The European School of Urology Boot Camp for First-Year Residents: The First Step to Standardization in Surgical Education

Surgical training is a complex process that requires academic and scientific learning as well as technical and nontechnical skills training. While academic and scientific learning is similar in all medical areas, technical skills training is the centerpiece of surgical education and has therefore been the focus of most surgical training curricula.

The traditional surgical training model, originally developed by Halsted and Churchill, has been the basis of most residency programs in Urology for more than a century.[1,2] Over the last decades, the traditional surgical training model faced several ethical and regulatory issues that considerably impacted surgical education.[3] In fact, not only was there a subjective decline in residents' performance (perceived both by program directors and residents themselves) but also there was also an objective decline in proficiency and autonomy levels at the end of residency programs.[4-6] On the other hand, the fact that traditional surgical training programs were based on learning from experience with patients posed severe ethical and insurance-related dilemmas regarding patient safety.[3,7] Altogether, these issues created a considerable challenge to surgical residency programs, ultimately leading to a major paradigm shift in surgical training worldwide.

Urology residency training is quite heterogeneous throughout the world, not only in terms of the total duration of training but also in terms of the length of core surgical training, the length of the specific urological training, research requirements, working hours, surgical exposure, and evaluation methods.[8,9] A study by Carrion *et al.* evaluated the current status of urological training among final-year residents in Europe.[10] Altogether, surgical exposure of residents for procedures seems low, with only 50% of residents performing more than 20 procedures such as TURP, TURBT, or circumcision and <5%–10% performing more than 10 procedures such as percutaneous nephrolithotomy, radical nephrectomies, partial nephrectomies, radical prostatectomies, or radical cystectomies during their training.[10] Overall, only 30% of residents were satisfied with their surgical training and 14% believed that they performed enough surgeries during their training.[10] A systematic review of laparoscopic training in Urology residency programs, encompassing evidence from almost 1000 residents, identified wide variations in terms of exposure to laparoscopy between training programs. Most residents scored their received training as inadequate, which resulted in low degrees of confidence to independently perform solo laparoscopic procedures at the end of their residency.[11] Altogether, these studies showed that current Urology residency programs have limitations that may seriously compromise the quality of urological training and subsequent patient care over the next years.

In light of these limitations of traditional surgical training, simulation-based training has been extensively explored over the past decades and used as an adjunct to traditional surgical training. This has led to the development of technical skills through individual hands-on practice.[7] Simulation-based training has been shown to improve operative skills in trainees, with evidence suggesting that the skills acquired through simulation-based training are transferable to an operative setting and that repetitive practice is associated with improved learner outcomes, with more practice yielding better benefits.[12-14]

The benefits of simulation in the acquisition of technical skills in Urology are well established.[15,16] Several simulation courses have been developed over the past decades, most of them being procedure specific and usually have a duration of some hours to 2 days. However, considering the complexity of urological training and the multitude of surgical procedures in which urologists must gain proficiency, there was the need to develop a more advanced and structured approach to simulation training.

One approach consisted of developing integrated simulation-based training curricula, comprising a series of validated training and assessment levels of progressive complexity. These training curricula supplement the conventional surgical training in a given area. In recent years, the European Association of Urology (EAU), the European School of Urology (ESU), the EAU Section of Uro-technology (ESUT), the EAU Robotic Urology Section (ERUS), and the EAU Urolithiasis Section (EULIS) have developed a series of standardized and validated training programs, such as the European Basic Laparoscopic Urological Skills, the Endoscopic Stone Treatment Step 1 (EST-S1), and the Certified Curriculum of ERUS (CC-ERUS). This has led to the implementation of several structured and integrated training curricula in laparoscopy, endoscopy, and robotics.[17-21]

Riding high on the clear success of these activities, ESU, ESUT, ERUS, and EULIS have created the Standardization in Surgical Education (SISE) program, a collaborative venture that aims to implement a comprehensive approach to all training activities within the ESU, encompassing a series of structured, standardized, and validated training curricula targeted at all trainee levels. To allow stepwise training from basic to advanced skills, laparoscopic skills will be provided as in the laparoscopic urology training curriculum, endoscopic skills will be covered by the

EST curriculum, robotic skills will be given through the CC-ERUS and transurethral skills by the transurethral training curriculum.[22] The first step in the SISE program is the ESU Urology Boot Camp.

The ESU Urology Boot Camp is a standardized course for 1st-year residents, comprising a full day of intensive hands-on training and organized into separate training modules. The aim is to provide high-quality hands-on training, within the framework of a standardized and integrated ESU training program, to give every European Urology resident the possibility to acquire the essential technical skills to perform the most frequent urological procedures before they start working with patients. The Urology Boot Camp model is well established in the training scheme within the United Kingdom, where the Urology Simulation Boot Camp for 3rd/4th-year residents was introduced in 2015 and became mandatory for all Urology residents in 2018.[23,24]

One of the most important hallmarks of the ESU Urology Boot Camp is the 1:1:1 training model, where each trainee has a dedicated training station and an experienced trainer for the entire duration of each module, therefore maximizing the learning experience. To this end, a series of different high fidelity models are used, as well as a considerable amount of state-of-the-art urological equipment. Trainees are provided with standardized hands-on training on laparoscopy, flexible, and semi-rigid ureterorenoscopy, transurethral resection of prostate and bladder tumors, flexible and rigid cystoscopy, bladder catheterization, suprapubic catheter placement, and scrotal examination.

Following a very successful pilot course in Portugal, in 2018, four additional courses have been made, in Portugal, Belgium, and Serbia. The aim of the ESU Boot Camp Board is to implement ESU Urology Boot Camps in every European country, to be held on an annual basis, to provide high-quality standardized hands-on training to every Urology resident at the beginning of their training.

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Original Article

A Simple Algorithm to Facilitate Improved Diagnosis of Nocturia

Abstract

Introduction/Aim: Traditionally, nocturia is considered a bothersome storage symptom, associated with prostatic enlargement. However, nocturia occurs also in a range of urological and non-urological conditions. Some other authors consider nocturia as a disease rather than a symptom. The aim of this article is to present the clinically relevant features of nocturia and to suggest a simple algorithm to facilitate its investigation. **Material and Methods:** A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, PubMed, EMBASE, the Cochrane Library and other libraries using the key words "nocturia", "nocturnal frequency", "nighttime voiding", in various combinations with the terms "etiology", "pathophysiology" "risk factors", "causes". We included reviews metanalyses and clinical studies. We considered full-text written papers. Bibliographic information in the selected publications was checked for relevant records not included in the initial search. **Results:** According to current litterature is a very common condition that affects millions of people worldwide. The rate of people affected increases with age. About 1 in 3 adults over the age of 30 experience nocturia. There is a predominance of female gender among younger patients however occurrence of nocturia is equal between men and women aged 50-59 years. Nocturia occurs in more than 50% of individuals over 60 years of age and the prevalence is greater in men than women. The impact of nocturia in overall health is highly significant. Additionally, to the decrease in quality of life due to the inconvenience that it causes, nocturia can be associated with long-term sleep deprivation and the subsequent exhaustion, mood changes, somnolence, impaired productivity, increased risk of falls and accidents, fatigue, lethargy, inattentiveness, and cognitive dysfunction. Despite its high frequency and significance, nocturia remains under-reported, and under-treated. The most usual reasons explaining the above is the variety of contributing factors and conditions. **Conclusions:** It is paramount that clinicians are aware of the multiple potential contributing factors in any given patient. A simplified algorithm may help to identify the underlying etiology (such as diabetes or nocturnal polyuria) leading to better treatment outcomes, improved quality of life scores, and substantial symptom resolution.

Keywords: *Convenience voiding, nocturia, nocturnal frequency, nocturnal voiding*

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Introduction

From a urological perspective, nocturia is technically a storage symptom, associated with a range of urological conditions including prostatic enlargement.[1] Since it is characterized by awakening to void, it is by far the lower urinary tract symptom (LUTS) with the greatest impact on quality of life of men.[2] However, nocturia occurs also in women and an important number of male patients suffering from nocturia have no significant prostate enlargement.[3] For this reason, several authors suggested nocturia as a symptom of-primary or secondary-overactive bladder syndrome (OAB). Nevertheless, most patients with nocturia do not have OAB, and conversely, most patients with OAB do have nocturia.[4,5] Some other authors consider nocturia as a disease rather than a symptom.[6] In this article, we discuss the clinically relevant features of nocturia and we present a simple algorithm to facilitate improved diagnosis of this common and bothersome disorder.

Materials and Methods

A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, PubMed, EMBASE, the Cochrane Library and other libraries using the key words "nocturia," "nocturnal frequency," "nighttime voiding, in various combinations with the terms "etiology," "pathophysiology" "risk factors," "causes." We included reviews meta-analyses and clinical studies. We considered full-text written papers.

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Bibliographic information in the selected publications was checked for relevant records not included in the initial search.

Results

Nocturia is defined as the need for a patient to get up at night on a regular basis to urinate. A period of sleep must precede and follow the urinary episode to count as a nocturnal void.[7] It is a very common condition that affects millions of people worldwide. The rate of people affected increases with age.[8] About 1 in 3 adults over the age of 30 years' experience nocturia. There is a predominance of female gender among younger patients however occurrence of nocturia is equal between men and women aged 50–59 years. Nocturia occurs in more than 50% of individuals over 60 years of age and the prevalence is greater in men than women.[7,9,10]

The impact of nocturia in overall health is highly significant. In addition, to the decrease in quality of life due to the inconvenience that it causes, nocturia can be associated with long-term sleep deprivation and the subsequent exhaustion, mood changes, somnolence, impaired productivity, increased risk of falls and accidents, fatigue, lethargy, inattentiveness, and cognitive dysfunction.[11]

Despite its high frequency and significance, nocturia remains under-reported, and under-treated. Reasons explaining the above include various reasons. The most usual is patients' embarrassment to mention this problem. In fact, it was shown that only a proportion of patients seek treatment and <10% of the US patients actually diagnosed with nocturia receive specific therapy for it.[7] Another important reason is patients' belief that nocturia is a normal part of aging. It should be mentioned that, in older adults, the proportion of total daily urine output that is produced at night is higher. However, the quantity of urine is not too much to cause nocturia.[12]

A possible reason is the relatively little attention paid to this symptom by healthcare providers.[5,7] This fact is probably associated to the peculiar nature of the gerontologic patient.

