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Original Article

Impact of the COVID-19 Pandemic on Functional Urology Practice: A Nationwide Survey From Turkey

COVID-19 Pandemisinin Fonksiyonel Üroloji Uygulamasına Etkisi: Türkiye Çapında Bir Araştırma

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ABSTRACT

Objective: Routine urology practice has changed with the coronavirus disease-2019 pandemic. We aim to determine the urologists' functional urology practice during the pandemic by an online questionnaire.

Methods: An online questionnaire was conducted to assess the functional urology practice of Turkish urologists' during the pandemic. The workplace, positioning as a pandemic hospital, involvement in pandemic clinics, and the relevance to functional urology were questioned. We also inquired about outpatient services, diagnostic tests, and elective surgeries during the pandemic compared with their routine practice.

Results: One hundred and fifty-two participants completed the questionnaire. Of these, 32.2% replied that more than half of their daily practice was related to diagnosing and treating incontinence, prolapse, and neurourology. According to 123 participants (80.9%), there was a decrease in outpatient clinics. Diagnostic tests were also reduced, such as uroflowmetry (68.4%) and urodynamics (81.3%). The majority of respondents declared a decrease in elective surgeries as Botox injection (92.1%), surgery for urinary incontinence (93.4%), and surgery for prolapse (85%). Nearly one-quarter of respondents' (28.9%) stated that their diagnostic methods for neurourology patients did not differ.

Conclusions: One of the most affected areas in urology during a pandemic is functional urology. Although diagnostic tests and surgery for functional urology are classified as "optional," the quality of life of patients will be affected by the delayed intervention.

Keywords: Coronavirus, COVID-19, functional urology, neurourology

ÖZ

Amaç: Koronavirüs hastalığı-2019 pandemisi ile rutin üroloji pratiği değişmiştir. Bu çalışmada pandemi sırasında ürologların fonksiyonel üroloji uygulamalarını çevrimiçi bir anket kullanarak belirlemek amaçlanmıştır.

Yöntemler: Türk ürologlarının pandemi sırasında fonksiyonel üroloji pratiğini değerlendirmek için çevrimiçi bir anket uygulandı. Bu ankette, katılımcıların görev yeri, pandemi merkezi olarak konumlandırılması, pandemi kliniklerinde görev alma ve fonksiyonel ürolojiye ilgi hakkında sorular soruldu. Ayrıca pandemi sırasında poliklinik hizmetleri, tanı testleri ve elektif ameliyatlar, pandemi öncesi günlük uygulamalarıyla karşılaştırarak sorgulandı.

Bulgular: Toplam 152 katılımcı anketi tamamladı. Katılımcıların %32,2'si günlük uygulamalarının yüzde ellisinden fazlasının inkontinans, prolapsus ve nöroüroloji tanı ve tedavisi ile ilgili olduğunu belirtti. Yüz yirmi üç katılımcıya (%80,9) göre poliklinik sayısında azalma oldu. Üroflovmetri (%68,4) ve ürodinami (%81,3) gibi tanı testleri de azaldı. Ankete katılanların çoğunluğu, botoks enjeksiyonu (%92,1), üriner inkontinans cerrahisi (%93,4) ve prolapsus cerrahisi (%85) gibi elektif ameliyatlarda azalma olduğunu bildirdi. Ankete katılanların yaklaşık dörtte biri (%28,9) nöroüroloji hastaları için tanı yöntemlerinin farklılık göstermediğini belirtti.

Sonuçlar: Pandemi sırasında ürolojide en çok etkilenen alanlardan biri fonksiyonel ürolojidir. Fonksiyonel ürolojiye yönelik testler ve ameliyatlar "opsiyonel" olarak sınıflandırılsa da hastaların yaşam kalitesi geciken müdahalelerden etkilenecektir.

Anahtar kelimeler: Koronavirüs, COVID-19, fonksiyonel üroloji, nöroüroloji

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INTRODUCTION

A novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), remains challenging for healthcare professionals worldwide. Although vaccinations are becoming widely available, to date, the number of confirmed cases is nearly 380 million people, and that of deaths from coronavirus disease-2019 (COVID-19) is 5.5 million people[1]. After World Health Organization declared the pandemic, healthcare providers faced management difficulties.

