

Exacerbation of Urinary Storage Symptoms by the Psychological Stress Induced by the COVID-19 Pandemic

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Abstract. *Background/Aim:* This study aimed to determine whether psychological stress associated with the COVID-19 pandemic might exacerbate lower urinary tract symptoms (LUTS) and decrease lower urinary tract function in outpatients with LUTS. *Patients and Methods:* We evaluated 104 patients who visited our hospital during the first wave of the COVID-19 pandemic. Psychological stress was evaluated by the Stress Response Scale-18 (SRS-18). Subjects were divided into aggravation and non-aggravation of psychological stress groups according to the SRS-18. LUTS was evaluated according to the International Prostate Symptom Score (IPSS). Lower urinary tract function was evaluated as the post-void residual urine volume (PVR). Comparisons of scores and changes in scores of each parameter before versus during/after the first wave of the COVID-19 pandemic were performed between the two groups. *Results:* Forty-two patients were included in each group. We observed no significant differences in the comparison of scores at each time point and in changes in total IPSS score, voiding symptom subscores and PVR between the two groups. Although no significant differences in storage symptom subscores were observed between the two groups, changes in storage symptom subscores increased significantly during the first wave of the pandemic in the aggravation of psychological stress group ($p=0.02$).

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However, no significant increase was observed after the first wave. Conclusion: Psychological stress during the COVID-19 pandemic might transiently aggravate storage symptoms in patients with LUTS. Physicians should be aware of the possibility of transient worsening of LUTS during future pandemics, and transiently additional medication might be effective in such patients.

To date, the Coronavirus Disease-19 (COVID-19) pandemic has caused much hardship worldwide and has been a public health concern since it was first confirmed in Wuhan, China in late 2019. Thereafter, it spread all over the world within a few months (1, 2), and was declared a pandemic by the World Health Organization on 11th March 2020. Since then, millions of cases and deaths due to COVID-19 have been reported.

Mild cases of COVID-19 experience upper respiratory tract symptoms, fever, and diarrhea (3), while more severe cases experience pneumonia, multiple organ failure and even death (4). Thus, COVID-19 can affect the entire body, including the lower urinary tract. Nabbeeh *et al.* reported that lower urinary tract symptoms (LUTS) worsened significantly after COVID-19 infection in patients with benign prostatic hyperplasia (BPH) (5). One report described the progression of BPH due to damage to the prostate gland after COVID-19 infection (6). On the other hand, another study reported no evidence of progression of BPH after COVID-19 infection (7). Thus, the association between LUTS/BPH and COVID-19 still remains unclear.

However, apart from the physical effects of COVID-19 infection, the COVID-19 pandemic itself has likely caused significant psychological stress in a lot of people. Previous natural disasters, such as the Great East Japan earthquake, reportedly caused a transient increase in blood pressure, number of suicides, *etc.* (8, 9) In addition, the incidence of nocturia increased transiently after the Great East Japan Earthquake (10). Thus, previous epidemiological studies demonstrated the occurrence of various morbid conditions due to psychological stress following the disaster. However,



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Table I. Baseline characteristics of patients stratified according to aggravation of psychological stress.

	Mean (±SD) and number of patients		p-Value
	Aggravation	No aggravation	
N	42	42	
Age (years)	76 (10)	72 (8)	0,06
Sex (M/F)	34/8	36/6	0,55
Current diseases			
BPH	31	32	0,9
OAB	6	4	
NB	3	4	
Others	2	2	
Height (cm)	160 (9)	163 (7)	0,23
Weight (kg)	60 (10)	63 (12)	0,22
SRS-18	6.5 (6.5)	7.5 (9.3)	0,55
IPSS	13.1 (7.6)	12.3 (7.2)	0,61
IPSS voiding symptoms	7.6 (5.2)	6.8 (4.8)	0,45
IPSS storage symptoms	5.3 (3.1)	5.9 (3.4)	0,4
Post-void residual urine volume	33 (41)	45 (56)	0,51

BPH: Benign prostatic hyperplasia; OAB: overactive bladder; NB: neurogenic bladder; SRS-18: Stress Response Scale-18; IPSS: International Prostate Symptom Score; SD: standard deviation.

although the COVID-19 pandemic is considered to be equal to a disaster, only a few reports have evaluated whether the psychological stress of the COVID-19 pandemic exacerbated LUTS and affected lower urinary tract function. The aim of the present study was to clarify whether the psychological stress related to the COVID-19 pandemic might have worsened LUTS and lower urinary tract function in the patients with LUTS.

Patients and Methods

This prospective, observational study included 104 consecutive patients with LUTS who visited our hospital during the first wave of the COVID-19 pandemic in Japan, from April 2020 to May 2020. The cohort size was limited to 104 patients in this study because our department introduced another study of LUTS after the end of this study. To clarify whether psychological stress resulting from the pandemic worsened LUTS and lower urinary tract function, the present cohort was divided into two groups according to the presence or absence of aggravation of psychological stress.