It is true that, older adults compared with younger adults are more likely to be prescribed diuretics and/or drugs causing pollakiuria. However, older patients' recall of medication information is generally inaccurate and they often provide confounding information regarding symptoms onset and duration.[13]

Regardless of the actual underlying etiology, initial treatment of nocturia by physicians is somewhat routine with men typically receiving alpha-blockers and women prescribed overactive bladder medications without any substantial diagnostic investigation. In fact, almost 84% of patients in an OAB study reported nocturia among their urinary symptoms and 71% of patients with benign prostatic hyperplasia experienced frequent nighttime voiding (ie, 2 or more episodes per night).[14,15] Nevertheless, medications to treat lower urinary tract dysfunction (LUTD) in men (a-1 adrenergic antagonists, 5-a reductase inhibitors, partial differential equation-5 inhibitor, phytotherapy) and OAB in women (antimuscarinics, beta-3 agonist) are not significantly better than placebo in short-term use.[16] Surprisingly, even when these initial measures fail, further evaluation and management of nocturia are often lacking.[17]

This happens because nocturia is multifactorial and it is difficult to identify the actual cause especially in older individuals who generally have multiple medical problems as well as subclinical changes in several physiologic systems.[18]

Literature review revealed various classifications of the etiology and the categorization of nocturia. In the topographic classification, nocturia is divided into two main categories: (1) upper urinary tract dysfunction owed to nighttime urine overproduction, resulting from renal, cardiovascular, or pulmonary factors and (2) LUTD involving the bladder, prostate, or urethra.[19] According to the International Consultation on Male LUTS the causative categories for nocturia are summarized as follows: (1) Bladder storage problems; (2) global polyuria (>40 ml/kg urine output over a 24-h period); (3) Nocturnal polyuria (nocturnal output exceeding 20% of 24-h urine output in younger patients, or 33% of urine output in people aged over 65 year); (4) sleep disorders and (5) mixed etiology.[20]

Currently, it is generally accepted that nocturia is caused by one of the abovementioned four main problems and by combinations of these.[7] However, each of them is associated with a vast variety of diseases and conditions [Table 1], and therefore making a diagnosis can be a tricky endeavor.[19]

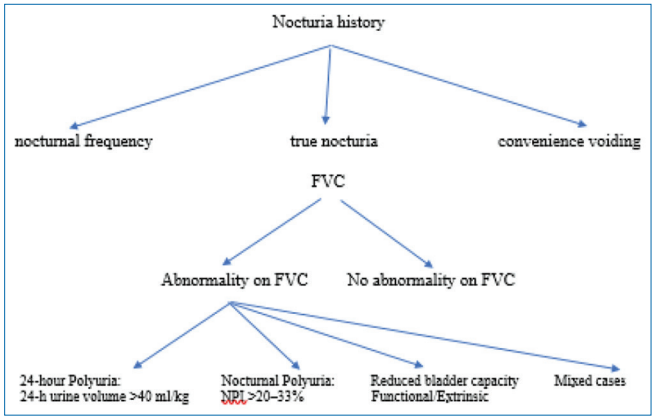
Discussion

Dealing with complaints of repeated nocturnal voiding, a physician should verify whether they represent true nocturia, nocturnal frequency, or convenience voiding. True nocturia occurs during bedtime and the voiding episodes are each preceded and followed by sleep periods. Nighttime voiding episodes without a desire to void and frequent nocturnal voiding when the person is awake are technically not nocturia.[21] Evaluation of nocturia history, focusing on how many times the patient wakes up at night to void and how much sleep disruption this causes, may distinguish the above situations. Initial evaluation includes also thorough medical history, physical examination, routine urine tests, and basic serum analysis and imaging.[22] Emphasis should be given to the presence of any peripheral or dependent edema, comorbid medical disorders, the presence of any other urinary tract symptoms, overall fluid intake, drinking habits, medications, caffeine and alcohol intake, high sodium intake, sleeping habits, and sleep disturbances as well.[7] The simple algorithm presented in can be used

Table 1: Etiologies of nocturia in association with frequency-volume chart[6] (modified)

No abnormality on FVC
Nocturnal frequency
Convenience voiding
Timing or dose of medicines:
Diuretics, cardiac glycosides (digoxin), β-adrenergic antagonists, tetracycline derivatives (demeclocycline), psychotropics (lithium), anesthetics (methoxyflurane), antiepileptics (phenytoin), opioids (propoxyphene), Vitamin D corticosteroids thyroid hormones
Sleep disorders
Primary sleep disorders (insomnia disorder, hypersomnolence disorder, narcolepsy, obstructive sleep apnea hypopnea syndrome, central sleep apnea syndrome), parasomnias (nightmare disorder, night terrors, bedwetting, sleepwalking) and periodic leg movements (repetitive jerking, cramping, or twitching of lower limbs during sleep)
Secondary sleep disorders (cardiac failure, chronic obstructive pulmonary disease, endocrine disorders)
Neurologic conditions (parkinson disease, dementia, epilepsy)
Psychiatric conditions (depression, anxiety)
Alcohol or drug use
Nocturnal polyuria: NPI >20%-33%
Evacuation of daytime fluid sequestration (peripheral edema, congestive heart failure, chronic venous insufficiency of the lower extremities, lymph stasis, hepatic failure, nephrotic syndrome, hypoalbuminemia)
Excessive evening fluid intake
Night-time drinking
Circadian abnormalities in antidiuretic hormone arginine vasopressin AVP secretion
CNS lesions of the hypothalamic-pituitary axis
Neurologic conditions (parkinson disease, multiple sclerosis)
Medicines: Diuretics, ethanol, steroids
Renal dysfunction: Tubular dysfunction, diabetic nephropathy, albuminuria
Obstructive sleep apnea
24-h polyuria: 24-h urine volume >40 ml/kg
Diabetes mellitus
Diabetes insipidus
Primary polydipsia
Excessive salt intake
Hypercalcemia
Medicines: Diuretics, selective serotonin reuptake inhibitors, calcium channel blockers, lithium, tetracycline, carbonic anhydrase inhibitors
Reduced bladder capacity (functional/extrinsic)
Urological diseases: Interstial cystitis, chronic prostatitis, chronic pain pelvic syndrome, benign or malignant outlet obstruction, overactive bladder syndrome, lower urinary tract calculi
Neurologic conditions neurogenic bladder parkinson disease, multiple sclerosis, spinal cord injury, stroke
Voiding dysfunction with high post-void residual

AVP: Arginine vasopressin, FVC: Frequency-volume chart, NPI: Nocturnal polyuria index, CNS: Central nervous system



Nocturia investigation algorithm

during the initial visit of patients complaining of nocturia for a focused selection of patients for further evaluation with the 24-h voiding diary (frequency-volume chart [FVC] or FVC). The remaining patients who either have nocturnal frequency or convenience voiding may be treated with anticholinergic drugs, β-3-adrenergic receptors agonists, minor tranquillizers, nonbenzodiazepine hypnotics or may refer for specific consultation. Of note, our anecdotal experience showed that <60% of patients complaining of nocturia have actually true nocturia

The cornerstone of nocturia diagnosis is the FVC. In fact, it is critical to correctly distinguish between global polyuria and nocturnal polyuria: Global polyuria is characterized by >40 ml/kg urine output over a 24-h period. In contrast, nocturnal polyuria is usually accompanied by a proportional decrease in daytime hourly urine production that results in a normal 24-h total urinary volume.[23] The nighttime urinary production is >20% of the total 24-h urine volume

in younger adults or more than 33% in older individuals. By dividing the total urinary volume from all nocturia episodes by the total urinary volume for 24 h and multiply by 100, one can calculate the nocturia episode percentage. Frequency is estimated with the nocturnal bladder capacity index, by subtraction of the actual number of voids from the predicted number of voids.[6,7] In Table 1, we present the main etiologies of nocturia in association with FVC findings. As shown in this table, further evaluation including flowmetry, urodynamics, urine cytology, and cystoscopy may be also helpful in diagnose certain disorders and diseases.[24]

Conclusions

It is paramount that clinicians are aware of the multiple potential contributing factors in any given patient. A simplified algorithm may help to identify the underlying etiology (such as diabetes or nocturnal polyuria) leading to better treatment outcomes, improved quality of life scores, and substantial symptom resolution.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

SARS-CoV-2 and Clinical Urology: There is no Dragon in this Story

Abstract

Covid-19 disease is caused by the coronavirus of severe acute respiratory syndrome 2. The disease has evolved into a global pandemic that continues to this day. Coronavirus basically causes acute respiratory illness, the symptoms of which may remain milder even three months after the onset of this acute infection. Many patients also experience cardiological, gastrointestinal, and neurological symptoms that last for at least two months. Some patients report worsening of certain urinary symptoms. In this paper, we review the current knowledge about the relationship between SARS-CoV-2 and urinary system. A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, PubMed, Embase, the Cochrane Library, and other libraries using the keywords "SARS-CoV-2," "COVID-19," and "pandemic," in various combinations with the terms "kidney," "bladder" "prostate," "testicles," "LUTS," "pain," and "infection." A considerable number of articles investigate the possible interaction between SARS-CoV-2 and the urinary system. In addition, to the well-documented involvement of the kidneys, testicle, and penile involvement seems to be possible. There are also studies investigating the development of benign prostatic hypertrophy (BPH) as a complication of SARS-CoV-2 infection and some studies examining the impact of COVID-19 disease on LUTS. In conclusion, the studies published so far do not provide conclusive evidence about a strong association between SARS-CoV-2 and the genitourinary system. Further investigation is warranted to better understand the nature of COVID-19 disease.

Keywords: *COVID-19, severe acute respiratory syndrome 2, urinary system*

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Introduction

COVID-19 disease is caused by the coronavirus of severe acute respiratory syndrome 2 (SARS-CoV-2). The disease has evolved into a global pandemic that continues to this day. Coronavirus basically causes acute respiratory disease, the symptoms of which vary and may remain milder even 3 months after the onset of this acute infection. In addition to systemic and respiratory symptoms, several patients also experience symptoms from the upper respiratory tract, skin, and eyes, as well as cardiological, gastrointestinal, and neurological symptoms, which last for at least 2 months.[1] The most common symptoms are fever, dry cough, and physical exhaustion. Less common symptoms are loss of taste or smell, nasal congestion, sore throat, headache, muscle or joint pain, skin rash, nausea or vomiting, diarrhea, chills, and dizziness.[1] Other less common symptoms include confusion, decreased consciousness, anxiety, depression, and sleep disorders.[2] The increase in cytokines that occurs during infection determines the severity of inflammation from COVID-19 disease. In fact, hypercytokinemia causes acute respiratory distress syndrome, stroke, myocardial infarction, acute renal failure, and vascular damage from vascular disease and serious manifestations due to nervous system malfunction.[3] Symptoms definitely attributed to this disease do not include lower urinary tract symptoms (LUTSs). However, some patients report worsening of some preexisting symptoms. There is currently no literature on a strong association between COVID-19 disease and the urinary tract. In this article, an attempt is made to present current evidence on the relationship between SARS-CoV-2 and the urinary system and to discuss the possible interaction.

Materials and Methods

A database and a manual search were conducted in the MEDLINE database of the National Library of Medicine, PubMed, Embase, the Cochrane Library, and other libraries using the keywords

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Table 1: Impact of severe acute respiratory syndrome coronavirus 2 on bladder function: The most relevant studies and their findings

Authors (study)	Patients	Instruments	Findings
Dhar *et al*. (observational)	39	OAB assessment tool	Frequency ≥13 episodes/24 h (85%) Nocturia ≥4 episodes/night (87%)
Can *et al*. (prospective)	94 (62 >50)	IPSS	IPSS score before COVID-19 (1.3±1.6) IPSS score during COVID-19 (5.1±4.1)
Kaya *et al*. (retrospective)	46	IPSS Urinary symptom profile	Male patients: Difference in storage IPSS Female patients: Difference in SI/OAB incidence
Chen *et al*. (prospective)	889	OABSS	Worse storage LUTS after vaccination (13.4%)
Mumm (retrospective)	57	Patients history	Onset of urinary frequency (12.5%)

OAB: Overactive bladder, IPSS: International Prostate Symptom Score, OABSS: OAB symptom score, LUTS: Lower urinary tract symptoms, SI: Symptom index

"«SARS-CoV-2," "COVID-19," and "pandemic," in various combinations with the terms "kidney," "bladder" "prostate," "testicles," "LUTS," "pain," and "infection." Two independent reviewers performed data extraction using identical extraction tables. We included all clinical studies with available information. We considered full-text written articles. We also included reviews and case reports. Bibliographic information in the selected publications was checked for relevant records not included in the initial search.

Results

SARS-CoV-2 has a specific three-dimensional spike protein structure characterized by strong binding affinity to the angiotensin-converting enzyme 2 (ACE-2). Given the mode of transmission through the respiratory tract and as ACE-2 is abundant in Type 2 alveolar cells of the lungs, the late are affected by the disease more easily than other organs.[4] However, ACE-2 main function is taking place in the renal vascular endothelium, therefore, kidneys can be easily affected by SARS-CoV-2. In fact, immunohistochemical studies in renal tissues obtained from infected individuals have confirmed the accumulation of SARS-CoV-2 antigen in the renal tubules.[5] Given that, the ACE-2 pathway is present in other organs of the genitourinary system, their involvement in COVID-19 disease has been investigated in a considerable number of articles. In addition, to the well-documented involvement of the kidneys, testicle and penile involvement were also reported. There are also studies investigating the development of benign prostatic hypertrophy (BPH) as a complication of SARS-CoV-2 infection and studies examining the impact of COVID-19 disease on LUTS and studies examining the impact of COVID-19 disease on LUTS [Table 1].

