clinics between 2015 and 2019. The detailed medical history of the study population was retrieved from the hospital medical records. Patients were categorized into three groups according to the IIEF score. Group 1 was formed of patients with an IIEF score of 22-25, without erectile dysfunction, Group 2 of patients with moderate-to-mild ED with an IIEF score of 12-24, and Group 3 of those with an IIEF score of 5-11 with moderate-to-severe ED.

Exclusion criteria were as follows; active malignant disease, systemic inflammatory or infectious disease, surgery or trauma within one month, end-stage renal failure (eGFR<15 ml/min/1.73m^2), liver failure, patients taking medications that may affect serum uric acid levels such as thiazides, furosemide, acetylsalicylic acid, etc. and medicines that may affect serum lipid levels such as statins, fibrates, niacin, etc., and that may affect erectile dysfunction such as beta-blockers, thiazide diuretics, and those with erectile dysfunction due to psychogenic and hormonal reasons.

Age, gender, smoking, and IIEF scores were recorded from the patient files and hospital medical records. Laboratory parameters, such as blood uric acid, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglyceride (TG), were measured using an automatic biochemical analyzer (Architect C8000, USA), and results were obtained from the same database and patient files. The uric acid to HDL ratio (UHR) is calculated by dividing serum uric acid level by HDL cholesterol.

Hypertension was accepted as systolic blood pressure (BP) of ≥140 mmHg or diastolic BP of ≥90 mmHg or both or the use of antihypertensive drugs. DM was defined as the use of anti-diabetic medications or fasting plasma glucose levels ≥126 mg/dL in at least two measurements or a glycated hemoglobin ratio (HbA1c) of ≥6.5%. The study was approved by the Institutional Review Board Ethics Committee of Dr. Sadi Konuk Training and Research Hospital (Approval no: 2021/342). Written informed consent was obtained from all patients.

Evaluation of Erectile Function

ED was evaluated by the Turkish version of the International Index of Erectile Function with five questions (IIEF-5) [16]. This is a self-administered questionnaire in which patient responses are based on their experience during the last four weeks and are scored on a 5-point Likert scale, with lower values representing the poorer sexual function. Total scores are classified as; 22-25: No erectile dysfunction; 17-21: Mild erectile dysfunction; 12-16: Mild to moderate erectile dysfunction; 8-11: Moderate erectile dysfunction; and 5-7: Severe erectile dysfunction [17]. This questionnaire has been shown to provide data on ED 98% sensitivity and 88% specificity [18].

Statistically Analysis

All statistical calculations were made using IBM SPSS statistics vn.25 software. The normality of data distribution was assessed with the Shapiro-Wilk test. Skewed data were expressed as median and minimum-maximum values. Since the data were not normally distributed, the Kruskal-Wallis test was used to compare the groups. ROC curve analysis was used to assess the predictive ability of UHR for ED. Univariate and Multivariate Logistic regression analyses were performed to investigate predictors of ED.

Results

The demographic and clinical data of patients are summarized in **Table 1**. Age was found to be significantly different in all three groups (Groups 1-2, p=0.001; Groups 1-3, p=0.000; Groups 2-3, p=0.001). The degree of ED was observed to increase with age. A statistically significant difference was determined between the three groups in respect of total cholesterol values. Post hoc analyses showed that this difference was between Group 1 (normal patients with IIEF 22-25) and Group 2 (patients with moderate-mild IIEF 12-21) (p=0.036). DM was observed at a higher rate in Group 3. No significant difference was determined between the groups in respect of triglyceride, LDL cholesterol, HDL cholesterol, and UA values (p>0.05 for all).

The laboratory data of the study groups are summarized in **Table 2**. The values of uric acid and HDL were similar in all groups (p>0.05). The UHR value was determined to be statistically significantly higher 0.15 (0.083-0.288, p=0.047) in Group 3 (moderate-severe ED).

Multiple logistic regression analysis was also performed to define the predictive value of variables for the presence of ED. UHR was not found to be an independent predictor of ED [p=0.216, 95% CI for OR:748.11, (0.021-2664.8)], but age predicted ED [p=0.002, 95% CI for OR:1.130 (1.044-1.233)] **(Table 3)**.

ROC curve analyses revealed that UHR predicted severe ED (IIEF 5-11) with 42.9 % sensitivity and 87.3 % specificity (AUC:0.66, CI 95 % 0.538-0.781, p=0.019) **(Figure 1).**

Discussion

The principal finding of the present study was that UHR was statistically significantly higher in patients with moderate-severe ED than in those with mild and mild to moderate ED. Also, UHD predicted severe ED.

Table 1. Clinical characteristics of the study population

	Mean ± SD	Median (min-max)
Age	49.93±9.24	50.00 (32-76)
Smoking (n)	62	42.2
Diabetes Mellitus (n)	39	24.5
Hypertension (n)	61	41.5
IIEF -5	16.90±4.758	18.00 (5-25)
Triglyceride (mg/dl)	159.80±83.373	136.00 (32-422)
HDL-C (mg/dl)	45.25±13.841	42.00 (25-136)
LDL-C (mg/dl)	123.98±37.407	127.80 (41-230)
TC (mg/dl)	198.85±42.621	205.00 (96-314)
Uric acid (mg/dl)	5.61±1.184	5.60 (3-13)
UHR (%)	0.13±0.049	0.12 (0.033-0.288)

IIEF: international index of erectile function; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; UHR: uric acid to hdl-cholesterol ratio

Table 2. Clinical characteristics and laboratory parameters of the study groups

	Group 1 (n=24)	Group 2 (n=102)	Group 3 (n=21)	P- value
Age	41.00 (32-57)	50.00 (33-75)	58.00 (43-76)	0.000
Smoking (n, %)	16 (66.7)	39 (39.0)	7 (33.3)	0.031
Hypertension (n, %)	3 (12.5)	41 (41.0)	17 (27.9)	0.000
Diabetes Mellitus (n, %)	2 (8.3)	21 (21.0)	13 (61.9)	0.000
TG (mg/dl)	140.00 (58-386)	131.50 (32-422)	141.00 (64-350)	0.841
HDL-C (mg/dl)	42.50 (32-136)	42.55 (25-113)	40.00 (28-50)	0.092
LDL-C (mg/dl)	102.00 (30-188)	130.60 (41-230)	120.20 (64-188)	0.103
TC (mg/dl)	170.50 (108-252)	211.00 (96-314)	196.00 (119-253)	0.029
UA (mg/dl)	5.30 (3-9)	5.60 (3-9)	6.12 (4-13)	0.599
UHR (%)	0.11 (0.033-0.201)	0.12 (0.347-0.270)	0.15 (0.083-0.288)	0.047

TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; UA: uric acid; UHR: uric acid to HDL-cholesterol ratio

Table 3. Univariate and multivariate logistics regression analysis for independent predictors of erectile dysfunction

	Univariate		Multivariate	
Parameter	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Age	1.157 (1.074-1.247)	0.000	1.130 (1.044-1.233)	0.002
Smoking	0.307 (0.122-0.773)	0.012	0.456 (0.166-1.253)	0.128
HT	6.444 (1.826-22.747)	0.004	3.171 (0.826- 12.172)	0.093
UHR	63.42 (0.039-1042.8)	0.193	748.11 (0.021-2664.8)	0.216

HT: hypertension; UHR: uric acid to HDL-cholesterol ratio

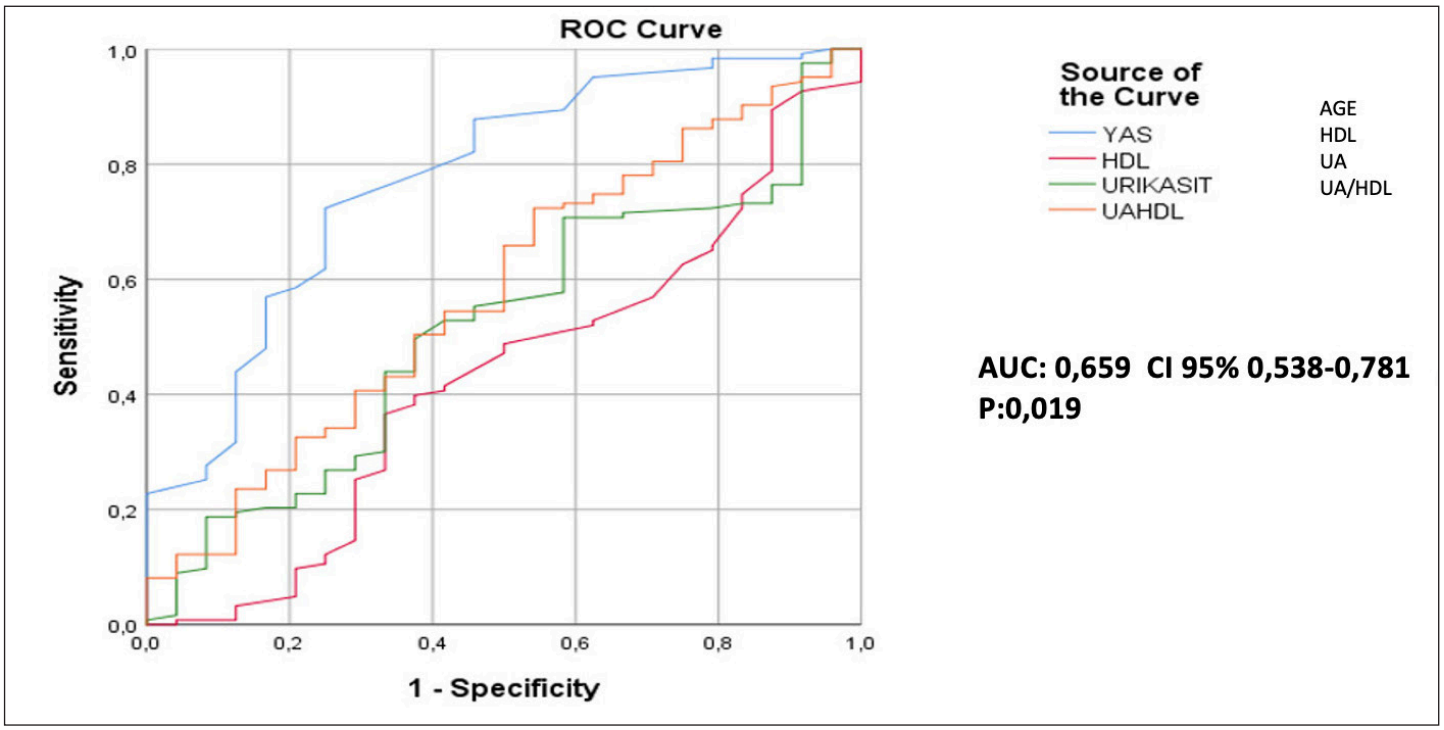

Figure 1. ROC curve of the study parameters in predicting severe ED

Multiple mechanisms such as androgen hormone levels, psychosocial factors, vascular damage, and endothelial dysfunction play a key role in the pathogenesis of ED. It is thought that uric acid may be associated with ED since it affects endothelial and vascular functions [19,20].

Meta-analyses have shown that UA is also a predictor of cardiovascular risk factors such as insulin resistance, HT and the development of renal disease (20-23). Therefore, all these risk factors that cause endothelial and vascular damage are also associated with ED.

UHR is a new marker consisting of two values, namely UA and HDL cholesterol. Using UHR, the degree of inflammation and endothelial dysfunction can be determined which may be involved in ED, indicated by a higher level of UA or a lower level of HDL cholesterol, or both. In a recent study, UHR was reported to be a predictor of metabolic syndrome in type 2 DM patients and was suggested as a marker of high sensitivity and specificity for the control of diabetes. Another study by Ruihua Liu et al. showed a significant association of UHR with cardiovascular mortality in peritoneal dialysis patients with age >65 years, malnutrition, DM, and CVD history [24].

ED may be an early predictor of CVD; thus, it may provide insight for clinicians in investigating risk factors. It was thought that the patients admitted to the cardiology department were reluctant to express complaints of ED. Therefore, it may be important to refer patients with high UHR to urology outpatient clinics for early diagnosis of ED. Thus, early detection of high-risk patients for ED and an early start to treatment will increase their quality of life, and most importantly, reduce the risk of CVD. Thus, early diagnosis of ED can accelerate the diagnosis and treatment of underlying risk factors and prevent major adverse cardiocerebrovascular events [5]. Our study is the first to examine the relationship between uric acid/HDL ratio and erectile dysfunction to the best of our knowledge.

