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Postoperative Microscopic Pyuria and Role of Damage-Associated Molecular Pattern: A Literature Review

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All patients who undergo transurethral prostate surgery exhibit pyuria and microscopic hematuria in postoperative urinalysis. Postoperative asymptomatic pyuria is associated with the inflammatory process and surface remodeling of the prostate, rather than infection. Various studies have investigated the incidence, duration, and risk factors for postoperative pyuria, noting that factors like age, surgery time, and prostate size can influence outcomes. Postoperative pyuria reflects tissue recovery and inflammation, and the use of antibiotics in asymptomatic patients may not be appropriate.

Keywords: Transurethral resection of prostate, Pyuria, Inflammation

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HIGHLIGHTS

Postoperative pyuria reflects tissue recovery and inflammation, and the use of antibiotics in asymptomatic patients may not be appropriate.

INTRODUCTION

All patients who undergo transurethral prostate surgery (TUPS) exhibit pyuria and microscopic hematuria in postoperative urinalysis, regardless of the surgical method [1]. However, there are few studies on the epidemiology and risk factors of pyuria and bacteriuria after TUPS. Clinicians, when encountering pyuria in a patient's urine during clinical practice, usually first consider the possibility of a urinary tract infection (UTI). UTI can often occur as a postoperative complication following urological surgeries [2]. However, pyuria that occurs after TUPS is different from UTIs as a postoperative complication. Table 1 demonstrates studies reporting pyuria after transurethral prostate surgery. Current evidence suggests that the persistence of white blood cells and red blood cells found in postoperative urinalysis is more likely due to an inflammatory process and remodeling of the prostate surface, rather than an infection [3]. Therefore, the authors have summarized the incidence and significance of pyuria that occurs after TUPS.

PYURIA

Urinalysis is a simple test frequently used in clinical practice, but it is a fundamental examination that should be performed on all urology patients presenting with urinary symptoms. The presence of white blood cells in the urine, known as pyuria, is a useful marker for evaluating UTIs in the general population [4]. Both pyuria detected through urinalysis and positive urine culture results can be appropriate diagnostic methods for UTIs. However, urinalysis is easier, faster, more convenient for patients, highly reproducible, and more cost-effective, which is why it is performed more frequently than urine culture.

Pyuria typically indicates an infection and/or an inflammatory response of the urothelium to bacteria, stones, embedded foreign bodies, or other conditions. Aseptic pyuria, or pyuria without bacteriuria, is commonly encountered in clinical practice, with reports showing that 2.6% of men and 13.9% of women in the general population have aseptic pyuria [5]. In cases other than genitourinary tuberculosis, it is important to differentiate the causes that can lead to a noninfectious inflammatory response, with common examples being urinary stones or genitourinary malignancy. Currently, various guidelines do not mention treatment for asymptomatic pyuria; however, in actual clinical practice, cases presenting with pyuria are often encountered [5]. It is particularly confusing to determine treatment plans for elderly patients who present with vague complaints [6]. The guidelines from the European Association of Urology and the American Urological Association do not provide clear recommendations regarding the utility of urine tests or urine cultures following TUPS for benign prostatic hyperplasia (BPH) [1]. The natural course of changes in urine analysis after TUPS has not been properly investigated.

1. Postoperative Pyuria

BPH is one of the most common causes of lower urinary tract symptoms in elderly men [7]. TUPS is recommended for patients who do not respond well to appropriate pharmacological treatment. Despite the development of various new minimally invasive surgical methods, transurethral resection of the prostate (TURP) remains the standard surgical treatment for patients with symptomatic BPH [8]. Despite improvements in technology, TURP carries several complications related to surgery, particularly the risks of bleeding, transurethral resection syndrome, and UTIs [8]. Even after effective TUPS, 5%–35% of patients may still complain of urinary symptoms postoperatively [9]. The most common cause of persistent symptoms is pre-existing detrusor overactivity, but it may also be due to UTIs that occur postoperatively. UTIs as a postoperative complication pose challenges for both patients and healthcare providers. The diagnostic methods for postoperative UTIs are not different from existing diagnostic approaches; they are characterized by the presence of symptoms and the detection of pyuria or bacteriuria in urine tests. Appropriate antibiotic treatment is necessary for UTIs as a postoperative complication [2].