National and international lockdowns were used to reduce the pressure on the healthcare system. Also, similar restrictions were approved for outpatient clinics and elective surgeries. Some urological associations released recommendations, and others published data for healthcare professionals in urology[2-6]. There was a decrease in outpatient and inpatient clinics and surgery[7]. The pandemic affected all cases, including oncological and emergency patients. However, elective outpatient clinics and surgeries were most affected, and were delayed for an unspecified period. The surgical practice of functional urology, including benign prostatic hyperplasia (BPH), all types of incontinence surgery, and genitourinary prolapse, were the initial cases to be postponed. Another limitation for functional urology was reducing or stopping all urodynamic studies[8].

The COVID-19 pandemic affected routine functional urology practice. Thus, we hypothesized that the routine practice of functional urology had been limited. Also, regulations and patient preferences decreased both the diagnosis and treatment of major functional urological diseases, such as urinary incontinence, prolapse, genitourinary fistula, neurogenic lower urinary tract dysfunction, and BPH. This study assesses the functional urology practice of the Turkish urologists, including outpatient services, diagnostic tests, and elective surgeries before and during the pandemic. We also evaluated the changes in functional urology practice in dedicated pandemic centers and respondents' interest in functional urology practice before and during the COVID-19 pandemic.

MATERIALS and METHODS

After the Ministry of Health and Istanbul Medeniyet University, Goztepe Training and Research Hospital Ethical Board's review (decision no: 2021-0083, date: 27.01.2021), an online questionnaire was conducted to evaluate the functional urology practice of Turkish urologists' before and during the pandemic. The questionnaire was developed by two (A.T. and R.O.) authors after reviewing the current literature for the health care service effect of COVID-19. A total of 45 questions was reviewed and discussed. Finally, the authors agreed on 30 items asking about the demographic of participants (two items), the hospital policy for COVID-19 (two items), the interest of functional urology (two items), examination routines (three items), diagnostic methods (five items), surgical interventions for overactive bladder, stress urinary incontinence, fistula, pelvic organ prolapse, BPH (thirteen items), treatment options for BPH (one item), evaluation options for their patients with new diagnosed high residual urine (one item) follow-up for neurourology patients (one item). The majority of the questions were multiple-choice close-ended.

We implemented measures on IP restrictions to avoid repetitive filling for the questionnaire. A list-based sample frame method was used for the online survey. The Turkish Urological Association's mailing list of urology experts and electronic software (Google Forms®) were used for administration. Participants were asked to compare their practice before and during COVID-19 to evaluate the decrease, same, or increase in functional urology practice. At the beginning of the survey, informed consent was obtained from all participants.

Some hospitals were converted to serve only COVID-19 patients during the pandemic because of government regulations. These hospitals are the so-called "dedicated pandemic centers" in this study. Physicians redeployed during the pandemic to care for COVID-19 patients were considered "participating in the pandemic." The participants' interest in functional urology in their routine practice was evaluated in three categories; less than 20% interest, 20% to 50% interest, and greater than 50% interest.

Statistical Analysis

All statistical analyses were performed using the SPSS program (IBM Corp. released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Multiple-choice questions in the survey are illustrated with bar charts. All categorical variables were compared with the chi-square test. Moreover, Fisher's Exact test was used in a small number of samples. The One-Way ANOVA test was used to analyze continuous data. Post-hoc analysis was done with the Bonferroni method to define variables with statistical significance. For all analyses, p-values less than 0.05 were considered significant.

RESULTS

The content validity was tested by three experts outside the study group using a non-face-to-face approach. The average scale-level content validity index

found was 0.9. One hundred and fifty-two participants completed the questionnaire (152/600, 25.3% completion rate). Most nonrespondents (440/448, 98.2% of nonrespondents) were not contacted for refusing and not completing the survey. Other reasons stated by the remaining nonrespondents were the inability to complete the questionnaire in the required time interval and the appropriate time to complete it. Almost 80% of respondents were in tertiary centers (45.4% in education and research hospitals, 34.2% in university hospitals), and only 7.9% of participants were from private clinics. According to respondents, 73.7% of hospitals were dedicated pandemic centers, and 70.4% of participants cared for COVID-19 patients. All participants had functional urology practices, and 32.2% had greater than fifty percent of their daily practice related to diagnosing and treating incontinence, prolapse, and neurourology (Table 1).