Limitations of the study: The cross-sectional and retrospective design of the study and the limited number of patients can be considered limitations of this study.

Conclusion

UHR may serve as an indicator of severe ED in patients admitted to the cardiology outpatient clinic since it has a significant association with a low IIEF score. More comprehensive prospective cohort studies may yield different results and show that UHR may be a predictor of ED.

Ethics Committee Approval: The study was approved by the Institutional Review Board Ethics Committee of Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey (Approval date, and registration number: 02.08.2021/342)
Informed Consent: An informed consent was obtained from all the patients.
Publication: The results of the study were not published in full or in part in form of abstracts.
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Original Article – Functional Urology

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Can We Use the Silodosin as Second Line Treatment of Benign Prostate Hyperplasia?

Benign Prostat Hiperplazisi Tedavisinde Silodosin İkinci Basamak Kullanılabilinir mi?

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Abstract

Objective: We aimed to investigate the efficacy of silodosin in patients with lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) refractory to previous α-adrenergic receptor (AR) blocker therapy.
Materials and Methods: Patients who did not benefit from alpha-blocker therapy but avoided surgical treatment constitute the population of our study. Seventy-five patients were studied in each group; Group 1 was given 8 mg of silodosin, while Group 2 continued the previous alpha-blocker treatment.
Results: The initial mean international prostate symptom score (IPSS) was calculated as 20.81±0.97 in Group 1, in the third month there was a decrease of 17.12±1.25 ($p<0.05$). No significant change was observed in Group 2. In addition, a significant decrease was observed in IPSS subscores (storage and voiding symptoms) in Group 1 compared to baseline at the third month. There was an improvement in residual urine in the silodosin group and no improvement in the other group.
Conclusion: In patients with BPH who refuse surgical treatment and could not achieve adequate symptom relief with other α-blockers in routine practice, silodosin was found superior in terms of LUTS recovery. Silodosin is also an effective option in patients who cannot undergo surgical treatment due to comorbidities.

Keywords: silodosin, alpha blocker, benign prostate hyperplasia, BPH treatment

Öz

Amaç: Daha önce alfa bloker tedavi ile iyileşme sağlanamayan benign prostat hiperplazisi (BPH) ile ilişkili alt üriner sistem semptomlu (AÜSS) hastalarda silodosin etkinliğinin ortaya konulması amaçlandı.
Gereç ve Yöntemler: Alfa bloker tedavisinden fayda görmeyen ancak cerrahi tedavi istemeyen hastalar bu çalışmaya dahil edildi. Kayıt sırasında, sırasıyla Grup 1 ve Grup 2'ye 75'er hasta kaydedildi. Grup 1 tedavide silodosin 8 mg alan, Grup 2 diğer α blokerleri alan grup olarak belirlendi.
Bulgular: Grup 1'de başlangıçta ortalama IPSS skoru 20,81±0,97 iken üçüncü aylarda anlamlı olarak 17,12±1,25'e düşmesine rağmen, Grup 2'de anlamlı bir değişiklik gözlenmedi. Grup 1'de ise her iki IPSS alt puanı için de düşüş gözlendi, üçüncü ayda başlangıca göre anlamlı olarak azaldı. Üçüncü ayın sonunda silodosine geçildikten sonra bu parametrede ilk değere göre ($p<0,05$) anlamlı bir iyileşme gözlendi. Rezidü idrar ile ilgili olarak silodosin grubunda iyileşme belirgin iken Grup 2'de anlamlı bir iyileşme gözlenmedi.
Sonuç: Bu çalışmada, cerrahi tedavi öncesi rutin klinik uygulamada diğer α-blokerlerle tatmin edici semptom kontrolü sağlanamayan BPH'li hastalarda silodosinin AÜSS iyileşmesi üzerinde etkisi daha fazla bulundu. Silodosin, cerrahi morbiditesi olan BPH'li hastalarda daha etkilidir. Böylece en azından farklı komorbiditeleri olan hastalar cerrahinin morbiditelerinden korunmuş olacaktır.

Anahtar kelimeler: silodsin, alfa bloker, benign prostat hiperplazisi, BPH tedavisi

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Introduction

Benign prostatic hyperplasia (BPH) is a widespread disease among elderly men. It was also known that in men beyond the age of 50 histological BPH will develop [1]. As a result of the proliferation of epithelial and stromal cells, prostate gland growth occurs and it is characterized with an increase in the micturition frequency, difficulties in initiating micturition, nocturia, urgency, a low stream of urine, and a prolonged period of micturition [2]. All these disorders should be called as lower urinary tract symptoms (LUTS). Stimulation of α-adrenergic receptors (ARs), resistance increases in hyperplastic prostate tissue, capsule, prostatic urethra and, bladder outlet. This is an important pathological mechanism in BPH-associated LUTS [3]. α1A-ARs and α1D-ARs mRNA are present in hyperplastic stromal prostate as well as in normal human prostate. Expression of α1A-AR is particularly increased in BPH [4-7]. The stromal α1A-ARs play an important role in the contraction of the prostate and, consequently, in the dynamism of BPH. Their antagonism may explain the relief of micturition difficulty [8]. In the prostatic contraction, the predominance of the α-1ARs subtype may play a primary role, so that this has led to investigation the α-1ARs-selective compounds in the notion of uroselectivity or prostate selectivity [9].

Studies have reported that silodosin has a higher affinity for the α1A-ARs than the α1B-ARs subtype and also higher selectivity for the lower urinary tract. Silodosin has >162-fold greater selectivity for the α1A over the α1B subtype and >50-fold greater selectivity for the α1A over the α1D subtype [10]. Thus, of all commercially available α1-AR blockers, silodosin is the most uro-selective and most potent relaxant in vitro to the prostate mediated by α1-ARs [5,11–14]. Oral silodosin is a highly selective α -1A-ARs antagonist which rapidly improves LUTS caused by BPH and allows the improvements in storage and voiding symptoms [15].

In our study, we evaluated the efficacy of silodosin in patients with LUTS caused by BPH refractory to previous AR blocker therapy.

Matherials and Methods

Prior to this study, approval was obtained from the Derince Training and Research Hospital Ethics Committee (Approval no: 2020/62). In our study, patients who switched to silodosin treatment were retrospectively examined. Patients whose alpha-blocker treatments other than silodosin were ineffective and who did not prefer surgical treatment were included in this study. Other inclusions criteria were as follows: international prostate symptoms score (IPSS) ≥8 points, quality of life (QoL) scale ≥3 points, prostate volume by ultrasonography <40 mL; maximal urinary flow rate (Qmax) <15 mL/s and post-voiding residual (PVR) ≤150 ml; prostate specific antigen (PSA) <4 ng/ml. Exclusion criteria were as follows: patients with a diagnosis of neurogenic bladder, with concomitant prostate or urethral carcinoma, with urinary tract infections, using drugs such as anticholinergic agents, beta-3 adrenoceptor agonists and 5-α reductase inhibitors, and those with a history of prostate surgery.

Study Setting and Design

This was a retrospective, single-center study conducted at urology clinic of Derince Training and Research Hospital.

Study Procedures

The patients were informed that silodosin is a new α-blocker that was recently released that could be more effective for their symptoms and could have a different side effect profile. When the patient agreed to undergo this change, we switched the drug after 2 weeks of washout period. Oral administration of silodosin at a daily dose of 8 mg started.

A total of 150 patients were divided into two equal groups of 75 patients each. Group 1 received silodosin 8 mg and Group 2 received their previous α blocker. The symptom scores and uroflowmetry with PVR evaluation were measured in both groups after 3 months.

Study Endpoints

The primary end-point of evaluation for efficacy was the change in total IPSS from baseline and the quality of life (QoL) scale; secondary end-points were changes in Qmax, residual urinary volume and evaluation of subjective symptoms as IPSS voiding and storage subscores and QoL scale. A 20% decrease in baseline IPSS and a 20% increase in baseline Qmax were considered as improvement [16].

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 15.0 for Windows program was used. For intergroup comparisons Student's t-test, and Mann-Whitney U test were employed. For the comparison of intragroup pre and post-treatment values, analysis of repeated measurements, and Wilcoxon Signed Rank Test were used. Level of statistical significance was accepted as p values lower than 0.05.

Results

Patient Population

There was no difference between the two groups in terms of age, prostate volume, IPSS and Qmax **(Table 1)**. The mean duration of previous drug use was calculated as 22.66±25.84 months. All of the patients in group 1 used silodosin (n=75) and in the Group 2 tamsulosin (n=25), alfuzosin (n=20) and doxazosin (n=30) were used . During the 3-month treatment period, no patients discontinued silodosin due to adverse effects.

Table 1. Comparison of baseline values of both groups (Mann-Whitney U test were used)

	Group 1 (mean±SD)	Group 2 (mean±SD)	P-value
Numbers	75	75	
Age (year)	67,1±2,06	64±2,11	0,989
PV (mL)	38,81±1,94	38,45±1,94	0,491
IPSS (total score)	20,81±0,97	20,77±0,78	0,871
IPSS – storage symptoms	11,09±1,18	11,21±1,19	0,818
IPSS – voiding symptoms	8,55±0,60	10,88±0,73	0,000
Qmax (mL/sec)	8,56±1,58	8,56±1,58	1,000
PVR (mL)	53,67±5,41	53,60±5,30	0,961
QoL	5,19±0,59	5,19±0,59	1,000

PV: prostate volume; IPSS: international prostate symptom score; Qmax: maximum urine flow rate; PVR: post-void residue; QoL: quality of life

Table 2. Comparison of changes in values in both groups (Wilcoxon Signed Rank test were used)

		Pretreatment (mean±SD)	Posttreatment (mean±SD)	Change between pre and posttreatment values (%)	P-value
Group 1	IPSS-total	20,81±0,97	17,12±1,25	17,6	0,000
	IPSS – storage symptoms	11,09±1,18	8,56±0,64	22,3	0,000
	IPSS – voiding symptoms	8,55±0,60	6,99±0,34	18	0,000
	Qmax (mL/sec)	8,56±1,58	11,69±1,20	39,9	0,000
	PVR (mL)	53,67±5,41	35,87±4,96	32,5	0,000
	QoL	5,19±0,59	3,09±0,47	40,2	0,000
Group 2	IPSS-total	20,77±0,78	20,96±0,48	1,0	0,070
	Qmax (mL/sec)	8,56±1,58	8,48±0,67	2,8	0,602
	PVR (mL)	53,60±5,30	57,41±3,65	7,7	0,000
	QoL	5,19±0,59	5,27±0,62	2,0 (%)	0,221

IPSS: international prostate symptom score; Qmax: maximum urine flow rate; PVR: post-void residue; QoL: quality of life

International Prostate Symptom Score (IPSS)

While the initial mean IPSS score was calculated as 20.81±0.97 in Group 1, this value decreased to 17.12±1.25 in the third month with a significant difference ($p<0.05$). No significant change was observed in Group 2. In addition, a significant decrease was observed in IPSS subscores (storage and voiding symptoms) in Group 1 compared to baseline at the third month. Data on IPSS scores are shown in **Table 2**.

Quality of Life Scale (QOLS)

At the end of the third month, a significant improvement in QoL scale was monitored after changing to silodosin, as compared with the first value ($p<0,05$).

Post-void Residue (PVR)

When PVR was compared compared, significant improvement was observed in Group 1 but none in Group 2. After 3 months evaluation , surgical intervention for BPH were applied in 10 (13,3%) patients of the Group 2. The flow chart of study is schematically illustrated in **Figure 1**.

Discussion

To the best of our knowledge, there is many studies for the treatment modalities of BPH with alfa blockers. The guidelines issued by the European Association of Urology (EAU) and American Urological Association (AUA) both states that alpha-blockers should be considered as the first-line medical therapy for men with bothersome, moderate to severe LUTS, and their clinical efficacy are similar in recommended therapeutic dose but for some of these drugs, studies reported that side effect profiles are more favorable [17,18]. Efficacy of all α-AR blockers in appropriate doses seems to be similar in clinical practice treatment efficacy but differs among individuals. Therefore, frequently applied application in clinical practice is switching intra-class α-AR blocker to another [19–21]. One of the surgical indication of BPH is a negative response to conservative pharmacological treatment [22].

