

# Increased post-voiding residue and recurrent acute epididymitis: Are they causally related?

## Rezidü idrar miktarı ve tekrarlayan akut epididimit arasında sebep-sonuç ilişkisi var mı?

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### Abstract

**Aim:** It is known that recurrent urinary tract infection (rUTI) is associated with increased post-voiding residue (PVR), however, the same relationship is yet to be shown in adults for recurrent acute epididymitis. To the best of our knowledge, there are inadequate studies on this subject and they are mainly focused on the retrograde flow of the infected urine into the ejaculatory duct in terms of pathophysiology. In this study, we aimed to evaluate the causal relationship between recurrent acute epididymitis and increased post-voiding residue.

**Methods:** In this retrospective cohort study, the data of 388 patients who received treatment for epididymitis in our polyclinic between 2015 and 2018 were evaluated to determine that 72 were examined for lower urinary tract symptoms (LUTS). Age, PSA level, Qmax value, uroflowmetric pattern, post-voiding residual volume, International Prostate Symptom Scores (IPSS), and prostate volumes were recorded. Patients were divided into acute (n=38, Group 1) and recurrent acute (n=34, Group 2) epididymitis groups for analysis. The patients in Group 2 were treated for epididymitis at least two times in the last six months or thrice a year. The patients in Group 1 were treated only once in a year. Chi-square (Fisher's exact test) and Student's t-test were used to compare categorical variables. A value of  $P<0.05$  was considered the threshold of statistical significance.

**Results:** Age, PSA level, prostate volume, IPSS score, and peak flow did not significantly differ between the two groups. However, there were significant differences in terms of post-voiding residual urine volumes ( $P=0.029$ ). The mean post-voiding residual volumes in patients with acute and recurrent acute epididymitis were 47.3 (16.2) ml and 178.2 (23.6) ml, respectively.

**Conclusion:** There is a relationship between increased post-voiding residual urine volume and recurrent acute epididymitis. Patients who present with recurrent acute epididymitis should be scanned for urological pathologies which may cause increased PVR.

**Keywords:** Epididymitis, Post-voiding residue

### Öz

**Amaç:** Tekrarlayan idrar yolu enfeksiyonunun artmış rezidü idrar ile ilişkili olduğu biliniyor. Yetişkinlerde tekrarlayan akut epididimit için ise böyle bir durum henüz gösterilmemiş. Bildiğimiz kadarıyla bu konuyla ilgili çok fazla çalışma yok ve bu yapılan kısıtlı sayıdaki çalışmaların çoğunda etyolojide ejekülör kanala retrograd idrar akışı üzerinde durulmuş. Bu çalışmada tekrarlayan akut epididimit ile artmış rezidü idrar (PVR) arasındaki olası nedensel ilişkiyi incelemeyi amaçladık.

**Yöntemler:** Çalışma retrospektif kohort olarak tasarlandı. 2015-2018 yılları arasında polikliniğimizde epididimit tedavisi gören 388 hastanın verileri retrospektif olarak incelendi. Bu hastaların 72'si aynı zamanda alt üriner sistem semptomları (AÜSS) açısından da incelenmişti. Yaş, PSA düzeyi, Qmax değeri, uroflowmetrik patern, işeme sonrası rezidüel hacim, IPSS Skorları ve prostat hacimleri kaydedildi. Hastalar, dahil edilme kriterlerine göre akut ve tekrarlayan akut epididimiti olanlar olarak iki gruba ayrıldı. Analiz için hastalar akut (n=38, Grup 1) ve rekürren akut (n=34, Grup 2) epididimit olarak iki gruba ayrıldı. Grup 2'deki hastalar epididimit için son altı ayda iki veya son bir yılda üç defa tedavi edildi. Grup 1'deki hastalar yılda sadece 1 kez tedavi edildi. Kategorik değişkenleri karşılaştırmak için ki-kare (Fisher's exact test) ve Student t-testi kullanıldı.  $P<0.05$  değeri istatistiksel anlamlılık eşiği olarak kabul edildi.