During the pandemic, 80.9% of respondents stated a decrease in outpatient clinic activities for functional urology. In a subgroup analysis, being or converting to a pandemic dedicated center was a significant factor for the decrease in outpatient clinical visits (p=0.001) (Table 2).

Regarding the stress test for diagnosing urinary incontinence during the urogynecological examination, only two-thirds of participants continued performing the stress test, and 83.3% of the respondents used personal protective equipment during the cough test. As an essential diagnostic tool, uroflowmetry continues to be used for diagnosis. Nevertheless, 68.4% of respondents reported a major decrease in their use of this test. There was no significant difference between centers and being a pandemic dedicated center regarding the ratio of the decrease in uroflowmetry tests. However, the interest in functional urology was a significant factor for the decrease in uroflowmetry (p=0.001) (Table 2). One hundred and seven participants (70.4%) responded as they had a urodynamic unit in their centers, but 81.3% of respondents had a decrease in urodynamic tests. A subgroup analysis found a significant correlation between the decrease in the number of urodynamic studies and the centers that participated (p=0.001). However, being a dedicated pandemic center or being interested in functional urology were not significant factors for the decrease in urodynamic studies (Table 2).

Table 1. Participant demographics (n=152).

Characteristics	n (%)
Centers of participants	
Education and research hospital	69 (45.4)
University hospital	52 (34.2)
Government hospital	19 (12.5)
Private clinic	12 (7.9)
Pandemic dedicated center	
Yes	112 (73.7)
No	40 (26.3)
Took part in the care of COVID-19 patients	
Yes	107 (70.4)
No	45 (29.6)
Interest in functional urology	
<25%	56 (36.8)
25-50%	47 (30.9)
>50%	49 (32.2)

COVID-19: Coronavirus disease-2019

All participants declared that they could perform anti-incontinence surgery, bladder botulinum toxin injections, prolapse surgery, and BPH surgery before the pandemic. According to participants, there was a major decrease in botulinum toxin injections (92.1%). The participant's center was the limiting factor decreasing botulinum toxin injections (Table 2).

Approximately 94% of participants stated decreased urinary incontinence surgery, and the participant's center was the only significant factor for the decrease (p=0.001) (Table 2). Participants' treatment options for patients requiring anti-incontinence surgery are shown in Figure 1. Of the participants, 85% stated that pelvic organ prolapse surgery decreased, but no significant factor was observed for this decrease (Table 2). Most participants preferred follow-up, medical treatment, or pessaries for patients requiring prolapse surgery (Figure 1). Of the participants, 93.5% who performed fistula repair surgery declared that it decreased, but there was no significant factor for this decrease (Table 2).

Of the participants, 84.2% stated that surgical interventions for BPH decreased, but there was no significant factor for this decrease. Of 143 participants, (94.1%) declared that they preferred medical treatment, intermittent catheter/suprapubic tube, and surgery in local settings for patients requiring BPH surgery (Figure 1). Participants' approaches to treatments for their patients with newly diagnosed high residual urine during COVID-19 are shown in Figure 1.

Participants' choices for managing neurourology patients during the pandemic were: "evaluate after the pandemic" (38.2%), "as usual as before the pandemic" (28.9%), "telemedicine to evaluate their situation" (17.8%), and "urodynamic studies but not invasive procedures" (15.1%).

Table 2. Decrease in functional urology practice according to centers of participants, being a pandemic dedicated center, and interest in functional urology.