The inclusion criteria were patients with LUTS and lower urinary tract dysfunction who had been regularly seen by a doctor at our tertiary hospital before the start of the pandemic. To clarify the effect of the pandemic-related psychological stress on LUTS and lower urinary tract dysfunction, the exclusion criteria were patients diagnosed with COVID-19 based on reverse transcription-polymerase chain reaction (RT-PCR) tests during the observation period. In addition, 20 patients were excluded from the present analyses, because LUTS and lower urinary tract function could not be evaluated during the observation period. Our purpose in the present

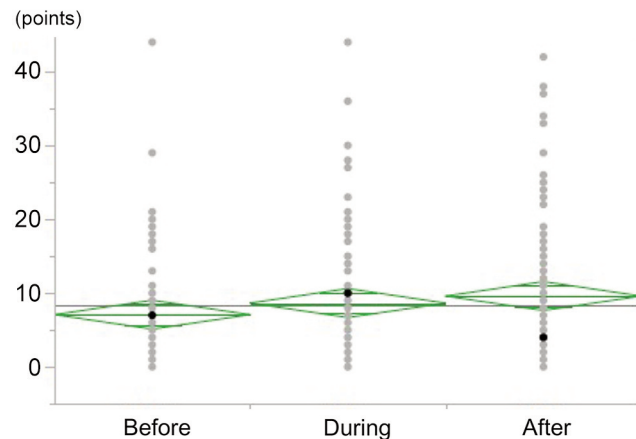


Figure 1. Time-course of changes in Stress Response Scale-18 scores during the first wave of the COVID-19 pandemic. Psychological stress was evaluated using the Stress Response Scale-18. There was no significant change in psychological stress during the observation period.

study was to investigate the association between psychological stress due to the COVID-19 pandemic and LUTS and lower urinary tract function. Informed consent was obtained from all the participants before the investigation after an explanation of its aim and methods. The investigation protocols were approved by the ethics committee of our institution (clinical trial registration number U20-07-006).

Evaluation of psychological stress. Psychological stress regarding the COVID-19 pandemic was evaluated by the Stress Response Scale-18 (SRS-18) (11). Before evaluating the psychological stress, the present cohort was asked to evaluate only the psychological stress regarding the COVID-19 pandemic during the past few days. SRS-18 was measured three times *i.e.*, before, during and after the first wave of the COVID-19 pandemic. Because psychological stress before the first wave of the pandemic could not be evaluated after the start of the first wave, psychological stress regarding the COVID-19 pandemic before the first wave was involuntarily evaluated during the first wave. Thus, psychological stress before the first wave and that during the first wave were concurrently evaluated during the first wave of the pandemic. The SRS-18 is composed of 18 questions. Higher scores indicate greater psychological stress. In the present study, if the SRS-18 score increased during the first wave of the COVID-19 pandemic compared with before the first wave, the subjects were grouped into the aggravation of psychological stress group. The remaining subjects were grouped into the non-aggravation of psychological stress group.

Evaluations of LUTS and lower urinary tract function. LUTS was evaluated using the International Prostate Symptom Score (IPSS). Moreover, IPSS subscores, such as voiding symptom subscore (sum of the intermittency score, weak stream score and straining score) and storage symptom subscore (sum of the frequency, urgency and nocturia scores), were also assessed as individual scores (11). Post-void residual urine volume (PVR) determined by ultrasonography during the observation period was also evaluated. Each parameter was evaluated three times, *i.e.*, before, during, and after the first wave of the COVID-19 pandemic in Japan.