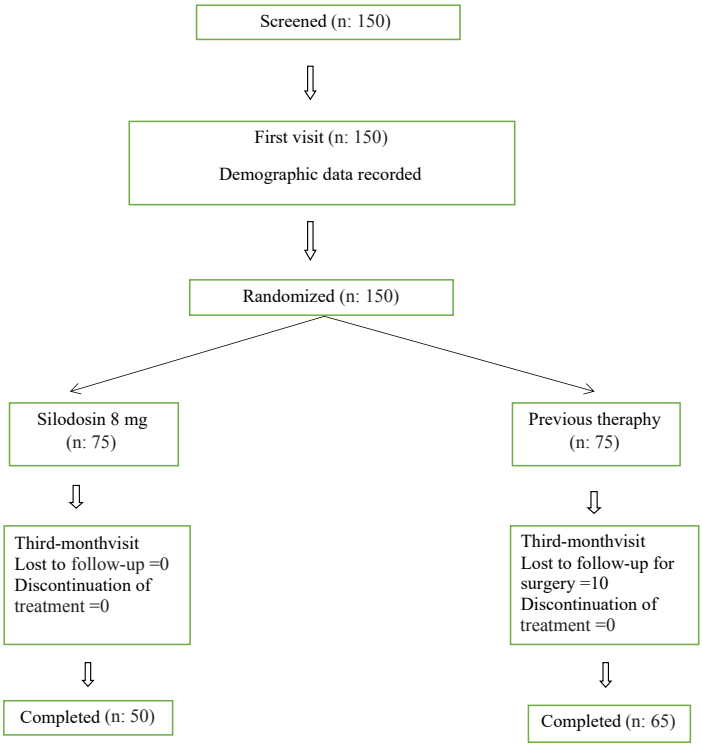

Figure 1. Flow of study participants through the study

In this retrospective study we evaluated the clinical outcomes associated with switching to silodosin in patients who did not respond to other α-AR blockers therapy. According to our study it has demonstrated that in patients refractory to α-AR blockers, silodosin 8 mg therapy can be an alternative for proceeding medical therapy. In LUTS/BPH patients with a poor response to at least 4 weeks of their own α-blocker, switching to silodosin 8 mg improves LUTS/BPH and related QoL.

There are different studies in the literature about switching α-AR blockers to another. Masciovecchio et al. assessed the clinical outcomes associated with switching to silodosin in patients who did not respond to tamsulosin therapy and after a 8-week treatment they found a significant improvement in IPSS total score, and QoL scale [21]. They also analyzed the specific subscores of the IPSS questionnaire and reported that a significant improvement was observed in storage symptoms, but not in voiding symptoms. On the other hand Tanaka et al. reported that switching to silodosin besides improving the other parameters exhibited a more strong effect on voiding symptoms than on storage symptoms, but they have found no significant improvement in the post-micturition symptoms [23]. Recently, a new study was published by Yoshida et al [24] whom declared silodosin as an effective first-line α AR blocker monotherapy, even in those who still have moderate lower urinary tract symptoms in their study. Silodosin, a highly selective α-ARs blocker, is the most recently approved of the commercially available α-blockers [10].

Overall, switching to a 3-months silodosin treatment determined a significant improvement in IPSS total score, and QoL scale was observed. All patients had been previously treated with a recommended treatment associated with LUTS, without showing response; therefore, an improvement in IPSS after switching to silodosin appears clinically relevant.

Noteworthy studies have shown that silodosin also improves the urodynamic parameters [25–27]. In this way silodosin improves voiding, and storage symptoms and Qmax in men with LUTS associated with BPH [15]. In our study, silodosin exhibited a strong effect on both voiding symptoms and on storage symptoms.

This present study has some limitations due to the number of patients which each study arm was relatively small, the short duration of observation, and the lack of a control.

Conclusion

In patients with BPH who did refuse surgical treatment and could not achieve adequate symptom relief with other α-blockers in routine practice, silodosin was found superior in terms of LUTS recovery. Decrease in IPSS, PVR and increase in Qmax and QoL scale were higher in the group receiving silodosin treatment compared to the group using other alpha blockers. Silodosin is also an effective option in patients who cannot undergo surgical treatment due to comorbidities.

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences, Derince Training and Research Hospital, Kocaeli, Turkey (Approval date, and registration number: 11.06.2020/62).
Informed Consent: An informed consent was obtained from all the patients.
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Review Article – Urological Oncology

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Focal Ablation Therapies in Prostate Cancer

Prostat Kanserinde Fokal Ablasyon Tedavileri

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Abstract

Focal ablation therapies in prostate cancer have been actively evaluated in the light of recent literature. According to published data,focal ablation therapies appear to be well tolerated and have an acceptable side effect profile. Moreover, while clinical outcomes were not homogenous, short-term oncological results of some focal ablation therapies such as laser and irreversible electroporation (IRE) have been found as good as curative ones. While waiting long-term oncological results, focal ablation therapies in prostate cancer are beinmg used increasingly.

Keywords: focal therapy, ablation therapy, prostate cancer, MRI

Öz

Prostat kanserinde fokal ablasyon tedavileri güncel literatür eşliğinde aktif olarak değerlendirilmiştir. Yayınlanan verilere göre, tedaviler iyi tolere ediliyor ve kabul edilebilir bir yan etki profiline sahip görünüyor. Dahası, klinik sonuçları homojen olmamakla beraber, lazer ve irreversible elektroporasyon (IRE) gibi bazı fokal ablasyon tedavilerinin kısa vadeli onkolojik sonuçları, küratif tedavinin sonuçları kadar iyi bulunmuştur. Uzun dönem onkolojik sonuçları beklerken, prostat kanserinde fokal ablasyon tedavileri giderek daha fazla kullanılmaktadır.

Anahtar kelimeler: fokal terapi, ablasyon tedavisi, prostat kanseri, MRI

Introduction

Localized prostate cancer is the most common cancer in males today [1]. Most commonly used curative therapy methods among the therapies applied for prostate cancer are surgery or radiotherapy-based treatment modalities. However, these therapies have severe short-, and long-term side effects [2]. Active surveillance and follow-up protocols aim to save the patients from treatment-related side effects. Known slow progressive course of prostate cancer can only enable follow-up through surveillance in some prostate cancer types. Severe side effects which may be caused by complete resection or treatment of especially low- or intermediate- risk prostate cancer may shadow treatment success. Although complete resection or radiotherapy of the prostate in high volume or high-risk prostate cancer is still an important treatment option, imaging-guided focal ablation therapies in other prostate cancer types have currently become important treatment alternatives [3].

Magnetic resonance (MR) imaging has made an undeniable contribution in popularization of focal ablation therapies in prostate cancer. Targeted biopsies have now replaced standard biopsies in prostate cancer thanks to multiparametric MR imaging. Focal ablation or hemiablation options has been started to be used in visible prostate lesions. Focal ablation therapies have become the standard treatment option in renal cell carcinoma and solid organ tumors such as thyroid, liver, breast and pancreas. Multifocal character of the tumor is the most important obstacle for the focal ablation therapies in prostate cancer. In addition, the close proximity of the tumor to rectum and nerves controlling erectile and the need to preserve continence mechanism are vital issues worth considering.

Lesions over 0.5 cm3 are known as clinically significant cancer markers in prostate cancer. Based on prostate cancer surveillance studies, prostate tumors less than 1.3 cm3 have a lower possibility of becoming clinically significant. It should not be forgotten that clinically insignificant tumors under 0.5 cm3 in size can be aggressive or can reach high volumes. Thus random biopsy is still the standard application in addition to the pathological samples taken from the target lesion [4].

The objective of this review was to compare the focal ablation techniques used recently in prostate cancer treatment.

Focal Ablation Types and Clinical Results

Irreversible Electroporation (IRE) (NanoknifeTM)

Many thermal-energy based techniques are used to induce cellular damage. While most of these operate with high thermal energy, some depend on cooling-based techniques. Irreversible electroporation (IRE) causes non-thermal cellular damage through a different system. Direct flow rhythmically applied with low energy on the cell induces cellular apoptosis by keeping all cell wall pores open. Energy used in IRE is provided through the needles inserted into the tissue. The energy applied through a special device is monitorized through ultrasound (US).

IRE was first applied in 16 locally advanced prostate cancer patients by Onik et al. Side effects such as erectile dysfunction and urinary incontinence were not observed in these patients [5]. Later on Valerio et al. published their IRE experience in 34 patients and mentioned inadequate treatment only in one patient [6]. In the study by Van den Bos et al., IRE treatment was applied one month before the operation in 16 patients who would undergo radical prostatectomy Histopathological evaluation of post-radical prostatectomy specimens showed satisfactory ablation in targeted areas without skipping any lesion [7]. IRE treatment was applied in 123 patients diagnosed with locally advanced prostate cancer in the largest biopsy- controlled study and ablation success rate up to 97% was achieved in the control biopsy samples taken from the treatment area at the end of 1 year. In this study, it was shown that urinary continence was achieved in 98.8% of the patients and potency didn't change in 76% of the patients at the end of 12 months [8].

Photodynamic Therapy (PDT)

In photodynamic tissue ablation tumoral tissue is destructed through the activation of vascular photo stimulators under light at certain wavelengths. As a result, the number of free radicals in the tissue increases. Following the intravenous application of photo stimulators, laser is applied transperineally or transrectally at certain wavelengths.

One hundred and sixteen stage cT1 and cT2b prostate cancer patients were treated in a prospective study performed using photodynamic therapy (PDT). Median PSA value was 6.4 ng/ml for patients with low and intermediate - risk prostate adenocarcinoma. While no clinically significant cancer was detected in any of the patients, clinically insignificant cancer was detected in 46% of the patients at the end of six months. While no continence data was available, 88.4% of the patients had maintained their potency [9,10].

High-intensity Focused Ultrasound (HIFU)

In high-intensity focused ultrasound therapy, tissue ablation through thermal energy is accomplished using focused ultrasound. Temperature over 60 °C is generally achieved in the tissue. HIFU induces formation of coagulation necrosis and cavitations in the targeted tissue. It is the only system among focal applications which doesn't use needles or electrodes. It can be applied transrectally or transurethrally using the new high-intensity focused ultrasound (HIFU) systems.

Many studies including more than 300 prostate cancer patients have been performed. The results are variable due to the non-homogeneous character of the studies and different application methods. Targeted prostate biopsies were performed in most patients. Secondary treatment starting rate was reported as 7.8% in the studies completing post-treatment 12 surveillance months. While continence rate was reported as 100%, potency was maintained in 88% of the patients [11–13].

Cryotherapy

This ablation system uses thermal energy. Extreme tissue cooling causes cell death by inducing osmotic cell injury. Cooling is performed on the targeted area using transperineally