	Centers of participants					Being a pandemic dedicated center			Interest in functional urology practice (%)			
	Education and research hospital (%)	University hospital (%)	Government hospital (%)	Private clinic (%)	p-value	Yes (%)	No (%)	p-value	Low (n=56) (<25%)	Medium (n=47) (25-50%)	High (n=49) (>50%)	p-value
Outpatient clinical visit												
Decrease	88.4	80.7	94.7	16.7	0.001	87.5	62.5	0.001	82.1	87.2	73.5	0.22
Same or increase	11.6	19.3	5.3	83.3		12.5	37.5		17.9	12.8	26.5	
Uroflowmetry												
Decrease	66.7	71.2	84.2	41.7	0.1	68.8	67.5	0.88	55.4	66	85.7	0.03
Same or increase	33.3	28.8	15.8	58.3		31.2	32.5		44.6	34	14.3	
Urodynamic studies												
Decrease	82.6	87.7	100	16.7	0.001	80.8	82.8	0.81	76.3	75.9	90	0.22
Same or decrease	17.4	12.3	0	83.3		19.2	17.2		23.7	24.1	10	
Botulinum toxin injections												
Decrease	97.1	88.5	100	83.3	0.004	94.6	85	0.08	94.6	93.6	87.8	0.41
Same or increase	2.9	11.5	0	16.7		5.4	15		5.4	6.4	12.3	
Anti-incontinence surgery												
Decrease	98.6	96.2	100	41.7	0.001	93.8	92.5	0.72	94.6	93.6	91.8	0.91
Same or increase	1.4	3.8	0	58.3		6.3	7.5		5.4	6.4	8.2	
Surgery for prolapsus												
Decrease	89.9	76.9	89.5	83.3	0.24	86.6	80	0.31	91.1	85.1	77.6	0.15
Same or increase	10.1	23.1	10.5	16.7		13.4	20		8.9	14.9	22.4	
Fistula repair												
Decrease	95.5	92.5	-	87.5	0.43	93	95.2	0.71	96.7	88.9	94.3	0.57
Same or increase	4.5	7.5	-	12.5		7	4.8		3.3	11.1	5.7	
Surgery for benign prostatic hyperplasia												
Decrease	84.1	92.5	82.7	83.3	0.94	83.9	85	0.87	82.1	85.1	85.7	0.88
Same or increase	15.9	7.5	17.3	16.7		16.1	15		17.9	14.9	14.3	