However, several studies have shown that pyuria and hematuria can be observed even in the absence of evidence of UTI postoperatively [1,10,11]. Additionally, no statistical correlation has been established between bacteriuria and pyuria [10,11]. Several studies have been conducted on the clinical significance and duration of persistent hematuria and pyuria after surgery; however, the results vary depending on the surgical method and the investigation techniques used [11-17].

1) Occurrence and duration of pyuria after TUPS

Some studies have reported that pyuria occurs immediately after surgery. Ikeuchi et al. [14] performed a retrospective analysis of 87 patients who underwent TURP and open prostatectomy. All patients included in the study had persistent pyuria up to 6 weeks after surgery, with an average duration of pyuria of 73.6±36.6 days. In a study by Olvera-Posada et al. [12], 274 patients who underwent monopolar TURP, bipolar TURP, or open prostatectomy were analyzed. Similarly, all patients ex-

Table 1. Studies reporting pyuria after transurethral prostate surgery

Study	Design	Surgical modality	Enrolled patients	Duration of pyuria	Risk factors
Ikeuchi et al. [14] (1987)	R	TURP Open surgery	30 57	75.5±46.0 Day 71.3±31.4 Day	Indwelling catheter, diabetes complications, preoperative pyuria, preoperative bacteriuria, resected weight, postoperative bacteriuria, anemia, postoperative complications
Okamura et al. [13] (1987)	R	TURP	54	70.1±24.7 Day	Preoperative infection, resected weight, postoperative infection
Fujita et al. [15] (1992)	R	TURP	395	57.2±30.8 Day	Postoperative infection, age, surgery time, prostate weight, postoperative catheter indwelling time, postoperative bacteriuria, resected weight/operation time
Oka et al. [16] (1998)	R	TURP	273	110.6±38.3 Day	Age, resected weight, operation time
Cho et al. [11] (2007)	R	TURP	49	4.12±4.51 Wk	Age, preoperative pyuria, resected weight
Olvera-Posada et al. [12] (2013)	R	TURP (M) TURP (B) Open surgery	44 27 14	266 Day 274 Day 176 Day	Resected weight
Yang et al. [17] (2020)	R	TURP (M) DiLRP	81 120	16 Wk 12 Wk	Operation method, age
Elshal et al. [1] (2024)	P	Resection Vaporization Enucleation Incision	77 22 31 22	19.1 Wk 20.1 Wk 15.8 Wk 14.0 Wk	Indwelling catheter, operation method

R, retrospective design; P, prospective design; TURP (M), transurethral resection of prostate (monopolar); TURP (B), transurethral resection of prostate (bipolar); DiLRP, diode laser vaporesection of the prostate.

hibited pyuria from the early postoperative period, with its prevalence decreasing over time. On average, it took 274 days for the pyuria to resolve.

However, other studies have reported a gradual increase in pyuria following TUPS. Okamura et al. [13] conducted a retrospective analysis of 54 patients who underwent TURP. In these patients, pyuria gradually increased after surgery, with all patients showing signs of pyuria around 5 weeks postoperatively. The pyuria resolved after an average of 70.1 days. In a recent study, Elshal et al. [1] reported similar findings, with the number of patients exhibiting pyuria gradually increasing postoperatively. By approximately 2 weeks after surgery, pyuria was observed in about 60% of patients. The pyuria resolved in all patients by 6 months.

In the studies by Oka et al. [16] and Cho et al. [11], the timing of the initial occurrence of pyuria or the peak incidence after TURP was not reported. However, the average duration of pyuria was 110.6 days and 4.12 weeks, respectively."

