REVIEW

Impact of coronavirus disease on the management of lower urinary tract symptoms and voiding dysfunction

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Purpose of review
Coronavirus disease (COVID-19) has caused a crisis in the entire healthcare system since its emergence. The urgency and priority of various diseases have impacted the medical and surgical treatment in this period. We aim to review the impact of COVID-19 on lower urinary tract symptoms (LUTS) and management.

Recent findings
There may be a relationship between COVID-19 and de novo or increased LUTS. Patients with LUTS should also be evaluated for COVID-19. Management of diseases has varied during the COVID-19 due to the density of the pandemic. Virtual consultations can mitigate patients who are postponed or cancelled, such as patients with LUTS. Patients suffering voiding dysfunction may manage with oral medications such as alpha blocker and 5-alpha reductase inhibitor via telemedicine. Minimally invasive procedures with a low risk of complications and a short hospitalization time should be considered in complicated cases such as the inability to catheterize.

Summary
Telemedicine should be implemented on managements of noncomplicated LUTS and voiding dysfunction. Each centre can schedule its LUTS management approach according to the density of pandemic. Virtual consultations need to be developed to compete with face-to-face consultations.

Keywords
coronavirus disease, lower urinary tract symptoms, urology healthcare, voiding dysfunction

INTRODUCTION

Coronavirus disease (COVID-19) is one of the biggest disasters recorded around the world and continues to have an impact on healthcare. The disease was first defined in Wuhan, China in the last of 2019. The World Health Organisation (WHO) declared the disease as a pandemic on 11 March 2020 after spreading to the majority of countries within a few months [1]. COVID-19 has become a life-threatening healthcare crisis. By now, COVID-19 has approximately infected 245 million and caused the death of 5 million people, and the numbers are increasing cumulatively [2]. Whether infected or not, billions of people have been socially and psychologically affected by this disaster.

The spread of outbreak could not be stopped although many countries had imposed strict rules such as curfew and closing borders. Many factors may affect the rapid spread of the pandemic. The symptoms of the disease were one of the main handicaps in early time of outbreak. Although the most well-known effect of COVID-19 is mainly on the respiratory system, other involvements also reported such as gastrointestinal, cardiovascular, liver, bone marrow and kidney [3,4]. Therefore, we may see presentations with loss of taste and smell, fatigue, myalgia, nausea, vomiting, diarrhoea in addition to fever and pneumonia [5,6].

Due to the high number of appointments of COVID-19 patients, the normal health system has lost its ordinal functioning. Triage of diseases has gained importance. How to manage lower urinary

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KEY POINTS

- COVID-19 has changed all clinical practice in medicine.
- Telemedicine is recommended for uncomplicated LUTS evaluation during COVID-19.
- Treatment of diseases that cause LUTS such as BPH, urethral stricture, urinary incontinence, interstitial cystitis can be delayed.
- Telemedicine is not yet a complete alternative to face-to-face examination.

tract symptoms (LUTS) have also been one of the topics of urology. Despite well-known features, every day we can hear the new symptoms and effects of COVID-19. Not all properties of COVID-19 have yet been defined and its effects on certain organs are still in question and continue to evolve [5]. There are studies in the literature examining the urinary tract, which is one of the systems affected by COVID-19. This review aims to present the effect of COVID-19 on LUTS, possible impact pathways and managements with current studies.

CORONAVIRUS DISEASE IMPACT ON LOWER URINARY TRACT SYMPTOMS

Although a small proportion of patients infected with COVID-19 develop acute progressive respiratory syndrome and multiorgan failure due to cytokine storm, mild and nonspecific symptoms are observed in most cases [7]. Even though LUTS are mostly considered urological symptoms, some studies associated it with COVID-19 in outbreak era. According to defining of International Continence Society, LUTS consist of voiding (obstructive) and storage (irritative) symptoms such as frequency, urgency, poor or intermittent stream, prolonged micturition, incomplete bladder discharging, dripping, urge incontinence and nocturia [8,9].

In one of the first studies in the literature on this subject, urinary frequency was seen as an increased symptom in a small case series in which urinary tract infection and acute kidney injury were excluded [10]. In other early case series, some patients infected with COVID-19 reported gross haematuria and acute urinary retention [11]. Later, the relationship between LUTS and COVID-19 has become a more researched subject by authors.