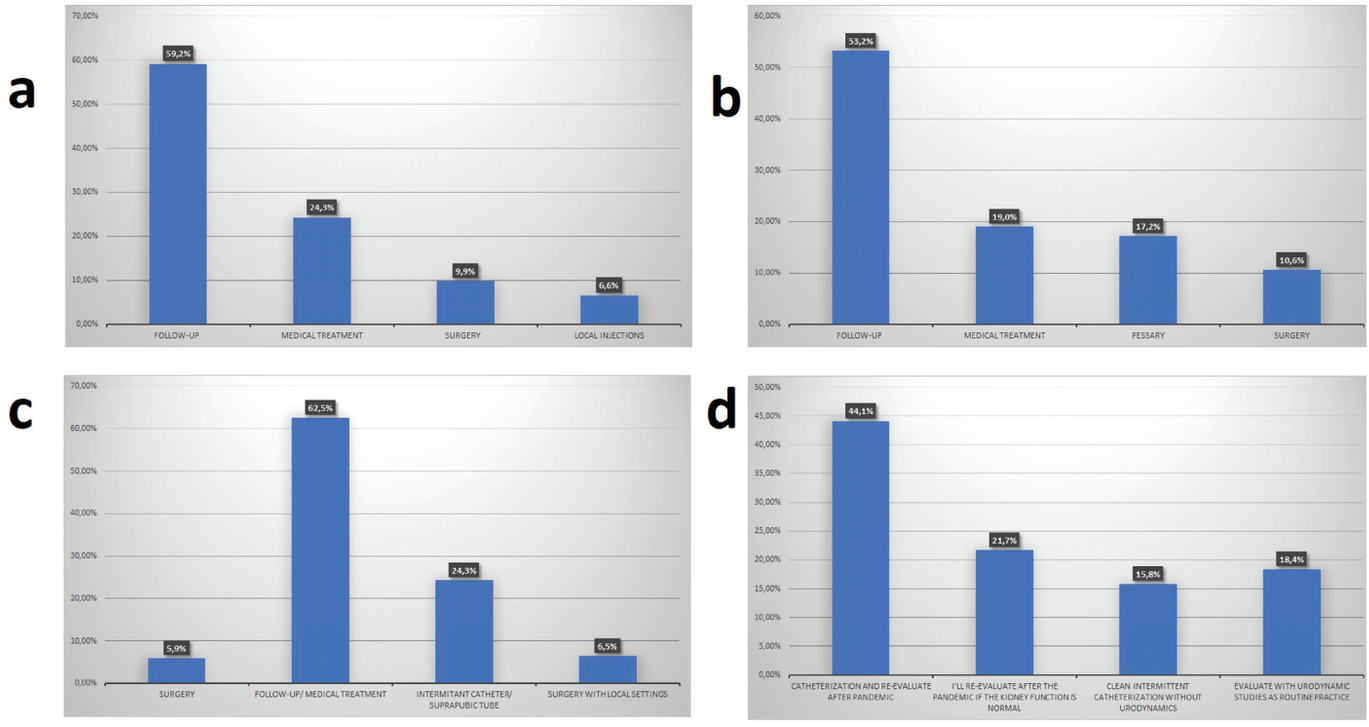

Figure 1. a) Participants' treatment options for the patients requiring anti-incontinence surgery. b) Participants' preferred option for the patients requiring prolapse surgery. c) Participants' approaches for their patients requiring surgery for BPH. d) Participants' approaches to treatments for their patients with newly diagnosed high residual urine during COVID-19.

BPH: Benign prostate hyperplasia, COVID-19: Coronavirus disease-2019

DISCUSSION

The novel virus, SARS-CoV-2, spread rapidly and presents a worldwide threat. Vaccinations and clinical drug trials for COVID-19 are promising, but devastation continues. During the first wave in Turkey (mid-March 2020), some government restrictions were set: national lockdowns, delays for all types of elective surgeries, restrictions for outpatient clinics, and reductions in the number of hospitalizations. In addition, healthcare professionals were repositioned during the pandemic. In Turkey, almost all the tertiary centers and government hospitals became dedicated pandemic centers. Major associations of urology and the Ministry of Health regularly published recommendations for urological practice during COVID-19[2,3,7,8]. These regulations and restrictions resulted in a major decrease in routine urological procedures.

One of the most affected areas in urology during a pandemic is functional urology. Thus, we hypothesized that routine practice in the era of functional urology would show major changes. This survey showed that functional urology practice was widely affected by the pandemic. This study assesses the functional urology practice of Turkish urologists, including outpatient services, diagnostic tests, and elective surgeries before and during the pandemic. We showed a considerable decrease in outpatient clinic (80.9% of respondents) diagnostic tests (68.4% and 81.3% of the participants stated uroflowmetry and urodynamics were reduced). The majority of the respondents declared a decrease in botox injections (92.1%) and incontinence (93.4%). We also evaluated whether the dedicated pandemic center was interested in functional urology and the respondents' places of work affect functional urological practice. Being a pandemic dedicated center was a significant factor for the decreased number of outpatient visits. An interest in functional urology was a significant factor for the decrease in uroflowmetry. Respondents' place of work was a significant factor for the decrease in the number of urodynamic studies, botulinum toxin injections, and anti-incontinence surgeries.

The completion rate of our study was similar to the online survey, which questioned the impact of a pandemic for the urologist. The authors stated that 18.2% of the invited population completed the online survey[9].

In another online survey, the authors investigated the influence of the pandemic on the urologist's work and mental status with personal life. The response rate achieved for the online questionnaire was 28.63%[10].

Our results are consistent with a survey from Brazil where the authors found that 80% of participants reported a reduction of ≥50% in elective surgery[9]. Similarly, Paffenholz et al.[11] from Germany investigated the impact of the pandemic. They showed that 77.8% of participants stated their routine practice of surgical interventions changed, and they had not performed any surgery except for uro-oncology. In another online survey of Polish urologists, the pandemic also had negatively affected their routine practice[10].

All parts of urology practices were affected during the pandemic. Studies evaluating the effect of the pandemic showed a 40-82% decrease in the number of outpatient clinics[12,13]. This decrease can be attributed to guidelines and published data recommendations, measures taken by the government, and restrictions imposed at hospitals to maintain COVID patient care.