Discussion

Impact of severe acute respiratory syndrome 2 on the kidneys and renal drainage system

Up to the present day, approximately 30% of COVID-19 treated patients were found to have moderate renal impairment.[5] Although the exact mechanism by which SARS-CoV-2 causes renal impairment is currently unknown, glomerulopathy, damage of the proximal tubules, and accumulation of protein in Bowman's capsule related to the ACE-2 pathway activation are common findings in COVID-19 patients.[6,7]

Currently, there is no evidence of a pathogenic effect of SARS-CoV-2 on the renal drainage system. To our best knowledge, viral RNA was mostly detected in the urine of patients with moderate-to-severe disease; however, the detection of viral RNA in the urine of patients appears to be low to nonexistent and the presence of the virus in the urine is not related to the course of the disease.[8]

Impact of severe acute respiratory syndrome 2 on the bladder function

With respect to bladder function following COVID-19 disease, available information is somehow confounding. While Dhar *et al*. reported increased frequency and nocturia in more than 85% of patients with a history of overactive bladder (OAB), Kaya *et al*. and Can *et al*. did not detect significant differences in International Prostate Symptom Score (IPSS) comparing LUTS before or during hospitalization due to COVID-19. However, in the latter study, a slight increase of IPSS during hospitalization was assessed in the subgroup of patients >50 years old.[9-11] Selvi *et al*. recorded urodynamically proven lower urinary tract dysfunction following COVID-19 in three young patients. Mumm *et al*., in a small series of 57 cases, reported a significant increase of urinary frequency in 12.5% of the patients. The remaining studies did not find significant differences in LUTS severity before and during SARS-CoV-2 infection.[12-16] Interestingly, Chen *et al*. showed that COVID-19 vaccination worsened storage LUTS in up to 13.4% of patients with preexisting OAB. The mechanism by which SARS-CoV-2 infection could impact of bladder function remains unknown. Recently, Lamb *et al*. documented an elevation of proinflammatory cytokines in the urine of COVID-19 patients, that is possibly related to urgency and urinary incontinence.[14]

Impact of severe acute respiratory syndrome 2 on prostate enlargement

There is currently no evidence on a direct association between COVID-19 disease and prostate enlargement. Nevertheless, the worsening of obstructive LUTS shown in some of the aforementioned studies indicates a possible impact of SARS-CoV-2 on the prostate gland. According to the literature, various mechanisms such as alteration of ACE-2 signaling, alteration of androgen receptor-related mechanisms, inflammation, and metabolic disorders during or after the course of SARS-CoV-2 infection may lead to worsening of LUTS related to BPH.[17] Although the exact cause of BPH development is unknown, changes in male sex hormones occurring during aging are reputed to be the most probable causative factor. Remarkably, studies have shown that men are more prone to SARS-CoV-2 infection and the elderly population appears to develop more severe COVID-19 disease.[18,19] The most likely pathogenic mechanism that indirectly associates COVID-19 with BPH has already been described: the co-expression of ACE-2 and TMPRSS2 in an organ is vital for the virus to infect it. Co-expression of ACE-2 and TMPRSS2 occurs not only in the lungs but also in the prostate.[19,20] However, to date, no presence of SARS-CoV-2 RNA has been reported in the prostate secretion of patients with COVID-19.[21] Given the age-dependent increase in the prevalence of BPH, one can assume that a significant group of elderly male COVID-19 patients may have BPH as a comorbid condition and that this condition may be exacerbated by COVID-19. In confirmation to the above Luciani *et al*. reported a worsening of BPH-induced hematuria greatly after contracting symptomatic COVID-19 infection during hospitalization in two patients. On the other hand, studies that have investigated trends in urological emergencies during the first wave of the epidemic have shown a marked reduction of chronic kidney disease-related urinary retention cases in emergency departments.[22-26]

Impact of severe acute respiratory syndrome 2 on the genital system

With respect to testicle involvement, Chen *et al*. studied 142 COVID-19 patients and found orchitis in 4.2% of cases, epididymitis in 4.9%, combined orchitis–epididymitis in 13.3%, and scrotal infections in 19.8%. The last two were more common in severely ill patients. However, this association was not statistically confirmed.[27] The studies of Ning *et al*. (112 patients) and Alkhatatbeh *et al*. (253 patients) reported neither testicular edema nor orchitis.[28,29] Ediz *et al*. reported orchitis–epididymitis/testicular pain in 10.9% of cases and testicular edema in 9.9% of cases in a cohort of 91 COVID-19 patients, while Pan *et al*. and Holtmann *et al*. in two smaller studies reported testicular discomfort in 17.6% and 5,5% of cases, respectively.[30-32] Individual reports of testicular pain and orchitis[33-36] do not add more evidence on the association between SARS-CoV-2 infection and testicular involvement.

Nineteen studies investigated the presence of SARS-CoV-2 in semen.[21,28,31,32,37-50] The sample size was very small in most of these studies. The severity of COVID-19 between cohorts varied and semen samples was collected in different periods of the disease. Only 3 out of 19 studies provided positive results. However, the possibility that the virus found in semen was actually originated in the urine could not be ruled out. Of note, the fact that the sperm quality of patients with moderate COVID-19 infection was lower than that of both patients with mild infection and healthy controls may be associated with fever and inflammation.[51,52] Furthermore, no viral RNA was detected in testicular biopsy material from dead patients.[53]

Penile involvement has been also documented through case reports describing priapism development in seriously ill patients.[54-58] Although priapism is the result of the hypercoagulable state of all these patients, given the rarity of these cases, priapism could not be recognized as a systematic side effect of COVID-19 disease.

Conclusions

The studies published so far do not provide conclusive evidence about a strong association between SARS-CoV-2 and the genitourinary system. Further investigation is warranted to better understand the nature of COVID-19 disease.

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Conflicts of interest

There are no conflicts of interest.

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Research Paper

A Cross-Sectional Study on Factors Determining the Current Practice of Prostate Biopsy among Government and Private Urologists in Malaysia

Abstract

Background: Prostate Biopsy remains a gold standard among urologist to diagnose prostate cancer. It is a field that is undergoing massive change. Our study allows us to have a glimpse into the current practice of prostate biopsies in Malaysia and would allow us to make improvements in the right direction. **Methods:** A 34 set multiple choice question was created using a web based programme and posed to all doctors in the Urology Field under the Malaysia Urological Association. The questions targeted various aspects of the practice of prostate biopsies. Data's were then collected and analysed using a validated statistical manner. **Results:** 94 responses were returned with a standard deviation of 18.15. **Conclusion:** This study provides an insight into the current practice of prostate biopsy among members of the Malaysian Urological Association (MUA). Although TRUS biopsy without additional imaging was still the most typical approach, MRI and TPT biopsy were commonly used. These two diagnostic methods are likely to increase in the future. Quinolone prophylaxis was widely used, but selective use of prophylactic carbapenems was also common, indicating concerns about quinolone-resistant pathogens and their infectious complications.

Keywords: *Prostate biopsy, prostate cancer, questionnaire, urologist*

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Introduction

Prostate biopsy remains the gold standard for the diagnosis of prostate cancer.[1] The information obtained from a prostate biopsy is undisputedly the most crucial for clinical decision making regarding further treatment options. In recent years, the field of prostate biopsy has changed rapidly. Prostate biopsy is not only used to diagnose cancer, but also routinely used to monitor the disease in men undergoing low-risk active surveillance. Prostate biopsy is no longer performed only transrectally, but also transperineally. The optimal number and location of cores is still unclear. Since prostate biopsy is not standardized,[2] it is believed that there is a wide range of practices. This study aims to provide an insight into the current practice of prostate biopsy in the Malaysian Urological Association (MUA).

Materials and Methods

A 34-question multiple-choice survey was created using a web-based survey provider, freeonlinesurveys.com. The survey addressed a series of questions about prostate biopsy. Wherever appropriate, multiple response options were provided. The survey questions are listed in Table 1.

Permission to distribute the survey was obtained from the Malaysian Urological Association (MUA). The survey was then linked to the MUA official email sent to its 169 members. The survey was launched in July 2021. A link to the survey was also posted in posts on the MUA WhatsApp Group.

Completed survey results were automatically collated by the survey website software. Data was then collected for different groups and comparisons were made between these groups. Groups compared included consultants and trainees, clinicians aged 30-40 years, 40-50 years or over 50 years, clinicians working in a government setting, in a university setting and private setting, and clinicians performing TPT biopsy and those not performing TPT biopsy.

Statistical comparisons were made using the chi-square test for equal proportions or Fisher's exact test when numbers were small. A two-sided P value of less than 0.05 was considered statistically significant.

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Results

General demographics

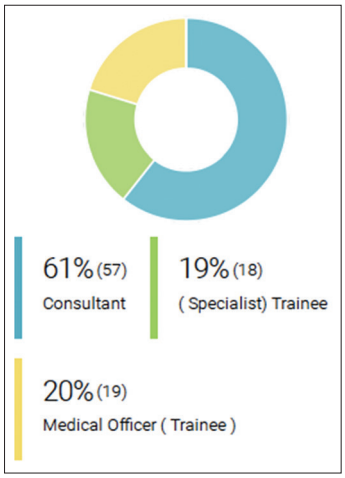
Of the 169 Malaysian Urological Association (MUA) members to whom the survey was distributed, 94 completed questionnaires were received, for a response rate of 55.62%. 61% were consultants, 19% were specialists, and 20% were medical officers [Graph 1]. Of them, 45% were 30–40 years old, 27% were 40–50 years old, and 28% were older than 50 years. 89% of the respondents were male, and 11% were female. 46% of respondents were from the government sector, 20% from the university sector, and 33% from the private sector.

Biopsy technique

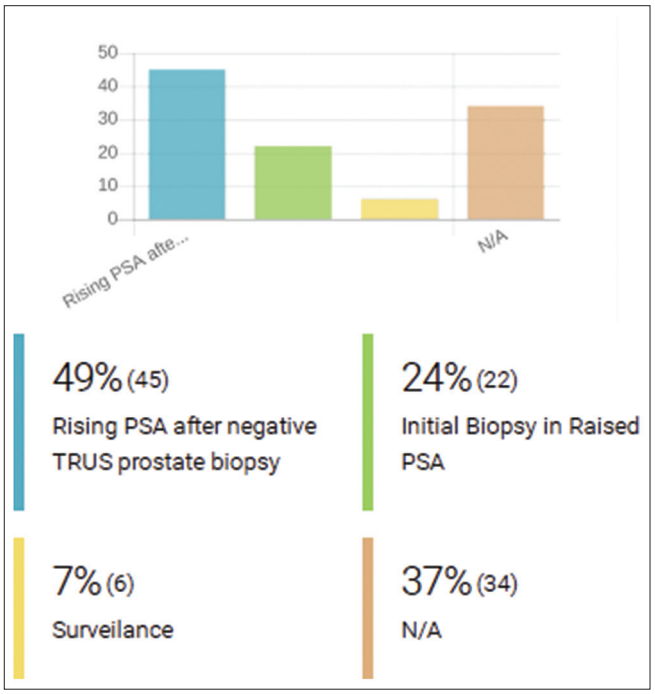
Ninety-three percent of clinicians responding to the survey perform transrectal ultrasound-guided (TRUS) biopsies themselves, 97% perform 1–20 TRUS biopsies per month, 54% perform tranperineal biopsies themselves, and of these, 49% use them when there is an increase in prostate-specific antigen (PSA) after an initial negative transrectal biopsy, while 24% use them in biopsy-naive patients [Graph 2]. As many as 24% use the magnetic resonance imaging (MRI)-US fusion biopsy, while 37% use the cognitive biopsy technique to perform the transperineal biopsy. Fifty-nine percent of physicians perform their TRUS biopsy in the outpatient center, while 6% perform it in the operating room, while 53% perform TRUS biopsy in the operating room.