A recent study evaluating both genders showed that storage symptoms worsened in men and stress incontinence and overactive bladder symptoms increased in women due to COVID-19 infection [12]. Cough, a common symptom of COVID-19, may have worsened existing stress incontinence in female patients. However, this study has poor statistical data or evidence to demonstrate it clearly. In their study of a relatively large number of patients, Can *et al.* showed that elderly male patients had an increased total International Prostate Symptom Score during COVID-19 infection [13]. However, it was not specified whether irritative or obstructive symptoms were dominant in the study. Both of these studies emphasized that increasing LUTS may be an early sign of COVID-19.

No radiological data indicating to urinary tract involvement due to COVID-19 have yet been reported. In line with this, it has been reported that increased LUTS in COVID-19 patients is not correlated with disease severity [13]. On the other hand, Karabulut *et al.* reported that increased LUTS was associated with the severity of the disease and even predicted the intensive care unit admission time [14].

POTENTIAL IMPACT PATHWAYS OF CORONAVIRUS DISEASE ON LOWER URINARY TRACT SYMPTOMS

In the first publications, angiotensin-converting enzyme 2 (ACE2) receptors came to the fore front for the virus to bind to the host cell [15]. However, the affinity of the COVID-19 virus to cells has been shown to depend on the degree of co-expressions of ACE2 and Transmembrane serine protease 2 (TMPRSS2) [16–21]. ACE2 and TMPRSS2 receptors are effective in the penetration and spread of the virus into cells [22,23]. Zou *et al.* defined a risk scale of organs for COVID-19 infection according to expression levels of ACE2 receptor. Organs above a threshold determined as 1% defined high risk for infection. The urothelium with an ACE-2 expression rate of 2.4% was determined as potentially at risk for COVID-19 [24]. The urinary tract may be already a target for COVID-19 in this aspect.

The cause of de novo or worsening LUTS may be related with prostatic or nonprostatic reasons during COVID-19 infection. Benign prostatic hyperplasia (BPH), is one of the most common causes of LUTS, affects frequently elderly patients. BPH causes voiding dysfunction and storage symptoms. Prostatic inflammation is a risk factor for the development of BPH. Inflammatory mediators have been shown to play an important role in the progression and severity of BPH and LUTS [25,26]. According to a hypothesis, virus binds to ACE2 receptors in prostate cells and causes ACE2 downregulation. BPH and LUTS progression develop with proliferation and inflammation mediator activation due to ACE2

downregulation [15,27]. However, the exact mechanism is still unclear.

The other possible pathway may be the basis of the relationship between BPH and androgen receptors [28,29]. It is considered that COVID-19 is more severe and fatal in men due to androgen-based immunological response and additional factors [30]. With the hypothesis that COVID-19 infection may be androgen-mediated related, there are studies showing that LUTS may increase with COVID-19 infection as a result of BPH progression [31,32]. Increased bladder outlet resistance after the aggravation of BPH may lead to deterioration in bladder functions by overtime, leading to storage function disorders in addition to voiding symptoms [33].

Mumm *et al.* reported cases of microhaematuria in a small series of COVID-19 patients in early publications of the outbreak [10]. Then, Hossam *et al.* showed accompanying microscopic and/or macroscopic haematuria in their study; however, the symptoms were not found to be statistically significant [34▪▪]. Viral infection of the bladder is usually seen in immunocompromised patients, for example, haemorrhagic cystitis may be seen in transplant patients due to viral invasion [5,10,35]. The best indicator of this situation is undoubtedly the determination of the viral pathogen in the urine sample. Although there are studies showing that COVID-19 was isolated in human and animal urine, some studies indicate otherwise [36–41]. Since it is unclear whether the expression of ACE2 is in the luminal cell or basal cell in the bladder, COVID-19 virus might not isolate in all patients. In this regard, it is still unknown whether the virus can be isolated routinely in the urine, and if possible, at what stage of the disease it passes into the urinary system. It may not be correct to consider viral cystitis in all cases with LUTS. A prospective, multicentre, observational study showed us that although approximately 25% of the patients have positive viral RNA in the urine, no patient had reported LUTS, urinary retention or incontinence [42]. Local inflammatory processes and endotheliitis may be also one of the reasons of increased LUTS in COVID-19 patients [43].