**Bulgular:** Yaş, PSA düzeyi, prostat hacmi, IPSS skoru ve pik akım iki grup arasında anlamlı farklılık göstermedi. Bununla birlikte, işeme sonrası rezidüel idrar hacimleri açısından anlamlı farklılıklar vardı ( $P=0.029$ ). Akut ve rekürren akut epididimitli hastalarda ortalama işeme sonrası rezidüel hacimler sırasıyla 47.3 (16.2) ml ve 178.2 (23.6) ml idi.

**Sonuç:** Artan işeme sonrası rezidüel idrar hacmi ile tekrarlayan akut epididimit arasında bir sebep-sonuç ilişkisi vardır. Tekrarlayan akut epididimit ile başvuran hastalar, artmış PVR'ye neden olabilecek ürolojik patolojiler için taranmalıdır.

**Anahtar kelimeler:** Epididimit, Artmış rezidü idrar

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## Introduction

Epididymitis is an inflammation of the coiled tube (epididymis) at the back of the testicle that stores and carries sperm. Its incidence ranges from 25 to 65 cases per 10,000 adult males per year [1]. Signs and symptoms of epididymitis might include a swollen, hyperemic, or warm scrotum, scrotal pain, tenderness usually on one side, painful urination, an urgent or frequent need to urinate, and less commonly, fever. It can be acute, chronic, or recurrent [1,2]. Acute epididymitis is a clinical syndrome consisting of pain, swelling, and inflammation of the epididymis that lasts for less than 3 months. Chronic epididymitis is characterized by symptoms of discomfort and/or pain in the scrotum, testicle, or epididymis for more than 3 months [2]. Recurrent epididymitis considered as chronic epididymitis, but according to some authors, it is a clinical condition involving pain, swelling, hyperemic and warm scrotum, tenderness, fever lasting for less than 3 months like acute epididymitis, that is treated with antibiotics but can recur due to urological pathologies and anomalies after clinical recovery [7-9]. The pathophysiology of epididymitis remains unclear, although it is postulated to occur secondary to retrograde flow of infected urine into the ejaculatory duct [2]. Chronic infectious epididymitis is most frequently seen in conditions associated with a granulomatous reaction. Mycobacterium tuberculosis (TB) is the most common granulomatous disease affecting the epididymis and should be suspected, especially in men with a known history of or recent exposure to TB [3]. The most common isolated pathogens are *C. trachomatis* and *N. gonorrhoeae* along with sexually and non-sexually transmitted pathogens [4,5]. Non-sexually transmitted infectious causes of acute epididymitis are uncommon and include obstructive urinary disease, urinary tract surgery, prostate biopsy, urinary tract catheterization, systemic disease, and/or immunosuppression [5]. Epididymitis is diagnosed with clinical findings, but urine dipstick test, urine culture, urethral smear, and scrotal ultrasonography are helpful [5]. The treatment of epididymitis includes bed rest, scrotal elevation, analgesics, nonsteroidal anti-inflammatory drugs, empirical antibiotics, correcting the underlying cause, and surgery [1,6]. To the best of our knowledge, there are a few published studies about the underlying causes of recurrent acute epididymitis in adults. Due to inadequate studies on this subject and the fact that authors are mainly focused on the retrograde flow of the infected urine into the ejaculatory duct in pathophysiology, we aimed to determine underlying causes of recurrent acute epididymitis and its relationship with post-voiding residual urine volume in order to choose the best treatment for patients and avoid epididymectomy.

## Materials and methods

In this retrospective cohort study, 388 patients treated for epididymitis between June 2015 and May 2018 were evaluated. Patients who were older than 18 years of age were all included in this study. All patients had low urinary tract symptoms and were diagnosed by ultrasonography, urinalysis, and physical examination. All patients had swollen, hyperemic or warm scrotums, testicle pain, tenderness, and positive urine