Use of magnetic resonance

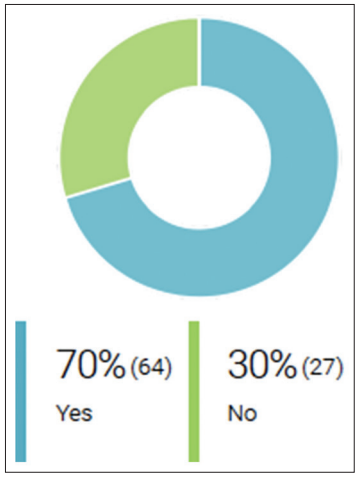
Seventy percent of respondents had ordered magnetic resonance (MR) of the prostate before an initial



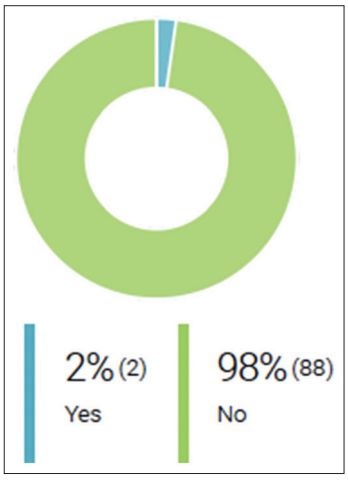
Graph 1: What is your position within Malaysian Urological Association?



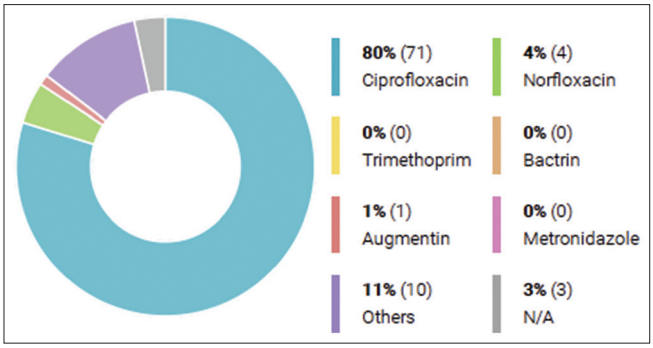
Graph 2: What are your indications for Tranperineal Prostate Biopsy? (If you perform this)



Graph 3: Have you ever ordered a MRI of the prostate prior to an initial TRUS biopsy? MRI: Magnetic resonance imaging, TRUS: Transrectal ultrasound-guided



Graph 4: Do you take a rectal swab prior to TRUS? TRUS: Transrectal ultrasound-guided



Graph 5: If so, what do you prescribe?

Table 1: Questionnaire

Page 1 Clinician information:
What is your position within MUA?

What is your age?
What is your gender?
Where do you predominantly work?

Page 2 Biopsy techniques
Do you perform TRUS yourself?
How many prostate biopsies/month do you do?

Do you perform TPT yourself?
Have you referred patients elsewhere for TPT?

What are your indications for TPT?

Page 3 The use of MR
Have you ever ordered a MRI of the prostate prior to an initial TRUS biopsy?
Do you order a MRI of the prostate before a repeat biopsy?

Page 4 Patient preparation
Do you take a rectal swab prior to TRUS?
If so, does it influence your antibiotic prophylactic regime?

Do you routinely order a standard enema?
An antiseptic enema?

Page 5 Prophylactic antibiotics
Do you use oral prophylactic antibiotics?
If so, what do you prescribe?
How many days prior to biopsy do you start prophylactic antibiotics?

What duration do you prescribe prophylactic antibiotics?
Do you use IV prophylactic antibiotics?
If so, what do you prescribe routinely?
Have you ever prescribed a carbapenem?
Do you routinely prescribe a carbapenem as prophylaxis if a patient has travelled to Asia or used a quinolone within the last 6 months?

Page 6 Analgesic regimes
What analgesia do your patients receive for TRUS?

Page 7 Prostate sampling and analysis
How many cores do you take in an initial TRUS biopsy?
Does prostate volume influence your decision regarding numbers of cores taken?
How many cores do you take in a repeat TRUS biopsy? (including active surveillance patients)
Who do you send the biopsy specimens to?

Page 8 Clinician preferences
If you yourself needed an initial prostate biopsy what would you choose for analgesia?
And which technique would you choose for yourself?

MUA: Malaysian urological association, TRUS: Transrectal ultrasound

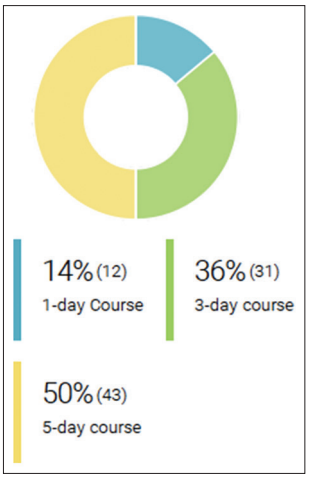
biopsy [Graph 3] and 92% routinely used MR before a repeat biopsy. For MRI, 57% of physicians use a general radiologist and 43% use an experienced uroradiologist.

Methods of patient preparation

Only 2% of clinicians routinely performed a rectal swab prior to prostate biopsy [Graph 4]. 60% ordered a standard enema before prostate biopsy, and 11% ordered an antiseptic enema before prostate biopsy.

Antibiotic prophylaxis

Ninety-five percent used prophylactic antibiotics before prostate biopsy. Graph 5 shows the most commonly



Graph 6: What duration do you prescribe prophylactic antibiotics?

prescribed prophylactic antibiotics. Prophylactic antibiotics were most commonly prescribed the day before the procedure (79%) or the day of the procedure (16%). 50% of clinicians prescribed prophylactic antibiotics for 5 days, 36% for 3 days, and 14% for 1 day [Graph 6].

Thirty percent of clinicians used intravenous (IV) prophylactic antibiotics. Sixteen percent of clinicians used IV carbapenems and 54% used them routinely within 6 months.

Analgesic regimen

Eighty-two percent of clinicians use periprostatic local anesthesia (LA) for TRUS biopsy, while 23% use general anesthesia and 20% use regional anesthesia for transperineal biopsy. A small minority of 15% use periprostatic LA for transperineal biopsy.

Collection and analysis of the prostate biopsy

For an initial prostate biopsy, 52% of clinicians harvested 10–12 prostate cores, while 48% harvested 12–20 cores. Prostate volume influenced the decision of how many cores were taken in 55% of clinicians. For repeat biopsy, including patients who underwent repeat biopsy as part of active surveillance, 16% of clinicians took more than 20 cores, while the majority (61%) took 12–20 cores. 88% of clinicians used general pathologists to analyze specimens, while 13% used specialized uropathologists. For transperineal biopsy, 84% would perform a targeted and systemic biopsy.

Urologists' preferences

Overall, 67% of clinicians would prefer a transperineal biopsy of the prostate if they needed a biopsy, while 46% would have chosen a periprostatic LA if they had had a TRUS performed.

Discussion

Prostate biopsy remains the mainstay in the diagnosis

of prostate cancer. Standard prostate biopsy is performed under ultrasound guidance. In most cases, prostate biopsy is performed transrectally. However, the transperineal approach, with comparable cancer detection rates to TRUS biopsy, seems to be gaining acceptance and has even improved recently.

There is no clear standard for other aspects of prostate biopsy. Therefore, prostate biopsy practices vary from urologist to urologist. This is not limited to biopsy technique, but also extends to patient preparation, antibiotic prophylaxis, analgesia, prostate sampling and analysis, and use of MRI.

A response rate of half of the fraternity to the survey provides a good insight into the trends in prostate biopsy practice in our region that have emerged.

Antibiotic prophylaxis

When a TRUS biopsy of the prostate is performed, rectal flora can enter the prostate and from there into the bloodstream. The most common organisms include *Escherichia coli*, Streptococcus faecalis, and Bacteroides. Several studies have demonstrated the efficacy of prophylactic antibiotics in TRUS biopsy, making them the standard of care.

According to the current EAU guidelines, quinolones are the antibiotic of choice for TRUS biopsy because they are well absorbed orally and penetrate well into prostate tissue. Our data suggest that quinolones in the form of ciprofloxacin and norfloxacin are most commonly used for prophylaxis in this region.

Infectious complications after prostate biopsy have been reported to occur in 1%–6% of patients and range from life-threatening sepsis to fever, urinary tract infections, acute prostatitis, and epididymo-orchitis. Quinolone-resistant infections following prostate biopsy are becoming increasingly common worldwide. They are a significant problem and have even been declared a public health emergency.

The cause of this worrying trend is thought to be the widespread improper use of quinolones.[11] Use of quinolones in the 6 months prior to biopsy has been associated with an increased risk of fecal transmission of quinolone-resistant bacteria.

Quinolone-resistant bacteria are usually sensitive to carbapenems. In this survey, 46% of clinicians reported using IV carbapenems for prophylaxis. Sixteen percent said they routinely use carbapenems in patients at some point. This prophylactic use of carbapenems underscores the concern about sepsis with quinolone-resistant bacteria in our region. Even more concerning than quinolone-resistant pathogens is the emergence of carbapenem-resistant Enterobacter (CRE), which the 2013 CDC report categorized as an "urgent threat." These strains are likely promoted by the increasing use of carbapenems for prophylaxis because "antibiotic use is the single most important factor leading to antibiotic resistance worldwide."[13] Treatment options for these organisms are very limited.

Previous studies without antibiotic prophylaxis are small and have shown a variable incidence of infections with fever. Gustafsson *et al*.[3] reported nine of 145 (6.2%) patients who developed fever, but these patients had undergone not only 2–4 18-G core biopsies but also three aspiration biopsies with a 22-G needle. Vallancien *et al*.[4] reported 15 of 145 (10%) patients with fever; these incidences are higher than in the present study. In contrast, others reported a low incidence.

Norberg *et al*.[5] reduced febrile reactions from 3.5% to 1.4% in groups of 199 and 148 patients, respectively, by giving antibiotics for 3 days instead of 1 day, and Aus *et al*.[6] reduced them from 4.9% to 2.8% in groups of 245 and 246 patients, respectively, by giving antibiotics for 1 week instead of 1 day. Aus *et al*.[6] concluded that the reduction in the number of infections was significant only for the subgroup with risk factors. In this group, febrile reactions were reduced from 9.5% to 1.1% in 84 and 90 men, respectively. Patients without risk factors developed fever in 2.5% and 3.8%, respectively.

The timing and duration of antibiotic prophylaxis varied widely in some of the reported studies. Some studies, e.g., Norberg *et al*.[18] and Aus *et al*.,[19] gave the antibiotic in immediate relation to the examination, whereas the others gave it between 15 min and an hour before the examination; this could make a difference.

Some studies show slightly fewer febrile reactions with prophylactic antibiotic therapy for 3 days. However, Aus *et al*. reported seven of 246 (2.8%) patients with fever despite 7 days of antibiotics. This suggests that regardless of the regimen of prophylactic antibiotic therapy, a few patients will still develop an infection with fever.

Transperineal biopsy of the prostate gland

Transperineal biopsy has an equivalent tumor detection rate and has been reported to improve cancer detection in the anterior zone.[8] Transperineal template (TPT) biopsy has an extremely low infection rate. This is especially important considering the increasing incidence of serious infections following TRUS biopsy. A recent worldwide survey found that the infection rate after TPT biopsy was 0.07%.[9] In our region, TPT was used very frequently, especially in cases of rising PSA levels after negative TRUS biopsies (49%), with 54% of clinicians performing the TPT biopsy themselves. It was most commonly performed by physicians in private centers, followed by universities.

Of note, when asked which biopsy technique they would choose themselves if they needed a prostate biopsy, both

consultants and trainees were more likely to choose a TPT biopsy of their prostate than specialists, at 88% and 83%, respectively. This could lead to more frequent use of this technique in the future.

Systematic biopsy plays an important role in the diagnosis of prostate cancer because the disease is multifocal and confined to small lesions in many cases. Since Hodge *et al*.[10] reported, systematic sextant prostate biopsy has become very popular in the United States. Previous studies have shown that transrectal sextant biopsy has a cancer detection rate of 20% to 32% for PSA levels of 4–10 ng/ml.[11] Increasing the number of biopsy cores and target regions could improve the cancer detection rate. Eskew *et al*.[11] reported that increasing the number of target regions by three (each far lateral and in the middle of the gland) compared with conventional sextant biopsy and the number of cores by at least seven significantly improved the cancer detection rate from 26% (31 of 119) to 40% (48 of 119).