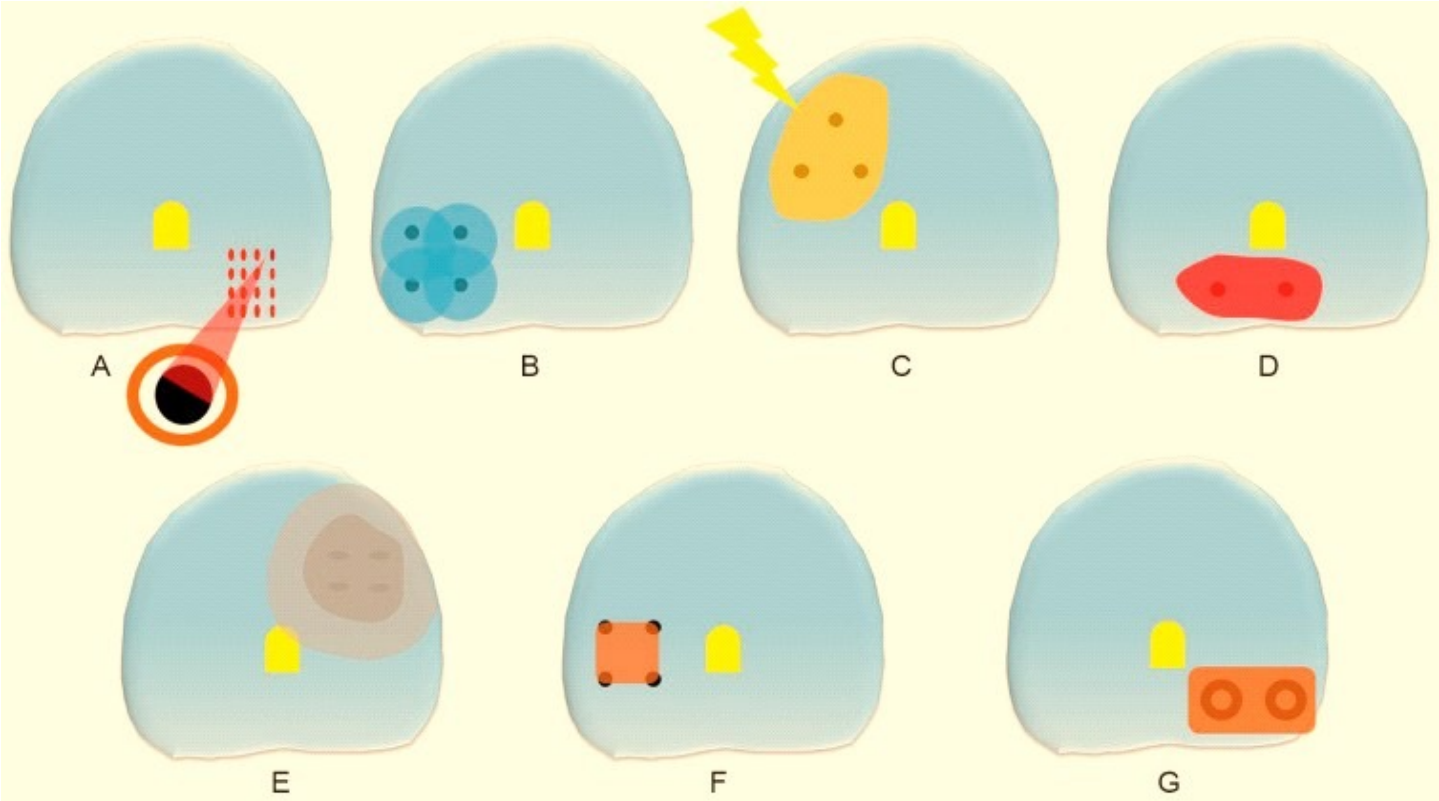

Figure 1. Focal ablation therapies used for prostate cancer treatment. A: high-intensity focused ultrasound (HIFU); B: cryotherapy; C: photodynamic therapy (PDT); D: focal laser ablation (FLA); E: brachytherapy; F: irreversible electroporation (IRE); G: radiofrequency ablation (RFA) (Valerio M, et al. New and Established Technology in Focal Ablation of the Prostate: A Systematic Review. Eur Urol 2016 reproduuced with permission obtained from authors).

inserted needle electrodes. Ice ball image is seen between cryo-needles.

A quite high number of patients have been treated and followed up for longer periods of time. Most of these studies had a retrospective design. Secondary treatment has been started at a rate of 7.6% in the studies with one-year follow-up period. Severe side effects were reported in 2.5% of the cases. Continence was preserved in 100%, and, potency was maintained in 81% of the patients [14–17].

Focal Laser Ablation (FLA)

In FLA, laser therapy is directly applied on the targeted area. Interstitial coagulation necrosis in the tissue is generally formed through the use of neodymium or diode laser. Thermal energy applied raises the temperature in the targeted tissue up to 60 °C. Increase in tissue temperature is monitored through thermal receptors during the operation. A single laser probe is generally used in transperineal or transrectal applications.

FLA has been performed on patients with low and intermediate risk, and average PSA value was reported as 5.4 ng/ml. As the long-term results of the patients have not been acquired yet, secondary application rate is not certain. Continence and potency preservation rates were reported as 100% [18,19].

Radiofrequency Ablation (RFA)

In RFA tissue ablation is achieved through thermal energy. Coagulation necrosis of the tissue is performed through the provision of alternative flow in the targeted area using the transperineally inserted needles..

Pathological results were reported for 15 patients who had received RFA before radical prostatectomy. Tumor persisted in all patients. No other treatment aiming study was reported [20].

Discussion

There are six actively used systems now among focal ablation therapies **(Figure 1)**. Most of these uses a thermal energy source, and only IRE achieves tissue ablation using non-thermal energy. Radiation-based therapies used in brachytherapy should not be included, and evaluated within this group, because it is a locally applied alternative form of radiotherapy. Due to its adverse outcomes, RFA treatment is not actively used now. Transurethral applications can now be performed thanks to the renewed application apparatus of HIFU. The most important difference of HIFU from other methods is the direct energy focused by the probe without the use of any electrode or needle. Thermal damages which may form on nonlesioned areas can be more frequently encountered than other methods which is seen as a partial advantage of the method. This ablative effect was shown to continue at least 0.5 cm outside the targeted area in tissue ablations performed using thermal energy sources. It is known that the hotness of thermal energy source in cold or HIFU, laser treatments as in cryotherapy doesn't change this effect. Thus good mapping is required for the targeted areas to prevent treatment insufficiency.

Although the highest number of studies has been performed

with HIFU and cryotherapy, many recent studies on PDT, focal laser ablation and IRE also continue. Easy applicability and clearer prediction of the borders of the region of interest of thermal effect constitute the most important characteristics of laser ablation. The results of the continuing prospective studies will present the treatment efficiency more clearly. The studies performed with IRE known as non-thermal energy source were similarly found to be quite successful. The rates of succesful oncological results at the end of follow-up periods of over one year were found to be equivalent to those of the radical interventions [4,8].

Relatively higher side effect incidence and morbidities of established curative treatments constitute the most important justification for more frequent application of focal ablation therapies. These curative treatments become a severe burden both for the patient and the treating health units. If the same oncological result will be acquired through less invasive treatment methods and if the side effect profile is lower, whatever treatment method you use will be more popular. Side effect rates of focal ablation therapies in applied for prostate cancer are quite lower than known curative treatment methods. They have very good results especially in terms of preservation of continence and potency. Similar results were acquired in limited studies comparing oncological results of these treatment modalities [8,10,13,19,20].

A great progress has been achieved in prostate cancer diagnosis and treatment thanks to the high performance provided in multiparametric MR. We detect the lesions more clearly and correctly thanks to especially different diffusion characteristics of the tissues Thus, it is possible to recognize clinically important cancer focuses with rates up to 95% and to apply focal ablation therapy. In many multi-centered studies multiparametric MR has established its worth in the diagnosis and treatment follow-up in prostate cancer [21–23].

Conclusion

Conduction of the studies with different energy sources prevents making homogeneous comparisons among studies performed.. Standard patient approach couldn't be provided even in focal ablation therapies conducted with the same energy source. Thus, we couldn't get adequate, and accurate data from studies comparing outcomes of focal ablation therapies. But we expect that the focal therapy is now possible for the treatment of low-and intermediate-risk prostate cancer patients, and more importantly better results can be acquired.

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Review – Neurourology

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The Effects of the Autonomic Nervous System on Urogenital Disorders

Otonom Sinir Sisteminin Ürogenital Hastalıklar Üzerindeki Etkileri

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Abstract

The possible effect or activity of the autonomic nervous system (ANS) in urogenital disorders is still controversial. Day by day, further studies that have proved the association between chronic urological situations like chronic pelvic pain, premature ejaculation, etc., and autonomic dysfunction have been published. Understanding the actual role of the autonomic nervous system on chronic pelvic disorders will be of interest soon.

Keywords: autonomic nervous system, chronic pelvic disorder, urogenital disorders

Öz

Otonomik Sinir Sistemi'nin (OSS) ürogenital hastalıklardaki olası etkisi ve aktivitesi hala tartışmalıdır. Gün geçtikçe, kronik pelvik ağrı, prematüre ejakülasyon gibi kronik ürolojik durumlar ve otonomik disfonksiyon arasındaki ilişkiyi kanıtlayan çalışmalar yayınlanmaktadır. Otonomik sinir sisteminin kronik pelvik hastalıklardaki gerçek rolü, yakın gelecekteki ilgi alanlarından biri olacaktır.

Anahtar kelimeler: otonom sinir sistemi, kronik pelvik hastalık, ürogenital hastalıklar

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Introduction

Autonomic nervous system (ANS) consists of the sympathetic, parasympathetic, and enteric nervous systems. Despite the well-understood vital properties like energy storage and consumption, reproduction, and excretion, the possible effect or activity level in pathologic circumstances are still under investigation and have not been completely defined.

In this review article, the effects of ANS dysfunction on urogynecological problems like urinary incontinence, interstitial cystitis, infertility, premenstrual syndrome, pelvic pain, polycystic ovary syndrome (PCOS) were investigated. Also, the relationship between ANS and erectile dysfunction and premature ejaculation was discussed briefly. The issue of this review article was related to disorders that are mainly attributed as idiopathic disorders and/or those within physiologic limits. Pathologies like mechanical, anatomical, infectious, neuronal, or vascular damage were excluded.

Estrogen

Estrogen leads to vasodilatation in both arteries and veins. The levels of circulating estrogen may not reflect the total activity because their levels in the tissue and their intracellular activities are influenced by concentrations of enzymes like aromatases. The reduction in the estrogen levels causes sympathetic overactivity and an increase in norepinephrine levels in the blood [1]. It controls sympathovagal balance centrally and prevents sympathoexcitation. Estrogen receptors are localized on autonomic neurons from the spinal cord to the brain. The injection of estrogen to the rats increases vagal parasympathetic activity and decreases renal sympathetic activity [2].

However, there are still questions about the effects of estrogens on ANS and the cardiovascular system [3]. Sympathetic nerve activity does not change during the menstrual cycle in young eumenorrheic women but orthostatic stress causes different sympathetic responses in the early follicular and mid-luteal phases. Although the sympathetic baroreflex sensitivity remains stable, the sympathetic response increases during the mid-luteal phase [4]. This may due to vasodilatation in the mid-luteal phase as a result of elevated estrogen or regression of estrogen dominance by progesterone. Consequently, estrogen seems to have an impression on ANS but the accurate measurement and the way of affection are still undefined.

PCOS and Infertility

Polycystic ovary syndrome (PCOS) is a metabolic disorder with oligo/anovulation and hyperandrogenism [5]. Obesity, hyperinsulinemia, obstructive sleep apnoea are frequently associated with sympathetic nervous system (SNS) hyperactivity which can be an etiologic precipitant or a result. The local or widespread sympathetic predominance in ovary is correlated with testosterone levels. Weight loss, insulin sensitizers, electroacupuncture, continuous positive airway pressure can decrease sympathetic hyperactivity and are beneficial in the treatment of PCOS [5]. Tekin et al. found that PCOS patients have reduced vagal activity through decreased heart rate variability, impaired heart rate, and recovery of systolic blood pressure after exercise [6]. Yildirir et al. also showed similar results in the same patient group [7]. High sympathetic activity is strongly associated with testosterone level and in combination, they enhance vascular problems in PCOS [8].

Stener-Victorin et al. hypothesized that impaired β-endorphin function, its increased production, and release have a role in the PCOS process. Low-frequency electro-acupuncture (1-15 Hz) decreases central β-endorphin concentration and sympathetic tone [9]. This possibly regulates the secretion of gonadotropin-releasing and gonadotropin hormones in addition to the decline in ovarian androgen production [9,10]. Low-frequency electro-acupuncture and physical exercise exert similar effects on disease behavior in long-term follow-up, and partial healing with the decrement in the activity of the sympathetic nervous occurs [11].

For infertility, despite opposite results [4], we can accept a sympathetic tendency or mild elevation during the second half of normal menstrual cycles as Yuna et al. mentioned. They also declare that this tendency is essential for T helper balance for fertility. Sympathetic and T helper-2 activity-related disorders mostly worsen in the luteal phase [12]. Although ovarian hormones are accounted for this process, autonomic dysfunction also must be kept in mind. T helper-2 cells and related cytokines allow the development of allograft tolerance [12]. Smoking is a well-known risk factor for infertility [13,14]. Park et al. found that sympathetic nerve activity does not decline in the early follicular phase compared with the mid-luteal phase in premenopausal smokers which may be crucial for fertility. Smoking exerts its effects on the cardiovascular and reproductive system also via impaired SNS activity [15].

Urinary Incontinence and Interstitial Cystitis

ANS function is essential for normal urinary system functioning. The parasympathetic nervous system regulates bladder contraction, sphincter relaxation, and SNS does the opposite. Idiopathic overactive bladder syndrome (IOBS) causes urgency with or without incontinence. Both sympathetic and parasympathetic activity is attenuated in the overactive bladder and autonomic imbalance exists [16-19]. Hubeaux et al. declared a sympathetic ANS dysfunction especially in IOBS patients without detrusor overactivity [20]. However, Sauver et al. stated that men with lower urinary tract symptoms do not have a high sympathetic tone or ANS dysfunction [21].

Hyperthyroidism can cause increased sympathetic and decreased parasympathetic activity. The imbalanced ANS in hyperthyroidism may also cause lower urinary tract symptoms and in patients with hyperthyroidism urinary incontinence risk increases [22]. Hyperthyroid women have lower peak flow rates of micturition and this resolves in the euthyroid state [23].