Similarly, healthcare professionals concerned about themselves and their surgical teams concerning COVID-19 infections, and the absence of useful information regarding viral transmission in surgical procedures, might have encouraged the surgeons to delay surgery, especially for elective cases[14]. Becoming a part of pandemic clinics may also be another reason for the decrease in urological practice. Regional and interstate differences in the same country also affect the decrease of urological patients[9,12]. Our country is one of the most affected territories globally, with many coronavirus cases. During these challenging times of the pandemic, the Ministry of Health organized countrywide restrictions to high-risk groups, restricted elective surgeries, and the numbers of inpatients and outpatients. A single-center study from our country compared practices eight weeks before and during the pandemic. It showed a decrease in outpatient services and the number of surgical interventions[15]. In another trial evaluating the pandemic's effect on urological practice and the anxiety levels of patients on the waiting list for surgery, the authors found a significant decrease in inpatient and outpatient clinics and surgical interventions[16]. Similarly, in a large cohort from Turkey, Bozkurt et al.[17] evaluated urology practice during the pandemic in 51 centers from all geographical parts of the country. At the beginning of the pandemic, the authors found a decrease in inpatients, outpatient clinic examinations, and surgeries, especially in tertiary centers. They also evaluated the workload by comparing it with the same period before and during the pandemic. They found a considerable decrease in all fields of urology.

Functional urology seems to be one of the most affected urological practice subspecialties. Due to guidelines, published data, and measures taken by the government and/or hospital, it is very challenging to have regular clinical practice during the pandemic. In most centers, all kinds of interventions were delayed except for the second stage of sacral neuromodulation and infected patients with artificial urethral sphincter[2-5,8]. In one study, Çakıcı et al.[18] analyzed the pandemic effect on urological interventions in the first three months of the pandemic. They showed a cumulative decrease in admissions, but the most decreases were seen in incontinence, pediatric urology, and andrology subspecialties. They also found an approximately 75% decrease in surgical interventions and a significant decrease in the number of transurethral resections of the prostate, transvesical prostatectomy, and transobturator tape surgeries. In a survey that assessed the COVID-19 effect for urology practice, a delay of over eight weeks was observed for nearly 30% of outpatient examinations and surgeries[19]. The most affected delays were in benign conditions of urology practice and particularly BPH surgery (93%); female urinary incontinence (85%) had the highest rates of delays. An online survey from Brazil showed that 68.7% of participants did not perform nonessential surgery, which increased to 75.5% for participants in the high incidence states[9]. A study from Italy evaluated the pandemic effect on patients with pelvic floor disorders and showed that the overall cancellation rate was 78.4% for outpatient clinics and 82.7% for surgery. They also showed that the mean cancellation rate for intravesical botulinum toxin injections was 82.2%. It was 85.6% for stress urinary incontinence, 85.1%, for prolapse surgery, 77.9% for BPH, and 80.6% for perineal fistulas[20].

Although the survey was conducted at the beginning of the third wave of the pandemic in Turkey, it was almost one year after the first case was confirmed in Turkey. Based on their estimation, we questioned the participants' practice before and during the COVID-19 pandemic. In Turkey, the Ministry of Health organized the restrictions during the wave. Strong and rigid regulations helped decrease infections, which enabled physicians to their routine practice with some restrictions. While infections decreased, delayed uro-oncology patients on the waitlist were evaluated and treated. However, the practice of functional urology remains a "nonemergency situation" regarding the infection risk for patients undergoing surgery. Thus, there may be another reason for this decrease, especially for surgical interventions.

A urodynamic investigation is an important diagnostic tool in functional urology practice. After the first wave, authorities suggested delaying nearly all urodynamic studies[8]. Following these recommendations, Hashim et al.[21] presented adaptation guidelines for urodynamic studies for the pandemic if they were deemed crucial for patients. In our study, approximately 80% of respondents stated a decrease in urodynamic studies, and 68.4% stated a reduction in uroflowmetry. Similarly, in a global survey, Teoh et al.[19] showed an 87% reduction in urodynamic studies and an 83% reduction in uroflowmetry testing. Another survey showed that overall cancellation rates for uroflowmetry were 79.1% and 81.2% for urodynamic studies[20]. The decrease of urodynamic studies may be the uncertainty of the limitations, especially during the first wave of the pandemic. Protective equipment supplies, guidelines, recommendations, and the reduction in clinical visits may be other reasons for the decrease.