To compare the transperineal and transrectal approaches, Emiliozzi *et al*.[12] performed six transperineal and six transrectal biopsies in 107 patients with a PSA level of 4.1 ng/ml or more. They reported that the transperineal approach was more useful, as the cancer detection rate was 40% (43 of 107) with the combination of both biopsy methods, 38% (41 of 107) with the transperineal approach alone, and 32% (34 of 107) with the transrectal approach alone ($P < 0.012$). Jones *et al*.[10] also reported that the saturation technique did not improve cancer detection on initial prostate biopsy compared with 10-core biopsy.

Shannon *et al*.[13] reported that the transperineal approach was more successful in detecting TC cancer, as the rate of correct diagnosis was higher with the transperineal approach than with the transrectal approach (89% versus 68%). Furuno *et al*.[14] performed transperineal ultrasound-guided template biopsy in patients with PSA levels of 4–10 ng/ml. They reported that the rate of cancer nuclei was significantly higher in biopsies from the anterior prostate than in biopsies from the posterior region, suggesting that transrectal sextant biopsy may be inappropriate for detecting cancer in the anterior region.

Use of magnetic resonance imaging

Multiparametric MRI of the prostate is increasingly used to detect prostate cancer. If suspicious areas are found, they can be targeted with additional biopsies. Some centers even perform MR-targeted biopsies exclusively, although this remains controversial.[1]

There has been significant use of MRI among MUA members. 70% of members performed MRI prior to an initial prostate biopsy. The use of MRI was most notable among clinicians who performed a TPT biopsy of the prostate. 84% of clinicians performing a targeted and sytemic biopsy while 14% only perform targeted biopsy of the prostate performed MRI prior to the repeat biopsy. These results suggest some acceptance of MRI as a useful tool in the diagnosis of prostate cancer by urologists in the region and are consistent with the growing literature in this area.In men without prior biopsy.

Recent studies have demonstrated the beneficial role of MRI prior to initial biopsy. In a study of 555 patients with high PSA or abnormal DRE, Haffner *et al*. performed a 10-core TRUS biopsy and a cognitive TRUS biopsy of MRI-suspected regions.[13] Had only targeted cores been performed instead of standard TRUS biopsy, 37% of biopsies would have been avoided, an average of 3.8 rather than 10 cores would have been required, 13% of low-grade cancers would not have been missed, and detected cancers would have received more accurate grading (16% more high-grade cancers were detected) and volume determination. In a randomized controlled trial, Park *et al*. studied 85 biopsy-naive men with clinically suspected prostate cancer. The group with visually estimated TRUS-guided biopsy had a threefold higher cancer detection rate (29.5% vs. 9.8%) [odds ratio (OR): 3.9 (95% confidence interval (CI): 1.1–13.1, $P = 0.03$)] and a fourfold higher positive core rate (9.9% vs. 2.5%) [OR: 4.2 (95% CI: 2.2–8.1, $P < 0.01$)], suggesting more accurate detection and risk stratification.[14] In another prospective study of 351 consecutive patients with elevated PSA, Numao *et al*. reported that the incidence of significant cancers in men with a positive MRI compared with a negative MRI was much higher in the low-risk group (43%–50% vs. 9-13%) and in the high-risk group (68%–71% vs. 47%–51%).[15] An important finding of this study shows that in the low-risk group, defined as men with a PSA level of <10 ng/ml and normal DRE, the negative predictive power of a combination of negative MRI and prostate volume <33 ml for significant cancer was 95.1%–97.5%, suggesting that one-third of men with negative MRI and small prostate volume could avoid biopsy.

In men with previous negative biopsy

In patients with a prior negative biopsy, MRI-guided prostate biopsy can support treatment decisions by helping to overcome diagnostic uncertainty, as imaging can help localize a suspicious area, such as in the 30% of men with prostate cancer whose tumor arises in the anterior or transition zone. Lavrentschuk and Fleshner analyzed the combined data of 215 men from six prospective studies of MRI prior to rebiopsy as PSA levels increased and found that prostate cancer was detected only by the MRI-guided cores in 54% of men who received both standard and MRI-guided biopsies.[16] In a related study using MR-US fusion biopsy in 105 patients with prior negative biopsy and elevated PSA, Sonn *et al*. found a cancer detection rate of 34% (36/105), with 72% of these 36 cancers being clinically significant. On multivariate analysis, a highly suspicious MRI lesion was the most important predictor

of significant cancer with an OR of 33, with clinically significant cancer detected in 12/14 (86%) patients.[17] According to the National Comprehensive Cancer Network and European Association of Urology guidelines, multiparametric MRI is now recommended for men with a rising PSA and suspected cancer despite multiple negative biopsies.

For men at low risk of cancer

Targeted MRI biopsy may be a valuable tool in men with prostate cancer under active surveillance because of its high negative predictive value for intermediate-to-high-risk prostate cancer. Vargas *et al*. studied a cohort of 388 consecutive men with low-risk prostate cancer at initial biopsy who underwent MRI, followed by an initial surveillance biopsy and a confirmatory biopsy within 12 months. A negative MRI (score of 1–2 out of 5) had 98% specificity and negative predictive value for excluding Gleason staging, whereas a positive MRI (score of 5 out of 5) had 93% sensitivity for Gleason staging (20% of the cohort had Gleason staging at the first surveillance biopsy). In a series of 66 men who underwent MRI followed by re-biopsy within 3 months of enrolment in active surveillance, Berglund *et al*. examined pathologic upgrading and up-staging and found that 27% of men had presumed extracapsular extension on MRI, of whom 39% had high-risk upgrading on re-biopsy; none of the 73% with normal MRI had high-risk upgrading on re-biopsy.[18] Recently, multiparametric MRI with confirmatory biopsy has been associated with reclassification of men who would have been eligible for active surveillance, underscoring its role in the decision-making process when considering active surveillance.

Analgesic therapies

The EUA guidelines on TRUS biopsy describe periprostatic infiltration of LA as state of the art analgesia.[14] The majority of TRUS biopsies in our region were performed under periprostatic LA with 82%, while 8% IV sedation. This also highlights the significant resource expenditure associated with performing a prostate biopsy under IV sedation and GA. Further research is needed to find a commonly accepted and effective method of analgesia that can be performed outside the operating room. Most clinicians performing TPT rely on general anesthesia (23%) or periprostatic LA (15%) for some type of analgesia.

There is sufficient evidence in the literature that some form of anesthesia/analgesia during TRUS biopsy improves patient tolerance and comfort. However, the optimal method remains to be determined. Among the different techniques, periprostatic lidocaine infiltration has shown the best results in terms of pain control. Therefore, it could be accepted as the gold standard if the urologist/radiologist considers the prostate biopsy "painful enough" to proceed with an analgesia/anesthesia method. Nevertheless, periprostatic nerve block has some weaknesses. Although some believe that the rectal surface below the dentin line is painless, a prospective randomized study has shown that the pain of inserting the needle to infiltrate the anesthetic can be more painful than the insertion of the probe and the actual biopsy.[7]

Another important pain component results from the insertion of the ultrasound probe, on which periprostatic blockade has little effect. Indeed, the mean pain score was significantly lower in the combination group (2.03 vs. 2.57). In addition, more patients in the combination group had a pain score of 3 or less, although the difference did not reach statistical significance (87% vs. 75%).

Another disadvantage of periprostatic infiltration is its tendency to increase infectious complications and bacteriuria rates.[7]

There are few studies addressing the role of noninvasive pain-relieving methods in prostate biopsy. Although the use of sterile lidocaine gel is noninvasive, it has been shown to be inferior to nerve block in pain management. Masood *et al*. reported that Entonox (50% nitrous oxide-oxygen) is a safe and effective form of analgesia.[19] However, to our knowledge, it is not widely used in daily practice, likely due to its relatively impractical use in a practice setting. Entonox requires personnel trained in resuscitation techniques to establish an airway if needed. Chronic inhalation of nitrous oxide poses a risk of potential toxicity to personnel. In addition, patients with certain medical problems, such as severe chronic obstructive pulmonary disease or severe coronary artery disease, are not appropriate candidates for nitrous oxide analgesia.[20] Importantly, unlike other opioids, tramadol has no clinically relevant effects on respiratory or cardiovascular parameters at recommended doses.[21] Therefore, it may prove particularly useful in patients with poor cardiopulmonary function. Moreover, its efficacy is similar to that of periprostatic nerve block, which is currently the gold standard.

Previously, periprostatic infiltration was reported to be associated with higher infectious complications and bacteriuria rates. It was speculated that this was due to the additional punctures and infiltration through a highly colonized medium, the rectum.

Prostate sampling and analysis

In the majority of TRUS biopsies, at least 12 cores were obtained. This is in accordance with EAU guidelines on the standard number of cores to be taken. Some clinicians would take more cores depending on the size of the prostate at approximately 55%. For repeat TRUS biopsy, 61% of clinicians would use the saturation biopsy technique, which includes 20 or more samples. Depending on the clinician's institution, most would send their samples to a general pathologist.

Sextant technique

The sextant technique, introduced in 1989 by Hodge *et al*., has become the gold standard for prostate biopsy worldwide.[22] As originally described, the sextant method involves taking 6 biopsies of the prostate, bilaterally from the base, middle, and apex of the prostate in the parasagittal plane of the mid-lumbar region.

Although the sextant method was the first described systematic method of prostate biopsy, other methods have shown that the sextant technique as originally described has a false-negative rate of approximately 30%.[23] This false-negative rate is understandable because not only are fewer cores taken with this method, but also a smaller percentage of the peripheral zone of the prostate, where 80% of prostatic adenocarcinomas are found. More recently, the sextant method has been modified to perform more laterally oriented biopsies. These biopsies, which have been termed "lateral biopsies" in several studies, include areas of the prostate called the "far lateral region" and "anterior horn."

Multisite biopsy with eleven cores. Babaian *et al*. studied an 11-core biopsy method in 362 patients that included both sextant biopsies and 1 biopsy from the far lateral region (anterior horn), midline, and bilateral transition zones (adjacent to and anterior to the urethra).[24] This study showed a statistically significant 33% increase in the overall detection rate of prostate cancer.

Eight systematic biopsies. Presti *et al*. studied systematic prostate biopsy in 483 patients.[25] In this biopsy scheme, 10 samples are taken from the prostate, 6 samples from the traditional sextant regions and 2 cores each from the lateral regions (marginal zones). This method is similar to the 5-region technique, except that the midline biopsies are omitted. The authors found that with systematic sampling from the traditional sextant region, the lateral base, and the lateral midline of the gland, 96% of diagnosed cancers were detected. Elimination of the nucleus from the lobar base of the sextant biopsy, resulting in the 8-biopsy scheme of the peripheral zone, decreased cancer detection by only 1%. It is not known whether 8 systematic biopsies is the optimal number. However, this study is useful in determining which cores can be safely omitted (sextant in the middle of the lobe base) without significantly affecting the cancer detection rate.[25] In this study, traditional sextant biopsies missed 20% of diagnosed cancers. Since other studies have shown that cancer is also found at the midlines of the gland, this biopsy technique may have a higher false-negative rate than other techniques that have been reported.[24]

Although TRUS-guided systematic sextant biopsy is recognized as the "gold standard" for prostate biopsies, the efficiency of this technique is controversial; many studies have been performed to improve the detection rate of this procedure. Several authors claim that the sampling performed with sextant biopsy is not sufficient and suggest increasing the number of cores. Levine *et al*. have shown that two consecutive sets of TRUS-guided sextant biopsies of the prostate performed in a single consultation were a cost-effective biopsy strategy, increasing the number of carcinomas detected by 30%.[51] In another study, Babaian *et al*. reported that 20% to 25% of prostate carcinomas were not detected with the classic sextant biopsy protocol; they introduced an 11-core biopsy technique that improved the detection rate.[24] The current trend is to increase the number of cores; detection rates of prostate biopsies with 18, 20, and 24 cores have been studied.[26]

Conclusion

This study provides insight into the current practice of prostate biopsy among members of the MUA. Although TRUS biopsy without additional imaging was still the most typical approach, MRI and TPT biopsy were commonly used. These two diagnostic methods are likely to increase in the future. Quinolone prophylaxis was widely used, but selective use of prophylactic carbapenems was also common, indicating concern about quinolone-resistant pathogens and their infectious complications.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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A Complication Arising as a Result of a Severe COVID-19 Infection: Prostatic Infarction

Abstract

A 57-year-old male patient diagnosed with coronavirus disease nearly 2 months ago and started to be treated was admitted to intensive care after 2 weeks due to the deterioration of his general condition. The patient's general condition improved during 3 weeks of intensive care, and he was moved to the regular unit, and his catheter was removed. Three days after being discharged from the hospital, the patient went to the emergency department due to urethral bleeding and inability to urinate. The patient had urethrorrhagia and globe vesical. A cystofix was inserted as a catheter could not be inserted. Following the urology consultation, it was decided to perform a transurethral resection of the prostate surgery. The prostate was found to be fully infarcted during the operation. Three days after the surgery, his catheter was removed, and the patient urinated spontaneously. He was then discharged. It was understood that prostatic infarctions may arise as a result of COVID-19 infection.