culture for bacteria or fungi. The patients in Group 2 (recurrent acute epididymitis, n=34) were treated for epididymitis at least two times in six months or thrice a year. The patients in Group 1 (acute epididymitis, n=38) were treated only once in a year. Patients younger than 18 years, those with chronic epididymitis, sexually transmitted epididymitis, and negative urine cultures were excluded from the study. A total of 72 patients were included based on the inclusion and diagnostic criteria, thirty-four of which were treated for epididymitis at least two times in six months or three times in a year (Group 2). There is no definitive description of recurrent acute epididymitis. Therefore, we classified the patients into two groups based on the definition of recurrent urinary tract infection in the EAU guideline [13,14]: Acute epididymitis (n=38, Group 1) and recurrent acute epididymitis (n=34, Group 2). Age, PSA level,  $Q_{max}$  value, uroflowmetric pattern, post-voiding residual urine volume, IPSS scores, prostate volume, and underlying causes were recorded.

### Statistical analysis

Statistical analysis was performed with SPSS v25.0 for Windows (IBM Corp. Released 2018). Chi-square (Fisher's exact test) and Student's t-test were used to compare categorical variables.  $P < 0.05$  was considered statistically significant.

## Results

The mean ages of the first and second groups were 56.2 (15.2) years and 68.3 (14.6) years, respectively. The incidence of recurrent acute epididymitis was insignificantly higher in the older group ( $P=0.29$ ). Epididymitis is more common between the ages of 18-50 [12]. The reason for the higher age average is that only patients with lower urinary tract symptoms were included in our study, who were all above 40 years of age. Mean PSA levels were 3.67 (1.26) and 3.09 (2.11) ng/mL in the first and second groups, respectively, which were similar ( $P=0.47$ ). There were no significant differences in terms of prostate volumes, IPSS scores, and peak flow between the two groups ( $P=0.26$ ,  $P=0.18$ ,  $P=0.21$ ), although mean prostate volume and IPSS score were greater in recurrent acute epididymitis patient group, in which all patients had severe LUTS. Most patients had normal voiding patterns and  $Q_{max}$  values were lower in patients with recurrent acute epididymitis. The mean post-voiding residual volumes in patients with acute and recurrent acute epididymitis were 47.3 (16.2) ml and 178.2 (23.6) ml, respectively ( $P=0.029$ ). In addition, there were more underlying causes in patients with recurrent acute epididymitis ( $P=0.039$ ): 1 patient had undergone transurethral resection of the prostate (TURP), 2 patients had undergone hypospadias repair and 1 patient had urethritis secondary to urethral stricture. 5 patients had neurogenic bladder, 11 patients had benign prostate hyperplasia and 6 patients had prostatic surgeries, such as transurethral electrovaporization of the prostate, TURP, or biopsy. The results and the underlying causes are summarized in Table 1 and Figure 1, respectively.

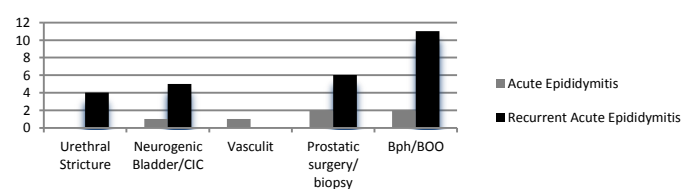


Figure 1: Underlying causes of AE and RAE ( $p=0.039$ ) (AE: Acute Epididymitis, RAE: Recurrent acute epididymitis)

Table 1: Characteristics of the acute and recurrent group

Parameters	Acute epididymitis (n=38)		Recurrent acute epididymitis (n=34)		P-value
	Mean	n	Mean	n	
Age	56.2(15.2)		68.3(14.6)		0.29
PSA Level (ng/mL)	3.67(1.26)		3.09(2.11)		0.47
Prostate volume (mL)	44.41(23.1)		61.33(21.95)		0.26
IPSS	8.1(4.7)		13.7(6.23)		0.18
Mild=0-7		16		12	
Moderate=8-19		19		12	
Severe=20-35		3		10	
Peak Flow (Q max)	18.2(11.1)		13.2(9.6)		0.21
Normal >15		30		21	
Obstructive <15		8		13	
Post voiding residual urine volume (mL)	47.3(16.2)		178.2(23.6)		0.029
Underlying causes		6		26	0.039
Urethral stricture		-		4	
Neurogenic bladder/CIC		1		5	
Vasculitis		1		-	
Prostatic surgery		1		5	
Following prostate biopsy		1		1	
BPH/BOO		2		11	