Interstitial cystitis is an idiopathic illness with visceral sensory hypersensitivity characterized by increased urinary frequency/urgency and pelvic pain [24]. Pelvic pain worsens as the bladder fills and resolves with emptying. Interstitial cystitis or painful bladder syndrome coexists with other central

and autonomic nervous system disorders like irritable bowel syndrome, fibromyalgia, chronic pain, migraine, syncope, and functional dyspepsia so it is like a part of systemic disorder or syndrome, and does not affect only bladder [25]. SNS dysfunction or predominance could be the underlying pathology of these disorders [26]. An extra information we can say about the urinary system and ANS is that the impairment of parasympathetic nerve function is associated with asymptomatic leukocyturia [27].

Evidence generally supports ANS dysfunction in IOBS, interstitial cystitis, etc. but possibly because of its nature we find sometimes contradictory results related to functions of ANS.

Pelvic Pain

Pelvic pain seems mostly a gynecologic complaint but it can emerge from pelvic floor muscle and viscera or surrounding structures like lumbosacral, hip, and sacroiliac joints [28]. There is limited, insufficient but supporting evidence about the existence of autonomic dysfunction in chronic pelvic pain. Dysmenorrhea, dyspareunia, pain with bowel movements accompany this prevalent disorder [29]. Baker et al. found that parasympathetic activity during sleep is decreased in premenstrual syndrome patients when they are symptomatic in the late luteal phase of the cycle [30]. Spinal cord stimulation seems an effective way of treatment in chronic intractable pelvic pain. One possible mechanism is the downregulation of the sympathetic outflow to the pelvis [31].

Yilmaz et al. found that ANS dysfunction exists in men with chronic prostatitis/chronic pelvic pain syndrome. They found findings related to heart rate variability similar to fibromyalgia [32]. Cho et al. also supported this information by pointing out that autonomic dysfunction may be one of the underlying mechanisms in the development of chronic pelvic pain [33].

Erectile Dysfunction and Premature Ejaculation

The parasympathetic nervous system causes penile arterial dilatation and relaxation of the smooth muscles of the corpora cavernosa [34]. Pelvic diseases like erectile dysfunction, premature ejaculation, benign prostatic hyperplasia, incontinence, overactive bladder, pelvic pain, colorectal motility disorders seem to have a connection with each other possibly via the ANS network. The deterioration of the function of a structure also leads to the inevitable impairment of the adjacent structures [35]. Erectile dysfunction is characterized by ANS imbalance/dysfunction and SNS hyperactivity [36-38]. In normal conditions, ejaculation is maintained by SNS, however premature ejaculation is also associated with SNS hyperactivity like erectile dysfunction [39].

Conclusion

The role of ANS dysfunction for all of the aforementioned disorders is still unclear. In general, we can not directly measure the status of ANS so we based our findings on only the clues we gathered. Studies have conflicting results which compel us to reconsider this issue. Rather than dysautonomia, autonomic dysfunction is mainly a disorder behind the mirror. However, there is still a question that needs to be answered about ANS dysfunction; “Is it a result or a cause of all these aforementioned disorders?”

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Case Report – Functional Urology

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Presentation of a Rare Case: Acute Kidney Failure Developed Following Complete Urinary Bladder Herniation and Management of Postoperative Voiding Dysfunction

Nadir Bir Vaka Takdimi: Komplet Mesane Herniasyonu Sonrası Gelişen Akut Böbrek Yetmezliği ve Postoperatif Miksiyon Bozukluğunun Yönetimi

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Abstract

Inguinal bladder herniation is seen in 1% -4% of all inguinal hernia cases; most of them are asymptomatic and come up with swelling in the groin. In symptomatic cases, nonspecific findings such as lower urinary tract symptoms or pain due to strangulation of the hernia sac are seen. Two-stage micturition (manual pressure to the scrotum to empty residual urine) is a pathognomonic sign for the advanced case. Vesicoureteral reflux (VUR), bilateral hydronephrosis, urinary tract infection, acute kidney failure and bladder wall necrosis are complications that may be seen if the problem is not appropriately managed. Preoperative diagnosis rates are low (<7%) and 16% of the cases are diagnosed in the postoperative period, and most cases are detected intraoperatively. Radiologic examination performed for other indications such as non-contrast abdominal computed tomography (CT) may diagnose the bladder herniation. CT, cystography and ultrasonography are the techniques that can be used in the diagnosis and differential diagnosis. Intraoperatively, reduction of the herniated bladder with herniorrhaphy is a routine procedure. Partial cystectomy has to be made in case of bladder wall necrosis, presence of a tumor in the herniated bladder and narrow bladder neck which don't allow reduction.
In this case report, our aim is to explain the management of left inguinoscrotal complete bladder herniation and postoperative voiding problem.

Keywords: bladder, herniaton, kidney, kidney failure

Öz

Kasık mesane herniasyonu tüm kasık fıtığı vakalarının% 1-% 4'ünde görülür. Çoğu semptomatik değildir ve kasıkta şişlik ile ortaya çıkar. Semptomları olanlarda; alt üriner sistem semptomları veya fıtık kesesinin boğulmasına bağlı ağrı gibi spesifik olmayan bulgular görülür. İleri evre herniasyonlarda iki fazlı işeme (artık idrarı boşaltmak için herniye bölgeye el ile bastırrma) bulgusu patognomonik bir işarettir. Vezikoüreteral reflü (VUR), bilateral hidronefroz, idrar yolu infeksiyonu, akut böbrek yetmezliği ve herniye mesane duvarı nekrozu, vaka uygun şekilde yönetilmezse görülebilecek komplikasyonlardır. Operasyon öncesi tanı oranları (<%7) düşüktür ve vakaların %16'sı postoperatif dönemde tanı almakta, çoğu vaka ise intraoperatif tespit edilmektedir. Kontrastlı olmayan abdominal bilgisayarlı tomografi (BT) gibi başka nedenlerle yapılan radyolojik incelemelerde mesane herniasyonunu teşhis edebilir. Tanı ve ayırıcı tanıda bilgisayarlı tomografi, sistografi ve ultrasonografi kullanılabilecek tekniklerdir. Operasyon sırasından herniye mesanenin redüksiyonu ve defektin onarımı yeterli olup, herniye mesanenin nekrozu, içinde tümör varlığı veya redüksiyona izin vermeyen dar mesane boyun durumlarında parsiyel sistektomi yapılmalıdır.
Bu olgu sunumunda amacımız sol inguinoskrotal tam mesane herniasyonunun ve postoperatif dönemde gelişen işeme sorununun yönetimini açıklamaktır.

Anahtar kelimeler: mesane, herniasyon, böbrek, böbrek yetmezliği

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Introduction

Inguinal bladder hernia was described first in 1951 by Levine [1, 2]. Although bladder herniation is seen in 1%-4% of cases with inguinal herniation, massive herniation of the bladder is very rare. Incidence of bladder herniation increases in obese people, males, and individuals aged >50 years [3, 4].

Most of the patients with bladder hernias are asymptomatic and diagnosed during inguinal hernia repair [5]. Less than 7% of patients are diagnosed preoperatively, and 16% of them postoperatively because of complications [6].

There are nonspecific urologic symptoms because of urinary retention , such as urgency, frequency, nocturia. Urinary tract infection, bilateral hydronephrosis, renal failure and bladder infarction may be seen if it isn't diagnosed timely and properly [7].

We present the case of a male patient who came to the emergency department with the complaint of scrotal swelling that had been present for one week. He had left inguinoscrotal hernia and the entire bladder of the patient was herniated into the inguinal canal, and also acute kidney failure developed.

Case Presentation

Fifty-six years old man who had scrotal swelling for seven days came to the emergency department. From his medical history we have learned that he had diabetes mellitus, hypertension and benign prostatic hyperplasia (BPH) and used an oral antidiabetic drug, calcium channel blocker for hypertension and alpha-blocker for BPH. Despite medical therapy used for BPH, he suffered from lower urinary tract symptoms. During his physical examination, bilateral pretibial grade 2 edema was found, and his biochemical analysis revealed higher urea and creatinine levels. His anamnesis revealed two stage micturition (manual pressure to the scrotum to empty residual urine). Nonenhanced computed tomography (CT) was taken by emergency department physicians before the urologic examination to explain postrenal etiology in acute kidney failure. CT scan revealed grade 2-3 bilateral hydronephrosis. Diameters of both ureters increased. A catheter balloon was observed in the bladder. The bladder was herniated into the left inguinal canal, and the ureters opened to the bladder at the level of the inguinal canal. Before the planned operation, cystography was taken **(Figure 1)**.

Intraoperative findings demonstrated a giant direct left inguinoscrotal hernia with total herniation of the bladder into the scrotum. The bladder was reduced into the abdominal cavity without complication followed by herniorrhaphy. A closed suction drain was placed in the scrotum, and removed on the postoperative second day. Antibiotic treatment was started due to fever on the third postoperative day. After ten days of intravenous antibiotic treatment which recommended by infectious disease department, the patient was discharged with a urethral catheter and normal renal function values. The urethral catheter was removed after the control cystogram obtained one week after discharge **(Figure 2)**. Cystogram revealed that the bladder was in its anatomical position. Unfortunately, urodynamics was planned because the patient was unable to urinate after the catheter was removed. In urodynamics, detrusor pressures did not increase despite 500 cc of isotonic fluid instilled during urodynamic examination, and the patient could not urinate **(Figure 3)**. Clean intermittent self-catheterization four times a day and maintenance of daily use of an alpha-blocker was recommended. At the control visit planned three months later, it was determined that the need for clean intermittent catheterization decreased to 2 times a day, and he started to urinate spontaneously.

Discussion

Herniation of the bladder accounts for approximately 1% -4% of inguinal hernias. After the 5th decade, the incidence of bladder herniation reaches up to 10% [2]. The inguinal herniation is often seen in males and into the right inguinal canal [2, 7-9]. The conditions that are thought to play role in the pathophysiology of bladder herniation as a risk factors in studies performed to date are as follows: a) aging, b) obesity, c) bladder outlet obstruction, d) decreased bladder tone and weakness in the pelvic muscles [3, 4, 10]. In our case, the patient was over 50 years old, obese and using alpha-blockers due to benign prostatic hyperplasia.

Patients with inguinal bladder herniation are generally asymptomatic, and the majority of patients present with complaints of swelling in the groin [5, 6]. In the anamnesis, usually accompanying lower urinary tract symptoms are detected. Addi-

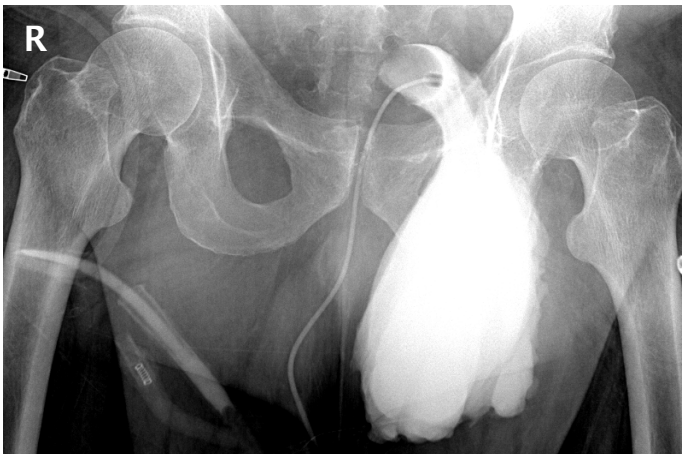

Figure 1. Preoperative cystogram

Figure 2. Control cystogram (postoperative 20th day)

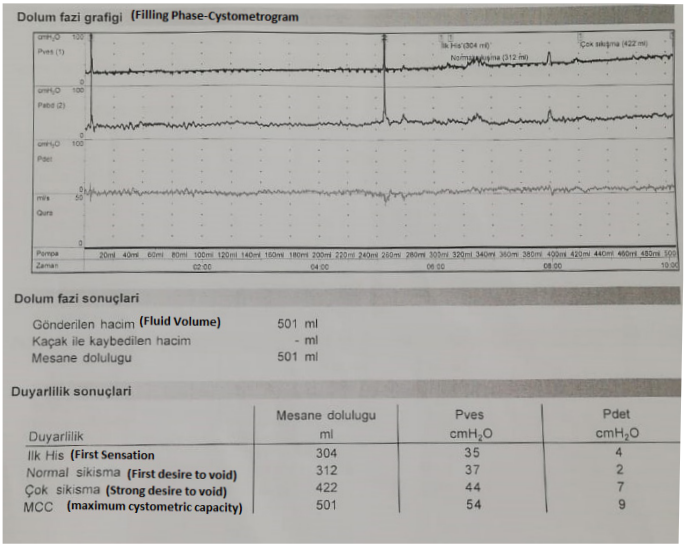

Figure 3. Urodynamic study (postoperative 22nd day)

tionally, pain due to strangulation of hernia, diminish in scrotal size after voiding and two-stage urination are seen in advanced stages [7, 11]. In our case, the patient applied with the complaint of scrotal swelling that had been present for one week. In the questioning, it was seen that the patient used alpha-blocker due to lower urinary tract symptoms secondary to benign prostatic hyperplasia.