Keywords: *Coronavirus disease, multiparametric prostate magnetic resonance imaging, prostatic infarction, transurethral resection of the prostate*

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Introduction

Coronavirus disease (COVID-19) has emerged as a severe health problem worldwide.[1] The mortality rate due to COVID-19 ranges from 0.9% in patients with no comorbidity to 10.5% in patients with comorbidity.[2]

The virus damages various organs, notably the lungs, kidneys, and brain. It has been determined that following COVID-19 infection, the damage causes cytokine storm, procoagulant activity and multiple organ failure, as well as affecting many organs.[3]

Age-related defects in T- and B-cells and overproduction of type II cytokines may induce prolonged proinflammatory responses and lack of control in viral replication, which could potentially lead to unfavorable outcomes.

Case Report

A 57-year-old male patient was diagnosed with COVID-19 nearly 2 months ago and provided with outpatient treatment. His general condition got worsened on the 12th day of the treatment. The patient with respiratory failure was intubated and admitted to intensive care. The patient was extubated after 3 weeks of intensive care and moved to the regular unit. His catheter was removed after completion of the treatment in the regular unit, and the patient was discharged. Later on, the patient went to the emergency department due to urethral bleeding and the inability to urinate. The examination presented urethral bleeding, suprapubic pain, and swelling. 16 Fr, 12 Fr, and 8 Fr catheters could not be inserted; therefore, a suprapubic cystostomy catheter was inserted. The rectal examination revealed a prostate with 1+ induration as well as pain, and a total prostate-specific antigen (PSA) and urine culture test were performed. A mpMRI of the prostate was performed on the patient as his PSA level was 4.25 ng/ml. The MRI exhibited a 53 g prostate with two hyperintense areas in the T1-weighted image without peripheral augmentation following contrast infusion or diffusion limitations, which suggested prostatic infarction. Prostate Imaging–Reporting and Data System category 2 lesion on the peripheral zone of the prostate gland; presacral space edema; stage II avascular necrosis in the anterior part of the femoral head on the right were detected [Figure 1]. Combined spinal-epidural anesthesia and plasmakinetic TUR were planned to be

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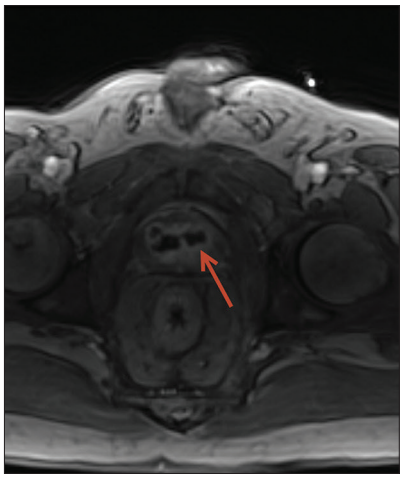

Figure 1: Gradient T1 sequence with dynamic contrast-enhanced is showed necrosis as no contrast enhancement on axial sequence

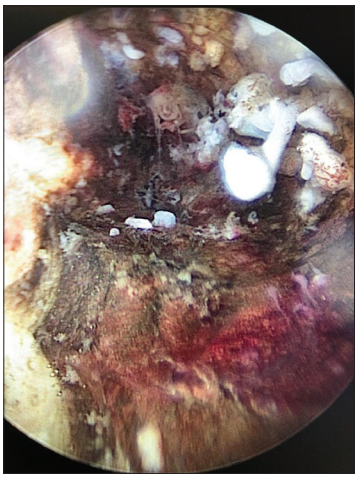

Figure 2: Endoscopic view of the prostate apical lobes with necrosis and hemorrhage

used on the patient. During the surgery, the prostate was found to be bleeding and infarcted [Figure 2].

Once a sample was resected, a fresh piece of tissue was sent to the laboratory to be tested for polymerase chain reaction-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it tested negative.

The patient's catheter was removed 2 days after the surgery, and he was discharged. Pathology results presented hemorrhagic infarct, chronic prostatitis, and adenomyomatous hyperplasia. The patient was on anticoagulants throughout the intensive care and afterward only except for the day of surgery.

Discussion

The new clinical symptoms of COVID-19 infection have been defined recently following the pandemic. It has been observed that the damage induced by the infection causes cytokine storm, procoagulant activity, and multiple organ failure, as well as affecting many organs. The virus inflicts damage on various organs, notably the lungs, heart, kidneys, and brain, among critical patients. Discussions relating to the use of anticoagulants on patients with COVID-19 have intensified as a result of increased evidence on hypercoagulation among this patient group.[3,4]

Recent studies have shown that hypercoagulation is caused through the activation of endothelial cells, thrombocytes and leukocytes, which possibly induce the tissue factor and then by stimulating the coagulation system attaching to the coagulation factor VIIa.[5] The coronavirus infects cells by attaching the viral S protein to the angiotensin-converting enzyme (ACE2) receptor located in the lungs, kidneys, intestines, and testicles. Studies have reported that ACE2, which is the receptor for COVID-19 in some organs, has high protein expression associated with organ failure in patients infected with SARS.[6] ACE2 is a constitutive product of adult-type Leydig and Sertoli cells and has an important role in protecting the lungs.[2] As there is more information available on COVID-19, studies increasingly show that patients with COVID-19 are at risk of deep vein thrombosis and pulmonary embolism.[7] Thromboembolic events appear to include both arterial and venous systems in patients with COVID-19.[8]

Studies have exhibited that SARS-CoV-2 was found in semen; however, it is yet unknown which organ is affected by the infection to what extent.[2,9]

The mechanisms involved in SARS-CoV-2/host cell interaction have key importance for cell infection and replication, leading to disease and related damage.

In a study, in order to detect SARS-CoV-2, a total of 205 samples were collected from the urine, semen, and prostate fluid of a 74-year-old patient who recovered from COVID-19; no viral nucleic acid was detected in the body fluids collected from the urogenital system.[10]

Screening PubMed for COVID-19 and thrombotic events over the past 5 years exhibits 354 studies, one of which reports a case of infarcted prostate tissue following incidence of acute urinary retention after COVID-19.[11] Unlike our case, the occurrence of urinary retention in the presented case was caused by the large volume of the prostate. In our case, the prostate weighed 50 ml, presented hemorrhagic infarction, and was infarcted in all apical lobes up to the capsule.

A number of factors have been suggested for the incidence of prostatic infarction. Some studies focus on the lack of blood supply in the prostate due to instrumentation, infection, thrombosis, embolism, atherosclerosis or enlarged prostate, or on venous drainage of blood vessels. Other studies address a significant correlation between prostatic infarct and some potential risk factors such as smoking and preexisting cardiovascular diseases.[12,13]

Although the relationship between prostatic infarction and acute urinary retention has been studied, no clear results

are as yet achieved. Baird *et al*. who carried out a study on the correlation between acute urinary retention occurring in patients with a large prostate and prostate infarct which occurred afterward found that enucleated parts of infarcted prostate weighed almost twice as much as the prostates which were not infarcted.[14] Another study revealed that enlargement of the prostate gland due to hyperplasia is not a common cause of prostatic infarction in the absence of the prostate gland.[15]

This article supports the views on embolism and thrombosis put forth with regard to prostatic infarction. COVID-19 thromboembolism has been determined to occur in the brain, heart, and kidneys in particular; however, the study demonstrates that prostate infarcts can occur following a thromboembolic event in the prostate.

Conclusion

It is understood through the reported case that ischemic events induced by COVID-19 in other organs can also occur in prostate tissue.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Use of a Small-Diameter Resectoscope on a Patient with Extensive Urethral Strictures for Transurethral Resection

Abstract

This case refers to a 60-year-old male suffering from an extensive circular urethral stricture throughout the whole length of the urethra, with the coexistence of a papillomatous tumor of the urinary bladder. The insertion of the resectoscope through the urethra was impossible, despite previous dilations with Benique. Therefore, an internal urethrotomy was performed. From May 2020 to September 2022, the patient was submitted to three TUR-BTs with the use of a smaller diameter resectoscope (22ch). The histology report resulted in TCC (Transitional Cell Carcinoma) stage pT1 high grade. The patient was then administered intravesical bacillus Calmette-Guerin installations. The last TUR-BT took place in October 2022. It was impossible to insert the conventional 22ch resectoscope through the urethra, so the Delmont gynecological resectoscope was used instead. This resectoscope by the French company Delmont has the same length as the conventional urological resectoscopes, but the important fact is its smaller diameter (18, 5 ch), allowing the surgeon to pass through the urethra and approach the papillomatous lesion in the bladder. The lesion was resected transurethrally, and the histological examination resulted in TCC with focal infiltration of the muscle layer, stage pT2 high grade. In this way, it was possible to complete the surgical procedure in a case that the conventional resectoscope could not enter the urethra, and the outcome was exceptional. In November 2022, following the Oncology–Urology Council of the hospital, it was decided for the patient to receive neoadjuvant chemotherapy followed by radical cystoprostatectomy.

Keywords: *Bladder cancer, resectoscope, urethral strictures*

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Etiology

There are many types of strictures, including iatrogenic strictures (such as those caused by catheterization, instrumentation, and prior hypospadias repair), infectious strictures (e.g., caused by gonorrhea or lichen sclerosis), traumatic strictures (including straddle injuries or pelvic fractures), and congenital or idiopathic strictures [Table 1].[1]

Iatrogenic causes have been shown to account for almost 50% of idiopathic strictures, which relates to about 30% of all strictures.[3]

As concern as the penile urethral strictures, about 15% are idiopathic, 40% are iatrogenic, 40% are inflammatory, and 5% are related to trauma.

For bulbar urethral strictures, about 40% are idiopathic, 35% are iatrogenic, 10% are inflammatory, and 15% are traumatic.[1]

In general, recurrence is more likely with longer strictures. The risk of recurrence at 12 months is 40% for strictures <2 cm, 50% for strictures between 2 and 4 cm, and 80% for strictures >4 cm.[4]

Aim

The aim of this publication was to present the management of patients with extensive urethral stricture, who need to undergo a transurethral bladder cancer resection, since the conventional urological resectoscopes cannot pass through the urethra.

Strictures are mainly caused by injury of the urethral epithelium and/or the underlying corpus spongiosum, which eventually causes fibrosis during the healing process.[5]

At the time of injury, this fibrosis may be asymptomatic; however, over time, the fibrosis process may cause further narrowing of the urethral lumen, resulting in symptomatic obstructive urination.[5]

The most commonly performed procedure for urethral stricture is dilation/urethrotomy. A survey of 1262 US urologists found that

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most urologists treat 6–20 strictures/year and over 90% perform dilation/urethrotomy.[6]

Urethral strictures are diagnosed either by ascending urethrocystography or with urethroscopy, using a flexible urethrocystoscope.