According to the other hypothesis, one of the reasons of storage symptoms may be related to depressive moods of patients during illness regardless of COVID-19 pathophysiology. Patients may feel fear and anxiety during hospitalization due to COVID-19 infection. It has been reported that LUTS may also develop due to psychological reasons [44]. However, studies investigating the relationship between LUTS and moods of COVID-19 patients are insufficient in the current literature.

MANAGEMENT OF LOWER URINARY TRACT SYMPTOMS

COVID-19 brought a heavy burden on all health systems especially in the first wave of outbreak. Therefore, face-to-face outpatient and nonurgent activities have been postponed in many hospitals. Telemedicine methods were recommended instead of outpatient clinics for less important symptoms that are not life-threatening during the pandemic period [45▪▪,46▪]. The main goal of telemedicine attempts during COVID-19 is to mitigate the postponed and cancelled patients burden on the health system.

From the perspective of urology, LUTS may be assessed as less important complaints compared to uro-oncological cases or benign urge diseases such as postrenal acute kidney injury and acute urinary retention. Therefore, urology centres also stopped outpatient applications for benign urological diseases in order to reduce admission to the hospital with spread of the outbreak [47▪]. Management protocols of LUTS and BPH during COVID-19 are limited due to insufficient study and data.

A group of experts on BPH from Spain reported that telemedicine should be encouraged and carried out with a combined protocol of primary care hospitals on diagnosis and treatment of BPH [45▪▪]. In the observational study of Somani *et al.*, LUTS patients constitute more than half of benign urologic diseases. More than 90% of these patients were managed with virtual consultation during COVID-19 lockdown. Determination of some diagnostic and reference criteria may be limited during virtual consultation. This study highlights that there is a risk of not being followed up or overlooked due to the lack of transfer of some vital clinical information. They also emphasized the need for training and professional development on how telemedicine should be implemented [48▪]. The other drawback of telemedicine may be a problem of accessibility and patient willingness. Most urology patients are elderly and need to be able to use electronic devices and an internet connection. Therefore, patients might not use telemedicine due to economic or social reasons. On the other hand, patient satisfaction was found high with video consultation in a cohort study [49]. According to another study evaluating patient willingness on telemedicine, although only 54% of patients were both eligible and wishful for the telemedicine method, approximately 84% of patients wished a telemedical consultation [50]. The lack of travel time and clinical waiting time may be the reasons for choosing telehealth.

According to some general evaluations and recommendations regarding voiding dysfunction, oral medications such as alpha blocker and 5 alpha reductase inhibitors, if ineffective, a suprapubic or urethral catheter and delayed surgery may be used to manage benign prostatic obstruction [46▪,51]. Ribal *et al.* reported that delaying treatment due to voiding dysfunction for 3–6 months would not cause any significant harm [52]. Similarly, Goldman and Haber highlighted that treatment other than noncatheterisable urinary retention could be delayed for 12 weeks [53]. In a recent study, approximately 78% of deferred functional urological interventions required rescheduling [54]. Therefore, although there is no change in medical treatments compared to the pre-COVID situation, delayed interventional procedures may cause a cumulation at a later time.

As mentioned in the previous section, there are studies showing viral pathogen in urine. Endoscopic procedures related to LUTS have been reported to be risky due to the risk of virus contamination by mixing urine and blood with the irrigation fluid. However, it has been reported that the surgical approach of BPH may be performed by prioritizing the safety of the patient and health staff, according to the availability of disposable materials and the epidemiologic COVID-19 status of location [55▪▪]. The Australian and New Zealand Association of Urology (USANZ) also reported that transurethral resection of the prostate can be performed in case of unsuccessful self-catheterization or indwelling catheter [56]. Hossam *et al.* managed with urethral catheterization in 26% of the patients due to acute urinary retention and with transurethral resection of the prostate in 30% of the patients due to increased LUTS in COVID-19 patients with BPH [34▪▪].

In this context, it is recommended that each hospital organize its work programs by minimizing, postponing or cancelling the necessary operations and consultations, considering the existing burden of the health system and the condition of the clinician [57]. A surgical intervention that combines the least complications and the shortest length of stay should be chosen to manage LUTS during COVID-19.

CONCLUSION

The burden of COVID-19 is different in various regions. Each centre can manage LUTS and voiding dysfunction according to the intensity of the pandemic and the health system. Telemedicine is an appropriate modality as LUTS can be a symptom of COVID-19. Further studies are needed comparing face-to-face examination and telemedicine consultation.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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