2) Risk factors for persistent pyuria after TUPS

Various researchers have shown interest in postoperative pyuria and have investigated this condition. Fujita et al. [15] identified several risk factors associated with the persistence of pyuria following TURP, including the occurrence of postoperative infectious complications ($r=0.4018$, $p<0.01$), patient age ($r=0.2169$, $p<0.001$), surgical duration ($r=0.1998$, $p<0.001$), and prostate size ($r=0.1769$, $p<0.01$). In the study by Okamura et al. [13], although patient age was not a significant factor, the presence of preoperative infection ($r=0.45$), the amount of resected tissue ($r=0.64$), and postoperative infection ($r=0.53$) were significant predictors of persistent pyuria even after multivariate analysis. Ikeuchi et al. [14] reported that preoperative factors such as the maintenance of a urethral catheter ($p<0.05$), the presence of diabetic complications ($p<0.01$), preoperative pyuria ($p<0.01$), and preoperative bacteriuria ($p<0.01$) were significant predictors. Surgical-related factors included the volume of resected prostate ($p<0.05$), postoperative bacteriuria ($p<0.05$), anemia ($p<0.05$), and the occurrence of postoperative complications ($p<0.05$) as risk factors for persistent pyuria. In the study by Oka et al. [16], patient age ($p=0.03$), the volume of resected prostate ($p<0.01$), and surgical duration ($p<0.01$) were found to be associated with the duration of pyuria.

According to a study conducted in Korea on the duration of pyuria after TURP, patients aged 70 years and older had a significantly longer duration of pyuria at 6.61 weeks compared to 4.12 weeks in patients aged 70 years and younger ($p=0.03$). Additionally, patients with preoperative pyuria experienced a longer duration of pyuria postoperatively ($p=0.04$) [11]. While no significant differences were found based on surgical duration ($p>0.05$), a greater weight of the resected prostate during surgery was associated with a longer duration of pyuria ($p=0.03$) [11].

Some researchers have studied the differences in pyuria based on the surgical method. Ikeuchi et al. [14] conducted a retrospective analysis of 87 patients who underwent TURP and open prostate surgery, but no significant differences were observed in the persistence of pyuria between the 2 groups. In a study conducted in Mexico, researchers retrospectively investigated the occurrence of pyuria after surgery among patients who underwent monopolar or bipolar TURP, as well as open prostatectomy. Among 85 patients, 44 underwent monopolar TURP, 27 underwent bipolar TURP, and 14 underwent open prostatectomy. The duration of pyuria was found to be longer than that of microhematuria (274 days vs. 176 days). The authors confirmed that the weight of the resected tissue was correlated with postoperative pyuria; however, there were no differences in the duration of pyuria between the surgical methods [12].

In a study conducted in 2019, the outcomes of monopolar TURP were compared with diode laser vaporization resection of the prostate in 189 patients who underwent surgery for BPH [17]. During the first 5 weeks postoperatively, there was no difference in the pyuria curves between the 2 groups. However, after 5 weeks,

the monopolar TURP group showed greater improvement in pyuria. Multivariate analysis regarding the persistence of pyuria revealed that the surgical method and age were significant factors. The authors suggested that the deep thermal injury caused by the diode laser could be a reason for the persistence of pyuria after surgery.

A recent prospective study reported results from 152 patients who were followed for 24 weeks after undergoing TUPS [1]. In this study, significant pyuria (white blood cell 〉5 high power field) was observed in urine tests before discharge, and at 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 24 weeks postsurgery, with rates of 52%, 96.1%, 94.1%, 71.7%, 78.9%, and 52.5%, respectively. In the final follow-up at 24 weeks, significant pyuria was reported in 80 patients (52.6%). None of the studied factors (age, body mass index, preoperative prostate size, preoperative urine culture results) were found to be significant predictors. However, the duration until the resolution of significant pyuria was longest in the vaporization group (20.1 weeks) and shortest in the enucleation group (15.8 weeks).

2. Is Postoperative Pyuria a Problem?

Persistent voiding dysfunction and pain following TUPS is one of the challenging issues for both patients and urologists. This can negatively impact the patient's quality of life and may also affect the patient-physician relationship. Nevertheless, the impact of postoperative pyuria on patient symptoms has only been reported in a few studies, and the results are inconsistent. The relationship between postoperative pyuria and urinary symptoms has been documented in 2 papers.

In the study by Cho et al. [11], the average duration of urinary symptoms after TURP was similar to the average duration of pyuria. Most of the symptoms reported by patients were irritative symptoms, including nocturia, increased urinary frequency, urgency, and dysuria. The correlation between symptoms and duration showed a significant result with a correlation coefficient of 0.579, and the relationship between the 2 values had a slope of 0.335, reflecting approximately 33% of the overall value.