BOO: Bladder outlet obstruction, CIC: Clear intermittent catheterization, BPH: Benign prostatic hyperplasia, n: Number of patients

## Discussion

Residual urine is defined as the volume of urine left in the bladder following urination. It is measured by the help of a catheter or ultrasonography. Catheterization allows for safer evaluation of PVR, however, it is time-consuming and carries complication risks, such as urethral injury, urinary tract infection and urethrorrhagia. Ultrasonographic examination of the bladder is a noninvasive, basic and easily-accessible method that requires a well-trained radiologist. However, its results depend on the performer, and it does not provide a definite result for PVR. Normal PVR urine volume is  $\leq 50$  ml, but there is no consensus on cut-off values. Increased PVR volume indicates problems with the emptying of the bladder. In men, it may be caused by various pathologies, such as benign prostate hyperplasia, bladder outlet obstruction, urethral or meatal stricture, underactive bladder, and neurogenic bladder [17]. The PVR volume significantly affects the quality of life due to the fact that increased PVR may reduce functional bladder capacity and cause symptoms of the lower urinary tract [21]. Current studies have shown that it is associated with many complications ranging from a simple lower urinary tract symptom to acute and chronic renal failure [24]. It is also reportedly associated with recurrent urinary tract infections. Dray et al. [23] reported that increased post-void urine residue was found to aggravate incontinence, as measured by the M-ISI (Michigan Incontinence Symptom Index) score and increase the risk of recurrent UTIs in selected MS (Multiple sclerosis) patients with LUTS. A PVR volume greater than 50 ml is considered an independent risk factor for rUTIs [18]. Some studies have shown that clinically asymptomatic adult men with a PVR of 180 ml or greater are at higher risk for bacteriuria [19]. High post-void residual (PVR) volumes can function as a reservoir for microorganisms because the infected urine cannot be emptied completely [20]. The pathophysiology of both acute and recurrent acute epididymitis remains unclear, but the theory of “retrograde flow of infected urine into the ejaculatory duct” is the most current one. All these studies and the pathophysiology of epididymitis suggest that there may be a relationship between the increased amount of residual urine and the development or recurrence of epididymitis. Some congenital abnormalities and low urinary tract pathologies have been associated with recurrent acute epididymitis in pediatric

populations [7-10]. In adults, there are a few studies on recurrent acute epididymitis [15,16]. Hoepfner et al. [16] reported that among 336 men aged over 60 years presenting with acute/recurrent acute epididymitis, lower urinary tract obstruction was identified in 187(56%) patients, which was caused by benign prostate hyperplasia, prostate cancer, and/or urethral stricture. Our study is important for the following two reasons: First of all, to the best of our knowledge, there is no sufficient study to date on recurrent acute epididymitis and secondly, we found a relationship between residual urine volume and recurrent acute epididymitis, which confirms the theory of “retrograde flow of infected urine into the ejaculatory duct” in pathophysiology.

## Limitations

However, our study has some limitations: Some data were missing due to its retrospective nature. Residual urine volume was measured only in patients with low urinary tract system symptoms, which decreased our sample size. Some of the patients in Group 1 may have had acute epididymitis attacks more than once, and it may not be recorded in the hospital registry, which may have led to statistically significant differences. It is not known whether the patients in Group 2 were previously treated for the pathologies leading to increased residual urine volume.

## Conclusion

Based on our study, we believe that solving the underlying pathology which increases PVR will be the best treatment choice in patients with recurrent acute epididymitis. It is possible that microorganisms migrate from the bladder due to high post-voiding residual urine increase in patients with recurrent acute epididymitis. Evaluating the PSA level, prostate volume, IPSS, peak flow and post-voiding residual volume in patients with recurrent acute epididymitis will determine the correct approach to treatment, even if there are no lower urinary tract symptoms. Further, prospective studies with large patient series are required to shed light on the issue.

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