Complications of inguinal bladder herniation include bilateral hydronephrosis with or without acute renal failure, vesicoureteral reflux, sepsis, cystolithiasis, strangulation and bladder wall necrosis [2, 6, 7, 12, 13]. In our case, there was acute renal failure developed together with bilateral hydronephrosis and, luckily, there was no ischemic appearance in the bladder wall.

Herniation of the bladder into the inguinal canal is usually detected during surgical repair of hernia [3, 14]. Less than 7% of the cases are diagnosed preoperatively, and 16% of them in the postoperative period due to postoperative complications [6]. Risk of bladder injury due to intraoperatively detected inguinal bladder herniation was reported in 12% of the cases [3, 6, 15, 16]. In our case, luckily, non-contrast CT was performed by emergency physicians to clarify acute renal failure detected in laboratory tests. In this way, preoperative diagnosis was made, and possible complications and surprises were avoided. CT, cystogram, IVU and USG are among the radiological methods that can be used for diagnosis [2, 3]. CT and cystogram were also used in our case.

After the reduction of the bladder to its anatomical location during the procedure, the repair of the defect with mesh is the routine treatment to prevent recurrence of inguinal herniation [6, 7, 14]. We didn't use mesh to repair the existing defect after the reduction of the bladder because of the deficiency of our equipment. Routine resection of the herniated bladder which is an older practice is only applied in cases such as bladder wall necrosis, the presence of tumor in the herniated tissue and a tight hernial neck [2, 5, 6, 12, 17]. We didn't make any resection.

In conclusion, inguinal herniation is not a simple entity. Herniation of the bladder into the inguinal canal should come to mind in the presence of risk factors. Before the hernia repair operation, at least a simple radiological examination should be requested to prevent undesirable results. It should be kept in mind that there may be voiding difficulties after the procedure and the patient should be monitored with conservative interventions.

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Case Report – Urological Oncology

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A Rare Prostate Pathology: Mantle Cell Lymphoma: A Case Report and Literature Review

Prostatın Nadir Bir Patolojisi: Mantle Cell Lenfoma: Bir Vaka Sunumu ve Literatür Taraması

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Abstract

Primary or secondary lymphoma of the prostate is a rare condition. Mantle cell lymphoma (MCL) represent 4-9% of all lymphomas. Prostate involvement with MCL is very rare, with only 11 reported cases up to now. Here we present a case with lower urinary tract symptoms and prostate-specific antigen (PSA) elevation diagnosed with MCL of the prostate. Prostate biopsy was performed in a 70-year-old patient due to increased PSA. After the pathology result was reported as prostatic MCL, imaging studies and sampling of additional pathological specimens were performed for staging. An improvement was observed in the urinary system complaints of the patient who started chemotherapy regimen. While prostatectomy was performed in some of the prostatic MCL cases reported previously, in some, no additional treatment was required after chemotherapy. Our case is the only prostatic MCL case with elevated PSA levels, but did not receive the diagnosis of prostate cancer. Physicians should keep in mind that, prostatic MCL can present with nonspecific symptoms. Staging should be performed in patients whose histopathologic diagnosis is lymphoma of the prostate so as to determine appropriate treatment options.

Keywords: mantle cell lymphoma, prostate, lymphoma, biopsy, diagnosis

Öz

Primer ve sekonder prostat lenfomaları nadir görülen hastalıklardır. Lenfomaların %4-9'unu Mantle cell lenfoma (MCL) oluşturmaktadır. MCL'nin prostat tutulumu oldukça nadir görülen bir hastalıktır ve şimdiye kadar yalnızca 11 vaka rapor edilmiştir. Bu yazıda alt üriner sistem semptomları ve prostat spesifik antijen (PSA) yüksekliği ile başvuran ve prostatik MCL tanısı alan bir vakayı sunmaktayız. Yetmiş yaşındaki hastaya PSA yüksekliği nedeniyle prostat biyopsisi uygulandı. Patoloji sonucunun prostatik MCL ile uyumlu olarak raporlanması sonrası evreleme için görüntülemeler ve ek patolojik örneklemeler yapıldı. Kemoterapi tedavisine başlanan hastanın üriner sistem şikayetlerinde düzelme izlendi. Daha önce rapor edilen prostatik MCL vakalarının bir kısmında prostatektomi uygulanmıştır, bir kısmında ise kemoterapi sonrası ek tedavi gerekmemiştir. PSA yüksekliği olan ancak prostat kanseri tanısı almayan tek prostatik MCL vakası bizim vakamızdır. Hekimler prostatik MCL vakalarının non-spesifik semptomlarla başvurabileceğini akılda tutmalıdır. Prostat patolojisi lenfoma olarak sonuçlanan hastalarda uygun tedavi seçeneklerinin belirlenmesi için evreleme yapılması gereklidir.

Anahtar kelimeler: mantle hücreli lenfoma, prostat, lenfoma, biyopsi, tanı

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Introduction

Lymphoma of the prostate, either primary or secondary is a rare condition. Prostatic involvement by lymphoma has been reported in less than 200 cases [1]. Mantle cell lymphoma (MCL) represents 4-9% of all lymphomas. Waldeyer's ring, bone marrow, peripheral blood, liver and the digestive tract, are commonly involved by MCL [2]. Prostatic involvement is very rare, with only 11 reported cases [3-12]. Here we describe a case presented with lower urinary tract symptoms (LUTS) and prostate-specific antigen (PSA) elevation, diagnosed with MCL of the prostate and literature review.

Case Presentation

A 70-year-old male with no known medical history presented with LUTS (frequency, dysuria and nocturia), and on physical examination no pathology was detected except that the prostate was firm and moderately enlarged. PSA was 8.2 ng/dL, and urinalysis was normal. Urinary ultrasound showed prostate measuring 120 cc. Uroflowmetry trace was consistent with obstruction, and Qmax was 7.2ml/s, so he was started on alpha-blocker regimen. He underwent prostate biopsy. During histopathologic examination of prostate biopsy specimens diffuse atypical lymphoid infiltration has been widely observed among cells of benign prostatic hyperplasia. The cells were observed to have partially large transparent cytoplasm and fine chromatin structure. Ki-67 index was up to 20% in the same areas. Tissue staining was strongly positive for CD20, CD5, Cyclin, CD79a, Bcl-6, and Pax-5, with rare areas positive for CD3 and CD43 consistent with MCL **(Figure 1,2)**. Then, the patient received a hematology consultation. Whole body CT-scans were obtained which revealed right pleural effusion requiring thoracentesis. No lymphadenopathy or spleenomagaly was detected. Cytology was consistent with low-grade B-cell lymphoma. Bone marrow biopsy report was consistent with MCL. He was treated with systemic chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine, prednisolone) per oncology clinic. In follow-up, patient experienced complete resolution of LUTS.

Discussion

The first study on prostatic involvement by lymphoma was made by Bostwick [13] in 1985 with a retrospective study of 13 cases, and it was emphasized that prostatic involvement by lymphoma should also be kept in mind in patients presenting with LUTS. Bostwick has set some criteria for the differentiation between primary, and secondary prostatic lymphoma. According to Bostwick's primary/secondary prostate lymphoma criteria; primary prostatic lymphoma will be diagnosed only if the following criteria are fulfilled: 1) primary symptoms are attributable to prostatic enlargement; 2) the major bulk of disease is localized to the prostate; and 3) lymph nodes, liver or spleen are not involved within 1 month of diagnosis. When previously reported cases are evaluated, 8 patients had secondary prostatic lymphoma and 3 cases had primary prostatic lymphoma **(Table 1)**. Our case is the fourth primary prostatic MCL case. Notably,

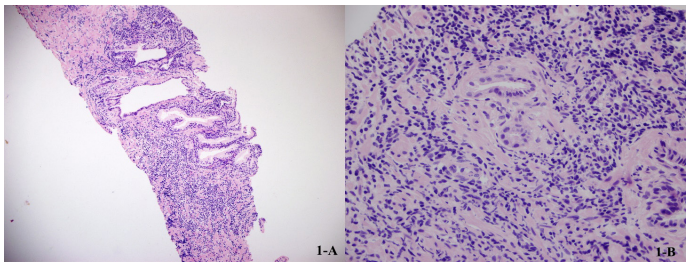

Figure 1. In prostate needle biopsy, small to medium- sized atypical lymphoid cells that efface the prostatic glands in some areas and show infiltration in a diffuse pattern around the glands in some areas are observed (H-E x100, H-E x400)

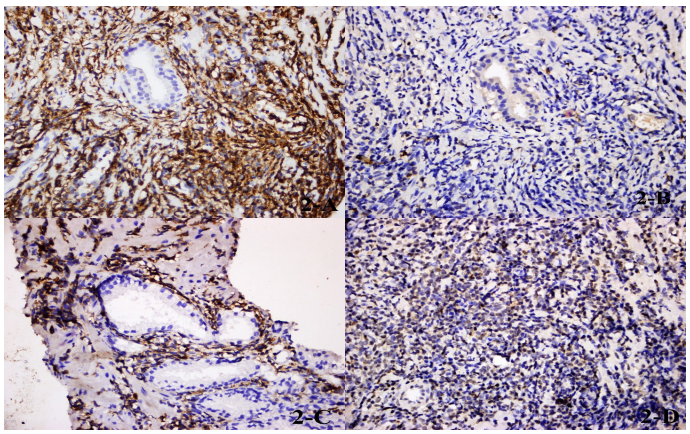

Figure 2. Immunohistochemical staining was commonly positive for CD20 in atypical lymphoid infiltration around the prostatic glands (2A, x400), whereas very rare lymphoid cell staining was detected with CD3 (2B, x400). Atypical lymphoid cell infiltration showed significantly positive staining with CD5 (2C, x400) and Cyclin-D1 (2D, x400)

the youngest of the patients was 59 years old. Lymphoma and prostate cancer are two common malignancies in elderly men. Three subtypes of MCL have been defined as classical, pleomorphic and blastoid. In our case, we observed "classical variant MCL" consisting of a monomorphic centrocyte-like atypical lymphocytes invading the prostate tissue with a diffuse growth pattern. This variant has a better prognosis than the blastoid/pleomorphic variant [14].

Prostatic involvement by MCL was reported for the first time in 2003 by Chim et al., (3), then ten more cases were reported in the literature. PSA elevation was noted in 3 cases with prostate cancer. In contrast, our case is the only prostatic MCL presenting with PSA elevation with no underlying prostate cancer. Prostatectomy was performed in 6 cases, obstructive symptoms resolved after chemotherapy in 3 cases, and sufficient information about the treatment of 2 cases were not available. LUTS is a common presenting symptom, and PSA elevation is not commonly seen. Our case contributes to the literature with its atypical presentation secondary to a rare prostatic pathology.

In some studies, a link was found between chronic lymphocytic leukemia, MCL, head and neck squamous cell carcinoma, bladder cancer and prostate cancer and a genetic basis was shown [15]. In this review, prostatic MCL- prostate adenocancer association was present in 3 patients [9,10,12] and MCL- bladder cancer association in 1 patient [6].