However, a recently reported prospective study found no significant correlation between the International Prostate Symptom Score and the presence of pyuria based on urine tests at various follow-up time points after surgery [1]. However, the degree of dysuria postoperatively showed a significant correlation with pyuria at 2, 8, and 12 weeks. This suggests that at least dysuria may be associated with pyuria after surgery.

Postoperative infected urine is common, and it can be challenging to completely eradicate it until re-epithelialization of the resected area occurs. It has been suggested that adequate antibiotic treatment is necessary for about 8 to 12 weeks after surgery [18]. During the treatment period, pyuria may occur, but it does not necessarily indicate an infection, and a urine culture test is essential.

In studies reporting the association between postoperative pyuria and urinary difficulties, pyuria was observed in urine tests for most of the time after TUPS. These data provide strong evidence that the degree and duration of leukocytosis after the procedure are related not to active infection but to the extent of inflammation in the prostatic urethra and the subsequent healing process associated with the surface area of the surgical site [1]. This suggests that postoperative pyuria should not be interpreted as a potential infection but rather recognized as a distinct postoperative inflammatory response, indicating that treatment may involve anti-inflammatory medications rather than empirical antibiotics. Clearly, routine screening urine tests may not be necessary for asymptomatic patients in the first few months after TUPS.

Postoperative pyuria is a surrogate marker for tissue repair and inflammation. Since aging is associated with increased inflammation, much of the tissue in elderly patients is likely to be in a state of chronic inflammation [19]. This aligns with findings from some studies that identify patient age as a risk factor for persistent pyuria after surgery.

3. Damage-Associated Molecular Pattern

The innate immune system is the first line of host defense that induces an immediate and nonspecific immune response against pathogens [20]. Inflammation is a component of the innate immune system and begins when the innate immune system recognizes invading pathogens or molecules resulting from tissue damage [21]. Inflammation is a protective response that removes harmful stimuli and initiates tissue repair to restore health; however, if not properly regulated, it can also contribute to the development of various diseases [22].

Damage-associated molecular patterns (DAMPs) are molecules released from damaged or dead cells and serve as factors in the innate immune response [21]. Throughout living organisms, DAMP-induced immune responses play a role in defense strategies aimed at maintaining and restoring homeostasis. They are considered endogenous danger signals because they activate the innate immune system during noninfectious inflammatory responses, leading to robust inflammatory reactions [23].

The systemic and local presence of DAMPs is essential for the immune response during traumatic injury. Following tissue damage from surgeries, the release of DAMPs can participate in the inflammatory response and fibrosis. DAMPs are released into the extracellular space during surgery, activating the NLRP3 inflammasome, which can lead to pyroptosis, recruitment and activation of immune cells, collagen accumulation, and fibrosis. This inflammatory activation may result in postoperative complications [24]. Although this mechanism has not been confirmed in the context of tissue repair following prostate surgery, it may operate in a similar manner.

DAMPs are essential for the normal functioning; however, excessive release of DAMPs and overactivation of pattern recognition receptors are recognized as contributing factors to the development of various diseases. Targeting DAMPs, their receptors, and downstream mediators may help regulate these diseases and reverse pathological deterioration [25,26]. In fact, there have been reports from animal experiments indicating that when DAMPs were removed prior to inducing ischemic renal injury, no kidney damage occurred [27]. Furthermore, DAMPs could be utilized as biomarkers to indicate or monitor the severity of diseases or injuries.

CONCLUSIONS

Pyuria occurs in nearly all patients following TUPS and can persist for around 3 months. Therefore, the clear value of routine urine tests post-TUPS requires careful consideration. However, in cases where UTI are suspected, conducting urine tests along with urine cultures may be reasonable. Instead of using antibiotics to treat dysuria in the absence of evidence for UTI postsurgery, it seems more appropriate to manage it with anti-inflammatory medications, considering the mechanisms behind pyuria. Understanding postoperative pyuria will be essential for improving patient satisfaction after TUPS.

NOTES

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