Ultrasounds can be used as a complementary examination to determine the length and degree of fibrosis of the corpus spongiosum of the urethra.[7,8]

Urethral strictures account for approximately 1.5 million office visits per year in the US.[2]

Case Report

This case refers to a 60-year-old male suffering from TCC. He was first diagnosed in April 2020, after reporting macroscopic hematuria and proceeding to computed tomography imaging and flexible cystoscopy.

The patient had an extensive circular urethral stricture, occupying the entire length of the urethra and the resectoscope insertion was impossible, despite previous Benique dilations, so an internal urethrotomy was performed.

From May 2020 to September 2022, three TUR-BTs were performed, with smaller diameter resectoscopes (22ch), and the histological examination revealed TCC, stage pT1 high grade.

The patient was administered intravesical bacillus Calmette-Guerin (BCG) installations. Since then, the follow-up includes cystoscopy every 3 months, BCG intravesical installations, regular imaging as well as urethral dilations.

The last TUR-BT was performed in October 2022 due to a 2 cm diameter papillomatous tumor of the posterior urinary bladder wall. Because the conventional 22ch resectoscope could not enter through the urethra, the French company Delmont gynecological resectoscope was used, which has the same length as the conventional resectoscope, with the important difference of a smaller diameter (18,5ch), thus allowing the surgeon to approach and resect the bladder tumor. The histology report resulted in TCC with focal infiltration of the muscle layer, stage pT2 high grade.

In November 2022, following the Oncology–Urology Council, it was decided to proceed with neoadjuvant chemotherapy followed by radical cystoprostatectomy.

Table 1: Incidence of strictures of different etiologies[2]

Etiology	Penile stricture (%)	Bulbar stricture (%)
Idiopathic	15	40
Iatrogenic	40	35
Inflammatory	40	10
Traumatic	5	15

After researching and contacting almost every urological endoscopic instrument manufacturer, it was impossible to find smaller diameter urological tools.

In our hospital, the gynecological department has a resectoscope (for biopsies and excision of polyps and uterine fibroids) by the French manufacturer Delmont featuring the same length as urological resectoscopes, but a much smaller diameter (18,5 ch). Figures 1-4.

In the past, we have successfully collaborated with the gynecologists in two of their cases, polyps resection and uterine fibroid biopsies.

Prior to the day of the surgery, the Delmont Company's representative was contacted for technical/further clarifications.

The patient received general anesthesia, and the insertion of the resectoscope (French manufacturer "Delmont") through the urethra was exceptionally smooth and easy, without causing any impact or damage to the tissue. The transurethral resection of the single bladder tumor was fully successful since the length of the resectoscope allowed an easy access to the papillomatous lesion.

The whole procedure was accurate and precise. Postoperation, the urine was clear and a 3-way Foley catheter with continuous saline irrigation was administered for a few hours.

On the next day, the Foley catheter was removed, and the patient's urination and urine color were satisfactory.

The cutting and coagulation brackets are smaller than those of the classic resectoscopes, while bipolar diathermy was also used. Their connections are similar to those of the urological endoscopes (cold light cable, cutting and coagulation electrodes, and washing fluids). The connection to the camera and monitor is compatible with our urological towers.

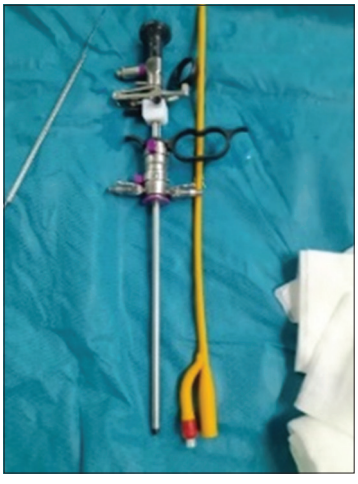

Figure 1: Comparison of the diameter of the 18.5 ch resectoscope to an 18 ch Foley urinary catheter

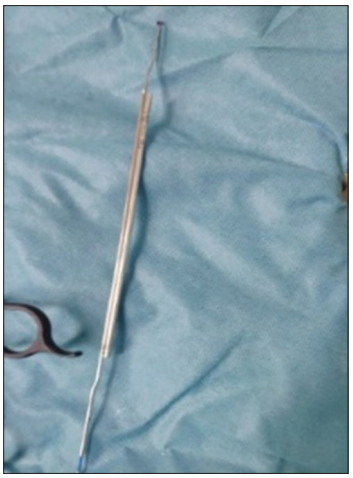

Figure 2: Resectoscope cut bracket

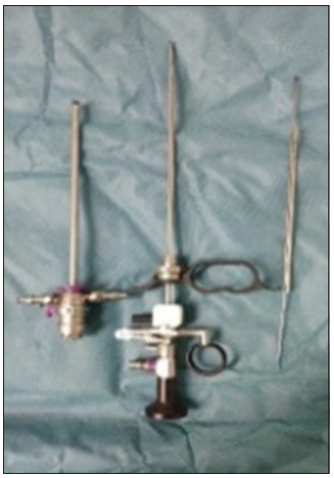

Figure 3: Full resectoscope set

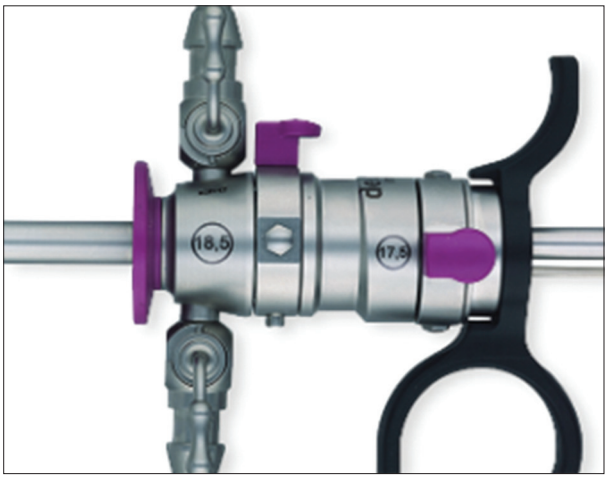

Figure 4: Resectoscope connection system

Figure 5: Bipolar diathermy

The bipolar diathermy power settings for cutting and coagulation range from 1 to 3; each power setting increases the output wattage accordingly. Initially, it was set for uterine polyps cutting and coagulation, while later on, the power was adjusted for a better safety and results to 2 for cutting and 3 for coagulation [Figure 5]. The cutting and coagulation brackets are comparatively smaller in diameter than the conventional resectoscopes; thus, the resection is consequently performed in smaller pieces of tissue compared to classic resectoscopes.

In general, for urethral strictures, the pediatric resectoscopes are also available, featuring a small diameter (8 or 9 ch), but also a much smaller length at 12 cm. It is their length that makes them inappropriate for use in urinary bladder cancer cases, while as mentioned above, in this case, the tumor was located on the posterior bladder wall.

Conclusions

This is an innovation of the Urology–Oncology Department of the Theagenio Cancer Hospital, concerning a transurethral surgery in a man with a severe stricture along the entire length of his urethra, and in whom it was impossible to insert 22 ch urological tools (minimum size of available conventional tools of all manufacturers internationally).

The French Delmont's 18.5 ch gynecological resectoscope system was used with an absolute success. Gynecological resectoscopes are used for the uterus and cervix. They are the same as urological resectoscopes and have the same length, but they are much thinner.

We suggest that large urological resectoscope manufacturers provide such smaller caliber resectoscopes to facilitate urologists in similar cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Quetiapine-Induced Chronic Priapism Needing Surgical Intervention

Abstract

Priapism is an uncommon but serious adverse effect of psychiatric medicines. Priapism is a urologic emergency defined by a prolonged, painful penile erection in the absence of sexual stimulation. It is seldom associated with the use of nonerectile dysfunction drugs. According to the findings, priapism can be caused by a variety of illnesses, including psychiatric medicines. One mechanism through which antipsychotics are thought to cause priapism is alpha 1-antagonism. This is distinctive and does not rely on long-term usage. The majority of the time, priapism resolves on its own or responds to conservative therapy. We discuss a rare instance of undiagnosed persistent priapism that required surgical intervention.

Keywords: *Antipsychotic, drug-induced, priapism, quetiapine, surgical intervention*

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Introduction

Priapism is described as prolonged penile erection that is not associated with sexual desire or stimulation and lasts for more than 4–6 h. It is deemed a urologic emergency that must be treated as soon as possible since it can cause erectile dysfunction in up to 90% of patients.[1] In general, there are two forms of priapism: high flow and low flow. High-flow priapism is nonischemic and is frequently induced by increased blood flow through arteries as a result of trauma. Low-flow priapism is caused by blood pooling inside the corpora as a result of erectile dysfunction drugs, hyperviscosity syndromes, injury, tumors, neurologic disorders, and prescription side effects. Several psychotropic medicines have also been linked to low-flow priapism, with trazodone being the most usually implicated. Quetiapine is an atypical antipsychotic that was initially developed to treat schizophrenia, but it is also used to treat a variety of other mental diseases, such as schizoaffective disorder, anxiety, bipolar disorder, and depression.[2] To date, the most widely accepted mechanism of this effect involves antagonism of alpha-1 adrenergic receptors leading to a relative decrease in local sympathetic tone concerning the local parasympathetic tone. The affinity of these drugs to alpha-1 adrenergic receptors varies significantly; the affinity of quetiapine compared to other antipsychotics is intermediate. Psychotropic drug-induced priapism does neither appear to be dose-dependent nor does it appear to correlate with the duration of the treatment.[3,4]

Prescribers must be aware of the possibility of drug-induced priapism as an adverse effect. Since ischemic priapism causes blood to stay in the penis for exceptionally lengthy periods of time, the blood gets starved of oxygen and can cause significant damage to the penile tissue itself, early suspicion, and diagnosis are critical. This can lead to erectile dysfunction, penile deformity, or impotence. In severe circumstances, priapism can lead to penile gangrene if the penis suffers a serious vascular condition.[5] Conservative care (watching, cooling, and resting), corporal aspiration, injecting of sympathomimetic drugs, and surgical treatment are the therapy options if the former therapies fail.[6] We present a case of priapism produced by quetiapine in a patient with bipolar illness who was in a euthymic condition.

Case Report

A 21-year-old man with mania-linked bipolar affective illness reported to the urology outpatient department with symptoms of a penile erection lasting 18 h. Before this appointment, he had

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erections exceeding 3 h daily morning for the previous month, which dissolved spontaneously. He put off going to the emergency room since he did not know about the adverse effects of the drug and expected it will go away on its own. There has been no history of trauma, sickle cell illness or trait, recent intercourse, vasoactive agents, including nitrates, or use of any sexual enhancement medicines or equipment. Destruction, angulation, fibrosis, lesions, or discharge was not identified in a nontender erect phallus. The patient had been on quetiapine 200 mg BD for manic-linked bipolar illness for 4 months before priapism. Tachycardia, QT prolongation, insomnia, and hyperglycemia were not present, indicating quetiapine intoxication.

On color Doppler ultrasonography, no flow was seen in cavernosal arteries with the symptoms of thrombosis [Figures 1 and 2]. Cavernosal veins were not seen distally on the penile angiogram [Figure 3]. Aspiration was performed, but tapping was unsuccessful. Al-Ghorab shunting plus dilatation of the both corpora cavernosa using Hegars dilators were performed, and priapism was resolved intraoperatively [Figures 4-6]. The patient was instructed to stop taking quetiapine and to schedule a follow-up appointment with his psychiatrist.