In conclusion, physicians should keep in mind that prostate lymphoma is rare, however it can present with nonspecific symptoms. Pathologists should be careful as lymphocyte

Table 1. Mantle cell lymphoma cases with prostate involvement

	Age	Primary (P)/ Secondary (S)	Case	Method of Diagnosis	Treatment	PSA	Prostate cancer (Yes/ No)
Chor S. Chim et al. 2003	73	S	A 73-year-old man presented to the emergency department with acute urinary retention. There were no systemic symptoms. Physical examination revealed generalized lymphadenopathy. Prostate biopsy was performed and pathology result was compatible with the prostate involvement of MCL.	Biopsy	Chemotherapy (cyclophosphamide, vincristine, procarbazine, and prednisolone)	-	No
Peiguo G. Chu et al. 2005	65	S	A 65-year-old male was already diagnosed with MCL. Prostate biopsy was performed and pathology result was compatible with the prostate involvement of MCL. There was no pathology other than axillary lymphadenopathy on the physical examination.	Biopsy	Adequate information on treatment has not been provided	-	No
	80	S	A 80-year-old male was already diagnosed with MCL. Due to LUTS, TUR-P was performed and pathology result was consistent with prostate involvement of MCL.	TUR-P	TUR-P	-	No
John D. Coyne et al. 2012	60	S	A 60-year-old male presented with LUTS and recurrent urinary tract infection. He was already diagnosed with MCL. Prostate biopsy was performed and pathology result was compatible with the prostate involvement of MCL.	Biopsy	Adequate information on treatment has not been provided	-	No
Binghai Chen et al. 2012	83	P	An 83-year-old male presented with LUTS. Cystoscopy revealed a moderately large prostate and bladder tumor size of 4x3 mm. TUR-P and TUR-B was performed and TUR-P pathology was consistent with prostate involvement of MCL. TUR-B pathology results was unclear due to the small size of the tumor specimen.	TUR-P	TUR-P	3,2ng/ml	No
Alberto Gurioli et al. 2013	83	P	An 83-year-old male was admitted to the emergency department because of gross hematuria. TVP was performed and pathology result was compatible with the prostate involvement of MCL.	TVP	TVP	-	No
Abuhjar Abdussalam et al. 2013	82	S	An 82-year-old male presented with increasing symptoms of bladder outlet obstruction. TUR-P was performed and pathology result was compatible with the prostate involvement of MCL	TUR-P	TUR-P	2,4ng/ml	No
Ashish. B. Rajput et al. 2014	74	S	A 74-year-old male presented with elevated PSA level and an enlarged prostate on digital rectal examination. Prostate biopsy was performed due to elevated PSA level. The pathology result was compatible with the prostate involvement of MCL.	Biopsy	Chemotherapy (bendamustine-rituximab)	17.16ng/ ml	Yes
Ivan Petković et al. 2016	64	S	A 64-year-old male initially presented with fatigue, splenomegaly, and bicytopenia. Prostate biopsy was performed due to elevated PSA level. The pathology result was compatible with the prostate involvement of MCL.	Biopsy	Chemotherapy (Cyclophosphamide, doxorubicin, vincristine, prednisolone)+Androgen Deprivation Therapy	52ng/ml	Yes
Preston A. Milburn et al. 2017	59	S	A 59-year-old male was referred by his primary care provider for progressive LUTS. Holmium laser enucleation (HoleP) was performed and pathology result was compatible with the prostate involvement of MCL.	HoleP	HoleP	1,2ng/ml	No
Eliška Tvrdíková et al. 2019	64	S	A 64-year-old male presented with increased PSA level. Prostate biopsy was performed and prostatic adenocarcinoma was detected. The patient had no systemic symptoms and no lymphadenopathy, splenomegaly or metastasis was observed in the imaging. MCL accompanying prostatic adenocarcinoma was detected in the final pathology of the patient who underwent RRP.	RRP	RRP	5,9ng/ml	Yes
Selman Unal et al. 2020*	70	P	A 70-year-old male with no known medical problem presented with LUTS and on digital rectal examination his prostate was firm and moderately enlarged. Prostate biopsy was performed due to elevated PSA level. The pathology result was compatible with the prostate involvement of MCL.	Biopsy	Chemotherapy (Cyclophosphamide, doxorubicin, vincristine, prednisolone)	8,2ng/ml	No

MCL: mantle cell lymphoma; LUTS: lower urinary tract symptoms; TUR-P: transurethral resectin of prostate; TUR-B: transurethral resectin of bladder; HoleP: Holmium laser enucleation of prostate; RRP: radical retropubic prostatectomy; TVP: transvesical prostatectomy; *: this case

infiltrates seen in prostate samples are possible signs of prostate lymphoma other than prostatitis. Staging should be performed in patients whose histopathologic diagnosis is lymphoma of the prostate so as to determine appropriate treatment options.

Ethics Committee Approval: N / A.

Informed Consent: Informed consent form was obtained from the patient for this case report.

Publication: The results of the study were not published in full or in part in form of abstracts.

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Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – S.U., H.U.; Design – S.U., H.U.; Supervision – S.U., A.A., A.K.; Resources – H.U., T.S., A.O.; Materials – H.U., T.S., A.O.; Data Collection and/or Processing – S.U., A.A., A.K.; Analysis and/or Interpretation – S.U., A.A., A.K.; Literature Search – H.U., T.S., A.O.; Writing – S.U., H.U.; Critical Review – S.U., A.A., A.K.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Case Report – General Urology

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COVID-19-Associated Retroperitoneal Hemorrhage: Same Complication, Two Different Types of Treatment

COVID-19 İlişkili Retroperitoneal Kanama: Aynı Komplikasyon, İki Farklı Tedavi

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Abstract

One of the reasons for the high mortality in COVID-19 patients is the increased risk of disseminated intravascular coagulation (DIC) and venous thromboembolism. For this reason, the use of anticoagulant treatments has become widespread. One of the rare complications of anticoagulant therapy is retroperitoneal hemorrhage. These hemorrhagies require immediate intervention. Retroperitoneal hemorrhage should be kept in mind among the many complications that develop in the patient who was followed up during the pandemic period. For this purpose, we present 2 cases who developed spontaneous retroperitoneal bleeding while clinically recovering under COVID-19 treatment.

Keywords: COVID-19, coronavirus, retroperitoneal hemorrhage, retroperitoneal hematoma, retroperitoneum

Öz

COVID-19 hastalarında yüksek mortalitenin nedenlerinden biri, yaygın intravasküler pıhtılaşma ve venöz tromboembolizm riskinin artmasıdır. Bu nedenle antikoagülan tedavilerin kullanımı yaygınlaşmıştır. Antikoagülan tedavinin nadir rastlanılan komplikasyonlarından biri de retroperitoneal kanamadır. Bu kanamalar acil müdahale gerektirir. Pandemi döneminde takip edilen hastada gelişen birçok komplikasyon arasında retroperitoneal kanama akılda tutulmalıdır. Bu amaçla COVID-19 tedavisi altında klinik olarak iyileşmekte iken spontan retroperitoneal kanama gelişen 2 olguyu sunuyoruz.

Anahtar kelimeler: COVID-19, koronavirüs, retroperitoneal kanama, retroperitoneal hematom, retroperiton

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Introduction

Spontaneous retroperioneal hematoma is a very rare, serious clinical condition defined as bleeding into the retroperiotenal area without associated trauma or surgical intervention [1]. The most important causes are anticoagulants, vascular diseases and renal tumors [2]. When the event occurs, the general condition of the patient may deteriorate due to weakness, flank pain, and hypotension requiring immediate intervention. In addition, hematoma can cause symptoms due to local compression on adjacent organs [3]. Although anticoagulants are useful in pulmonary embolism, stroke and deep vein thrombosis, they can cause bleeding in any part of the body [4].

Increased risk of disseminated intravascular coagulation (DIC) and venous thromboembolism are two of the leading causes of death in COVID-19 patients. Increase in D-dimer levels is often a herald of this situation [4]. The most important reason leading to multiple organ failure and death is hypercoagulability causing microvascular thrombus which is treated with antithrombotics such as heparin [5].

Anticoagulants are useful at therapeutic doses, but their common use increases the likelihood of spontaneous bleeding. While the probability of bleeding associated with anticoagulants is 4.8-8%, this rate has been reported as 3.5% in terms of major bleeding. Several cases of fatal retroperitoneal bleeding in COVID-19 patients receiving prophylactic or therapeutic doses of anticoagulant therapy have been previously reported in the literature [6–9].

Most cases are self-limited and resolve with cessation of anticoagulation and conservative treatment. The success rate of conservative treatment is dependent on the occurrence of these hematomas in confined spaces surrounded by adjacent structures [10]. In some cases, especially if there is a delay in diagnosis also non-adjacent vessels may rupture. And in such cases, the mortality rate is high [4]. In these special cases where persistent bleeding or hemodynamic instability despite conservative treatment occurs, transcatheter arterial embolization (TAE) may be required. Surgical treatment is applied in rare cases.

Herein, we describe two cases of life-threatening retroperitoneal hemorrhage developed during the clinical course of COVID-19. In both cases, respiratory distress caused by COVID-19 was improving when they developed retroperitoneal hemorrhage. Moreover, the patients were taking anticoagulants to prevent thrombosis. One of our patients recovered with TAE and the other with conservative treatment. Both of our patients were followed up without the need for intensive care, and were discharged.

Case 1

A 77-year-old woman without chronic disease was hospitalized because of severe respiratory distress and fever. Real-time reverse transcription polymerase chain reaction (RT-PCR) test performed to detect COVID-19 disease yielded positive results, and thorax computed tomography (CT) showed bilateral diffuse pulmonary infiltrates. The laboratory results at admission were as follows: ferritin, 1744 mcg/L (n: 23-336); procalcitonin, 0.45 ng/mL (n: <0.5); D-dimer , 0.42 mcg/mL (n: <0.5), and C-reactive protein (CRP), 118 mg/L (n: 0.3-10). Her platelet counts (n: 150-570 × 103/mcL), hemoglobin (Hgb) (n: 11.5-17.3 g/dL), and creatinine (0.74 mg/dL; n: 0.7-1.2) levels were within normal limits.

Her oxygen saturation (SpO2) was 88%. Physical examination on admission revealed bilaterally decreased pulmonary breath sounds. Arterial blood pressure (150/100 mm Hg), pulse rate (95 bpm), body temperature (38°C) and respiratory rate (24/min) of the patient were measured on admission. The patient was started on favipravir (loading oral dose of 1,800 mg on day 1, followed by 400 mg twice daily for 9 days), ceftriaxone (1 g/d IV), supplemental oxygen delivered through nasal cannula and prophylactic enoxaparin (40 mg/d SC). The patient felt palpitations. On electrocardiograph (ECG) atrial fibrillation with rapid ventricular response was observed. Her D-dimer level increased to 2.47 mcg/mL (reference range <0.5). The patient was started on therapeutic dose of enoxaparin (1 mg/kg SC) due to hypercoagulation concerns. Four days later, the patient started to complain about right flank pain, and on subsequently performed CT scan of abdomen, a large retroperitoneal hemorrhage was detected. Her blood pressure and pulse rates were 100/70 mmHg and 108/min, respectively.

Hemoglobin levels dropped from 14.7 g/dL to 10.2 g/dL and then to 7.1g/dL. Hypovolemia developed due to acute bleeding. After transfusion of 2 units of packed red blood cells (pRBCs), her Hgb raised to 9.5 g/dL. All anticoagulant agents were stopped. Contrast-enhanced abdominal and pelvic CT showed areas of hematoma (10.1x7.4 cm and 9.2x5.7 cm) in the right iliopsoas muscle spreading to the retroperitoneal space with extravasation **(Figure 1)**.

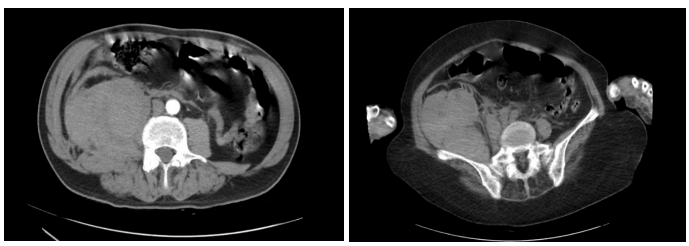

Figure 1. A 77-year-old woman; hematoma in the right retroperitoneal space was demonstrated in both abdominal and pelvic CT scans

The patient was treated conservatively, with blood transfusion. The patient was followed closely, her vital parameters and decrease in her hemoglobin values were monitored. In her new ECG, the rhythm returned to sinus rhythm. Although her D-dimer level was elevated, anticoagulant was not restarted in order to control bleeding. After one week of conservative treatment, the symptoms relieved and the retroperitoneal hematoma decreased in size.

Case 2

A 55-year-old male patient without any additional disease was admitted to the hospital with respiratory distress. The patient, whose complaints of fever and fatigue started 5 days before applying to our hospital, RT-PCR test for COVID-19 was found to be positive in another center, and favipravir treatment was started.