During the pandemic, telemedicine in clinical practice has been accepted as an alternative for consults and strategy development for diagnosis and disease management[11,12,20,22-25]. However, our survey showed that only 17.8% of participants decided to use telemedicine in neurourology patients. A study by Dubin et al.[26] revealed increased use of telemedicine by urologists, with most urologists declaring that they wanted to continue using it in their routine practice. Although our results showed a lower preference for telemedicine in Turkey, it seems to be increasing gradually day by day. This fact was supported by the survey that evaluated patients' perspectives on telemedicine during the pandemic and showed that most patients wished for telemedicine (84.7%) rather than clinical visits[27].

We found that functional urology was less affected in private practice. Although respondents from private practice constituted 7.9% of the cohort, 83.3% stated that the number of patients did not differ. There was a slight decrease in urodynamic studies and surgery for incontinence, but these ratios were lower than the other government reimbursed hospitals. Similarly, a survey by Gravas et al.[12] found that surgical interventions were less restricted in private practice than academic or public practice. In another study that compared the effect of the pandemic on private and public clinics, urological practice showed a similar reduction-except in surgery for BPH-in both centers[28].

In the first wave of the pandemic, the cancellation of routine functional urological practice was inevitable. The backlog of patients, especially those waiting for surgical interventions, seems to be a major problem. Many patients suffer from delays, and the long-term implications remain unknown. In an online survey, Sacco et al.[20] also showed that 87% of participants believed postponing services harmed patients' quality of life (QoL). Almost half of the respondents stated that there was a risk of potential health issues for patients. Based on projections, the estimated recovery for the backload of functional urological surgeries would require 28 to 64 months. Another study showed that anxiety and depression scores were higher for patients on surgery waiting lists[16]. Postponing surgery, especially for benign conditions, is widely accepted, but long-term outcomes, including anxiety, depression, and QoL, may be our challenge for the future. Delays in interventions during the pandemic may negatively affect clinical findings and overall outcomes, which will be another concern.

The main strengths of this study were that nearly 80% of participants were from tertiary centers and worked in dedicated pandemic centers reflecting the effects of the pandemic on all urology practices. The majority of the respondents were interested in functional urology, which could demonstrate real-life changes in functional urology during the pandemic. Although this study has several strengths, there were some limitations. The rate of respondents was lower than expected, and a single-country trial could not reflect real-world data. The design and questions were not validated and timeline changes of the pandemic were not evaluated nor questioned in any detail. The number of participants from private practice was low and, therefore, could not reflect the actual effect for private, practice which may differ from country to country.

CONCLUSIONS

The pandemic affected healthcare systems worldwide. One of the most affected areas in urology during a pandemic is functional urology. Various studies and urology associations recommended delaying diagnostic studies and treatments for almost all functional urology patients. In this study, most participants in several clinics declared a significant decrease in functional urology practice with reduced outpatient services, diagnostic tests, and elective surgeries. Although such surgeries may be categorized as "surgeries for benign reasons" or "elective," the healthcare system will eventually face the enormous patient load, consequences of delaying all procedures, and decreased QoL in patients.

Ethics

Ethics Committee Approval: After the Ministry of Health and Istanbul Medeniyet University Goztepe Training and Research Hospital Ethical Board's review (decision no: 2021-0083, date: 27.01.2021) an online

questionnaire was conducted to evaluate the functional urology practice of Turkish urologists' before and during the pandemic.

Informed Consent: Informed consent was obtained from all participants who completed the survey.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: A.T., M.D., R.O., Concept: A.T., M.D., R.O., Design: A.T., M.D., R.O., Data Collection and/or Processing: A.T., R.O., Analysis and/or Interpretation: A.T., M.D., R.O., Literature Search: A.T., R.O., Writing: A.T., M.D., R.O.

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

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