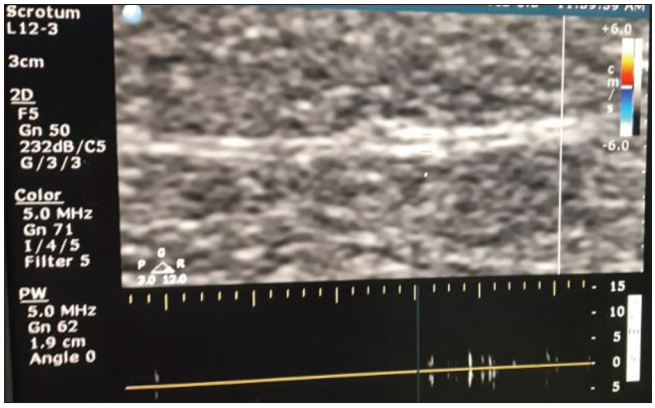

Figure 1: Penile color duplex Doppler ultrasonography, there was no flow noted in cavernosal vessels

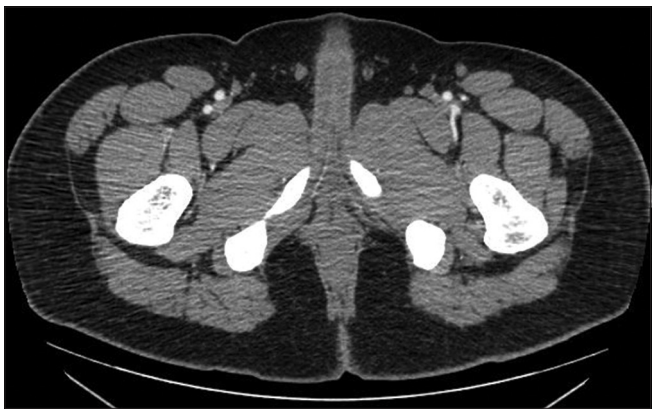

Figure 3: On penile angiogram, cavernosal vessels were not visualized distally

Discussion

Priapism may be classified into two types: high-flow priapism, which occurs when penile or pelvis trauma causes a shift in artery flow and low-flow priapism, which is more prevalent and is caused by medicines. Even after surgical surgery, around 40%–50% of people who acquire priapism become impotent. Medication-induced priapism accounts for 25%–40% of all instances, with antipsychotics and antihypertensives being the most typically related drug groups.[7]

Quetiapine is an antipsychotic second-generation medication that is used to treat bipolar disorder, schizophrenia, and serious depression. Priapism is a well-known adverse effect of first- and second-generation antipsychotics; however, quetiapine is seldom associated with the condition. In 2001, Paris and Ayvazian reported the first case of priapism: a 45-year-old man attempted suicide by eating 27 quetiapine (65 mg/tablet) tablets, resulting in priapism that required percutaneous cavernosal-glandular shunt to accomplish detumescence.[8]

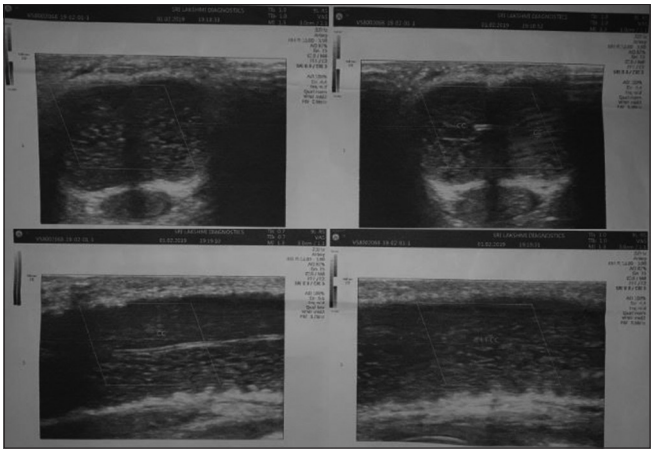

Figure 2: Penile color duplex Doppler ultrasonography, there was no flow noted in cavernosal vessels with signs of thrombosis present

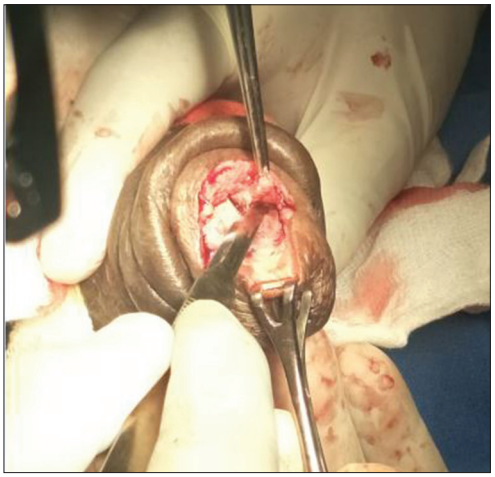

Figure 4: Intraoperative creation of Al-Ghorab distal shunt

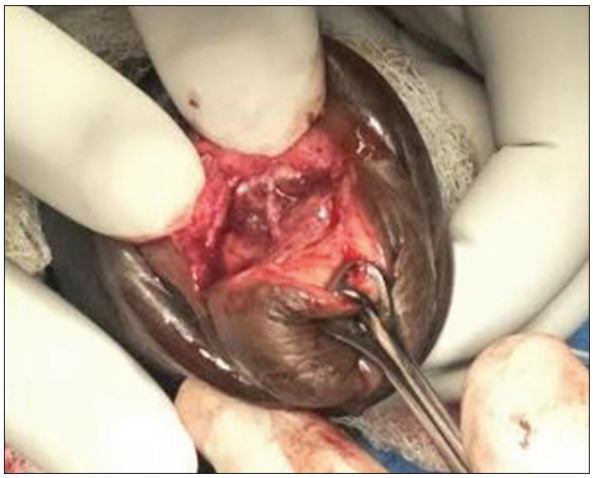

Figure 5: Al-Ghorab shunt

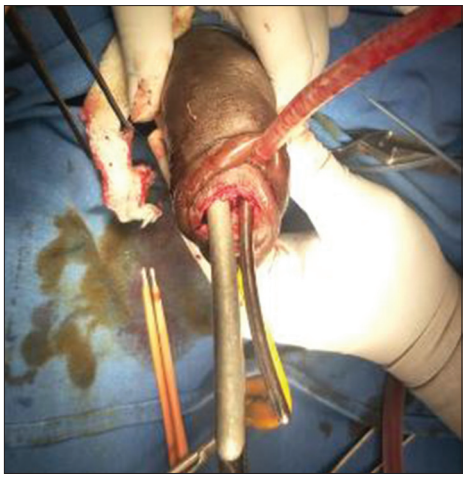

Figure 6: Al-Ghorab shunting with dilatation of corpora cavernosa with Hegars dilators

In 2004, Du Toit *et al*. described priapism caused by therapeutic dosages of quetiapine. Their patient experienced priapism 24 h after switching to quetiapine from risperidone and trazodone. Symptoms subsided after starting loxapine, an antipsychotic with a low alpha1 adrenoreceptor blockage. The patient had no problems with risperidone and trazodone for 2 years before to the occurrence, but acquired diabetes throughout his 2 years of medication. As a result, Du Toit *et al*. stated that "the risk of ischemic (low flow) priapism from a variety of atypical antipsychotics is exacerbated by diabetes."[9]

The final common mechanism in the pathophysiology of priapism is reduced venous outflow from the corpora cavernosa of the penis. The inhibition of the sympathetic alpha 1-receptor by antipsychotics appears to be associated to penile detumescence. It has been claimed whether psychotropic-induced priapism is produced by the medicines' alpha 1-adrenergic antagonism. Individual antipsychotics' likelihood to elicit priapism has apparently been evaluated based on 1-adrenergic blocking affinity.[10] Due to the amount of alpha 1-adrenergic antagonism, more instances of conventional antipsychotics, such as chlorpromazine, have been documented compared to high-potency medicines, such as haloperidol.[11] Ziprasidone and risperidone and have the strongest antagonism at alpha 1 among the atypical antipsychotics, whereas olanzapine has the lowest.[12] However, multiple documented instances of priapism with the other atypical antipsychotics with reduced alpha 1-antagonism, such as olanzapine, quetiapine, and clozapine, have been reported.[13] Despite the alpha 1-adrenergic affinity concept, antipsychotics with lesser (olanzapine, quetiapine, and clozapine) or greater (risperidone and ziprasidone) affinity were discovered to be the same priapism offenders.

Priapism is regarded to be an atypical response that is unrelated to medication dosage and can occur at any point of treatment. Although priapism can occur at any age, it is more common with in third and fourth decades of life, as in this example.[14] Recent dosage and medication modifications or reintroduction of medication following noncompliance, concurrent drug use, and/or other medicines while on medication may potentially be contributors to the development of priapism.[11] Another difficulty seems to be that priapism can develop at any moment throughout the medication, either at the start or later on, therefore, the length or therapeutic dose of medicine is not discovered to be connected.[15]

Quetiapine is metabolized by both CYP3A4 and to a lesser degree CYP3A5. Genetic variations in enzymatic activity can also result in increased blood concentrations of the medication and, as a result, priapism.[16] Enzymatic activity was not assessed in our case. It is difficult to forecast due to the lack of correlation between antipsychotic dose and duration and the start of priapism, and also the delay in patient reporting of priapism.

There is some indications that patients who have previously had priapism are more likely to have it again.[17] Penaskovic *et al*. described a case of priapism caused by a combination of atypical antipsychotics (risperidone, olanzapine, and quetiapine) that were stabilized with loxapine and no more priapism.[17] A medicine with reduced alpha 1-antagonism should indeed be evaluated and taken at the lowest feasible dose.[4] If required and approved to it by the patient, a full assessment of the risk versus benefit of therapy should be conducted with both the patient and also family members. Adequate patient education and acquiring accurate history information on pharmaceutical side effects are critical to prevent a recurrence.

Analgesia should be included in the initial therapy. Opioids and anxiolytics can be used as a preventative measure by parents. A dorsal penile nerve block with lidocaine without epinephrine done dorsally 1 ml distally to the pelvic bone and scrotal attachment may be a useful adjuvant in pain relief.

The first therapy includes the treatment of any main illness which may be producing the priapism. This therapy comprises hydration and oxygenation in sickle cell disease.

Since the arterial flow is maintained in high-flow priapism and there is no risk of rapid ischemia, a time of monitoring is recommended prior selective arterial embolization.[18] Another approach that has been tried effectively in case reports is to apply significant pressure toward the arteriovenous fistula while using Doppler ultrasonography guidance.[19] In any case, urologic advice should be obtained at the emergency department (ED) and will most likely guide therapy in high-flow priapism.

The most effective therapy for low-flow priapism is cavernosal blood aspiration and direct caversonal phenylephrine injection.[20] For phenylephrine, 1 mg of 1 mg/mL phenylephrine could be combined together into injection either with 9 or 99 cc of saline, resulting in a concentration of 100 mcg/1 cc or 100 mcg/10 cc.[21] A butterfly needle should be inserted into the corpora cavernosa perpendicular to the penis (the two corpora cavernosa are connected and thereby only a single-side approach is necessary). An empty syringe should be used to aspirate 5–10 cc of blood, and 100–200 mcg of phenylephrine should be administered. To reach a maximum dosage of 1000 mcg, continue this process every 5–10 min. Because some phenylephrine is taken systemically, vital indicators such as blood pressure must be monitored. Surgical surgery and the development of the cavernosal-corpora spongiosa shunt are the next steps if aspiration fails.

In all situations of juvenile priapism, chronic low-flow priapism, and high-flow priapism, a urologist should be consulted. Inpatient hospitalization is required for patients with chronic priapism or underlying diseases such as leukemia or sickle cell anemia. If the priapism is properly treated, the patient can be monitored and returned home with outpatient urologic specialist follow-up.

Conclusion

Antipsychotic medicines can cause priapism, which is an uncommon but well-known adverse effect. It can happen at any stage of a single antipsychotic medication, at normal dosages, and without any interaction with pharmacological medicines. Health education and physician acknowledgment of priapism as a significant adverse reactions of quetiapine are critical for avoiding difficulties while giving this medication. Given previous published studies and our case of recurring priapism, clinicians must learn to recognize priapism as a major side effect of quetiapine and also be ready to treat it effectively when it occurs.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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