Admission blood pressure (145/100 mmHg), pulse rate (106 bpm), body temperature (38.1°C) and respiratory rate (26/min) of the patient whose respiratory distress was added to his complaints were as indicated. The patient was hospitalized and transferred to the intensive care unit (ICU) because of severe respiratory distress. Laboratory data on admission were as follows: hemoglobin (13.6 g/dl [n:13-18 g/dl]), white blood cell count (6890/μL [n: 4300–10800 /μL]), platelet count (202 × 103/μL [n: 150–450× 103/μL]), ferritin (2550 μg/L [n: 23-336 μg/L]), procalcitonin (0.04 ng/mL [n: <0.5 ng/mL]), D-dimer (0.51 μg/mL [n: <0.5 μg/mL]), and CRP (6.65 μg/mL [n: 0.3-10 μg/mL). His D-dimer uptrended to 0.9 ng/mL. The patient was started on daily SC doses of 40 mg prophylactic enoxaparin treatment for concern of hypercoagulable state. On the 6th day of hospitalization, the patient started to complain of abdominal pain. There was tenderness on the right lower quadrant of the abdomen on clinical examination. Vital signs at that time (heart rate, 113 bpm; blood pressure, 74/45 mm Hg; hemoglobin, 8.9 g/dL) suggested the presence of hypovolemic shock. Noncontrast CT scans of the abdomen and pelvis demonstrated a hematoma measuring 18x8 cm all along the entire length of the right psoas muscle **(Figure 2)**.

Figure 2.A- A 55-year-old male patient; hematoma in the right retroperitoneal space was demonstrated in both abdominal and pelvic CT scans

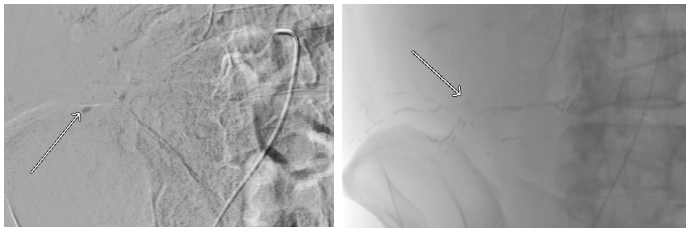

Figure 2.B- Angiography confirmed numerous sites of bleeding. Coil embolization performed achieved complete vessel obstruction and cessation of bleeding

Urgent transarterial embolization (TAE) was performed by interventional radiologists. Extravasation was identified from the right L2-L3-L4 lumbar arteries. Embolized using NBCA-lipiodol mixture. Complete embolization was achieved with no complications. After the procedure, no active contrast extravasation was observed. During his stay he received 3 units of packed red blood cells (PRBC).

Discussion

Spontaneous retroperitoneal hematoma is a well identified life-threatening condition, but its exact mechanism is not understood due to its uncommon occurrence. It is an undoubted fact that rupture of organs or vessels will cause bleeding in the retroperitoneal area without trauma or surgical intervention. Immune microangiopathy secondary to anticoagulation, intact vascular strain, and arteriosclerosis of small vessels are a few of the blamed etiologies [11]. Anticoagulation and antiplatet therapies have important roles in preventing thrombosis and thromboembolism in acute myocardial infarction, deep vein thrombosis and pulmonary embolism. Warfarin is the most commonly preferred anticoagulant agent that interferes with blood coagulation by inhibiting vitamin K epoxide reductase enzyme [3].

Due to the relationship between COVID-19 disease and thromboembolic events, anticoagulant treatment is used in all patients without contraindications in the management of hospitalized patients with COVID-19 disease in compliance with the guidelines. Spontaneous rectus sheath and retroperitoneal hematomas are rare complications of therapeutic anticoagulation and carry a mortality risk up to 20% [10]. There are few reports of these spontaneous bleeding in COVID-19 patients in the literature. With the increase use of therapeutic anticoagulation in those at high risk of thrombotic events, notifications of spontaneous bleeding cases will increase.

Asymptomatic retroperitoneal bleeding can occur. Diagnosis of this condition is mostly based on presenting symptoms and results of radiological studies [12]. Symptoms range from hip-leg pain to cardiovascular collapse and hypovolemic shock, although the Lenk triad, which includes symptoms of acute flank pain, tenderness, and internal bleeding, has been described for spontaneous retroperitoneum hematoma. Generalized weakness, headache, shortness of breath, syncope, and altered mental status are less common symptoms associated with the extent and duration of bleeding.

Therapeutic anticoagulant therapy is frequently used in patients hospitalized for COVID-19 disease, which may cause serious hemorrhagic complications. Vigilance is required in the diagnosis and management of this fatal complication. Administration of heparin at therapeutic doses may be risky in COVID-19 patients and we think that it should be administered with extreme caution. Therefore, vital signs and hemoglobin levels of these patients should be closely monitored.

The management mostly depends on the degree of bleeding and the underlying pathology. If the patient's condition is compromised or the underlying pathology is a kidney tumor, nephrectomy is recommended, but the clinical situation is much more complicated if the hematoma is associated with anticoagulant treatments [13]. It is difficult for the physician to make the decision because on one side there is a bleeding patient requiring surgical intervention, on the other hand, surgical intervention may further contribute to bleeding. In our cases, it was sufficient to remain conservative in the first case and hemodynamic stability was achieved only by transfusion. However, in the second case, TAE was required. There was no need for surgical intervention in both cases.

Thromboembolic events occurring in the course of COVID-19 increase mortality. For this reason, use of prophylactic and therapeutic doses of anticoagulant treatments has taken place in the treatment guidelines. Although rare, retroperitoneal

hemorrhages, which are complications related to this treatment, are life-threatening bleeding episodes. When a hemorrhage occurs, anticoagulation should be stopped immediately and, in case of need, it can be initiated again. In severe cases, department of interventional radiology should be consulted for TAE. These bleedings can be overlooked among many comorbidities encountered during intensive patient follow-up in the pandemic period. Therefore, anticoagulant therapy should be applied in selected cases and followed up carefully. We hope this case report will serve as a reminder of the risks inherent in anticoagulant therapy.

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Clinical Image – Genitourinary Radiology

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The Eternal Dilemma: Fat-poor Angiomyolipoma

Ezeli İkilem: Yağdan Fakir Anjiomyolipom

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A 55-year-old female patient admitted to the emergency department with one week long abdominal pain. In the physical examination of the patient, no clinical finding other than sensitivity was observed. The laboratory tests were normal. Because there was discordance between the patients clinical findings and laboratory tests, ultrasound exam was performed to exclude acute abdomen and a mass was detected in the anterior of left kidney's upper pole. There upon, the patient was discharged with recommendations and directed to the urology department. The patient had no history of malignancy or surgical history. Contrast enhanced abdominal magnetic resonance (MR) was performed for the lesion characterization. In the abdominal MRI, a lesion was detected in the anterior region of the left kidney's upper pole which is 36x20 mm in size. The lesion was hypointense on T2 weighted images (WI), slightly hyperintense on T1WI and had central cystic area. Since the mass was closely adjacent to the tail of the pancreas and had similar signal intensity with the pancreas on T2WI and postcontrast images, the origin of the lesion could not be made clearly between left kidney and pancreatic tail **(Figure 1-5)**. Therefore, histopathologic verification was recommended for preoperative management. It was reported as angiomyolipoma, wihch is rich in smooth muscle and poor in fat, after staining with actin and HMB-45 along with immunohistochemical staining obtained as a result of the biopsy procedure.

Renal angiomyolipomas are the most common benign kidney tumors. Non invasive diagnostic capacity between benign and malignant lesions is not yet at the desired standard. Approximately 10-17% of the resected kidney tumors are benign, and 2-6% of them are reported as angiomyolipomas [1]. Angiomyolipomas contain smooth muscle tissue, blood vessels and macroscopic fat areas in varying proportions [2]. In most cases, it is diagnosed radiologically without any further examination due to the macroscopic fat content. In the radiological diagnosis of angiomyolipoma, we use findings such as containing densities below -10 HU in computerized tomography (CT) examination

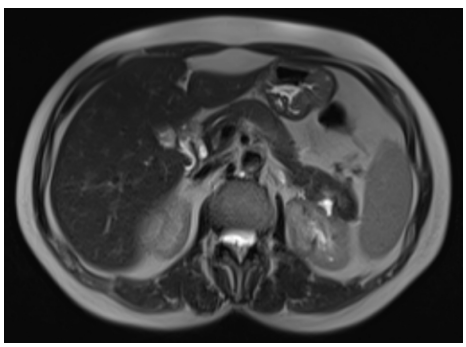

Figure 1. Axial T2 weighted (Contrast-enhanced abdominal magnetic resonance images of the patient)

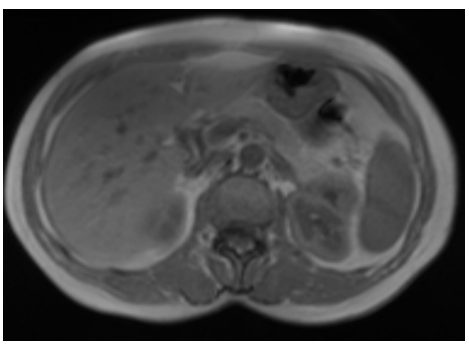

Figure 2. In phase (Contrast-enhanced abdominal magnetic resonance images of the patient)

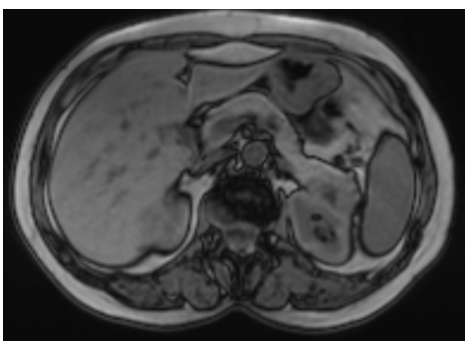

Figure 3. Out of phase (Contrast-enhanced abdominal magnetic resonance images of the patient)

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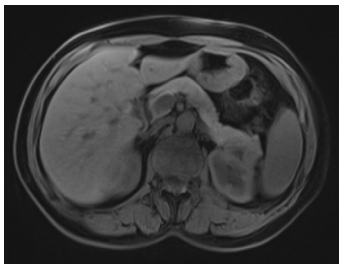

Figure 4. T1 Weighted, fat saturated T1 weighted (Contrast-enhanced abdominal magnetic resonance images of the patient)

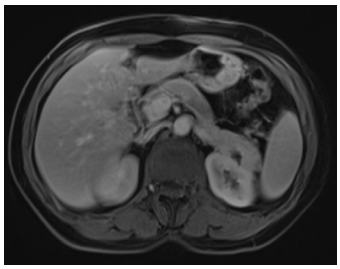

Figure 5. Post contrast images revealed a solid mass with central cystic area (Contrast-enhanced abdominal magnetic resonance images of the patient)

or showing suppression in fat saturated sequences in MRI [3]. In addition, chemical shift suppression techniques are useful in MRI in cases when there is a small amount of fatty tissue [4]. On the other hand, in 4.5% of angiomyolipomas, fatty tissue may not be seen radiologically [5]. Since the imaging findings of these fat-poor lesions, containing less than 25% fat, cannot be distinguished from RCC and they pose a serious problem [6]. RCCs, especially clear cell carcinomas, may also contain fat, but unlike angiomyolipomas, this adipose tissue is located at intracellular space and we use signal loss in out of phase MR sequence to differentiate RCC from angiomyolipoma [7]. Angiomyolipomas carry the risk of bleeding, especially in sizes over 4 cm and sometimes, fat densities can be overlooked due to intralesional bleeding and they can be confused with RCC [8]. Although new methods such as CT histogram [9] and specific MR sequences [4,10] have been used in the separation of fat-poor angiomyolipoma and RCC with new developments in radiology and technology, the application and reliability of these methods in daily practice are not sufficient.

Keywords: angiomyolipoma, renal cell cancer, chemical chift imaging

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Conflict of Interest: The authors declare that they have no conflict of interests.
Financial Disclosure: The authors declare that this study received no financial support.

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AAM TEDAVİSİNDE

uzun yol arkadaşınız

BETMIGA'ya başladığından beri 17. bisiklet yolculuğunu yapıyor.

TÜRKİYE'DE SINIFINDA İLK ve TEK[1,2]

Kısa Ürün Bilgisi için;

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Referanslar: 1. Khullar V, et al. Eur Urol 2013;63:283-95. **2.** Novara G, Cornu J-G. Eur Urol 2013;63:306-308.

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