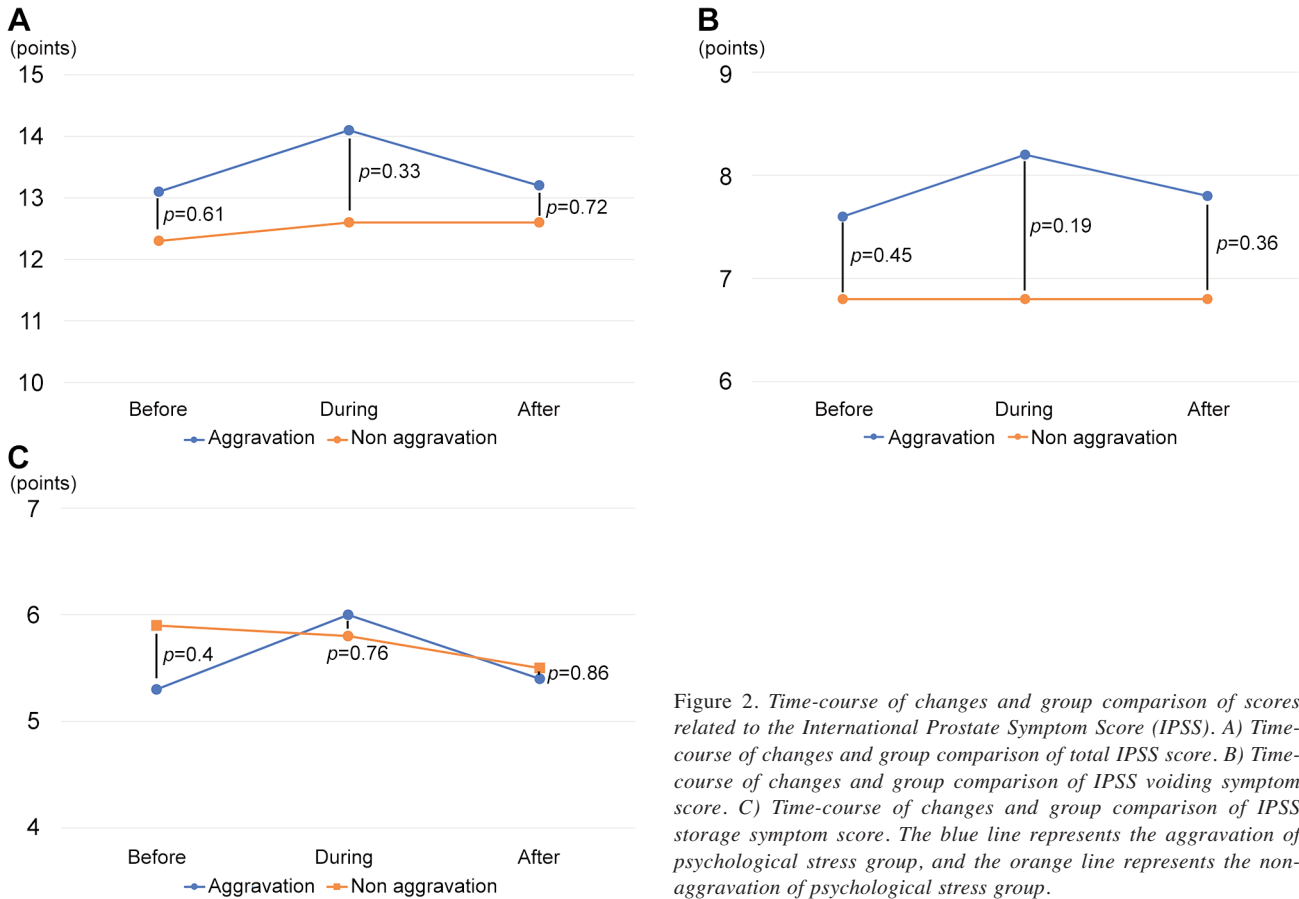


Figure 2. Time-course of changes and group comparison of scores related to the International Prostate Symptom Score (IPSS). A) Time-course of changes and group comparison of total IPSS score. B) Time-course of changes and group comparison of IPSS voiding symptom score. C) Time-course of changes and group comparison of IPSS storage symptom score. The blue line represents the aggravation of psychological stress group, and the orange line represents the non-aggravation of psychological stress group.

Two comparisons were performed between the aggravation of psychological stress and non-aggravation of psychological stress groups, as follows. First, comparison of scores at each time of assessment was performed between the two groups. Second, changes in the scores of each parameter from “before the pandemic” to “during” or “after the first wave of the COVID-19 pandemic” were evaluated using the formula: (score during or after the first wave of the pandemic – score before the first wave of the pandemic) for each parameter.

Statistical analysis. All the variables are presented as medians or means \pm standard deviation. Data were analyzed statistically using the Mann-Whitney *U*-test or one-way analysis of variance with Tukey’s test for continuous variables. The chi-squared test or Fisher’s exact test was performed for categorical variables. Linear mixed effect models were fitted to examine how the outcome data changed over time. Data were analyzed using JMP version 14 software (USA). A probability value of $p < 0.05$ was considered significant.

Results

The patients’ characteristics are shown in Table I. Forty-two patients each were included in the aggravation of physiological stress group and the non-aggravation of

physiological stress group. There were no significant differences in mean age, sex or current disease (BPH, overactive bladder, neurogenic bladder) ($p=0.06$, $p=0.55$, and $p=0.9$, respectively), and no significant differences in physical characteristics, such as height and weight, between the two groups ($p=0.23$ and $p=0.22$, respectively). The baseline SRS-18 score was not significantly different between the two groups ($p=0.55$). There were no significant differences between the two groups in total IPSS score, IPSS voiding symptom subscore and IPSS storage symptom subscore at baseline ($p=0.61$, $p=0.45$, and $p=0.4$, respectively), and no significant difference in PVR at baseline between the two groups ($p=0.51$). There was no significant time-course change in psychological stress during the observation period in the entire cohort ($p=0.55$) (Figure 1).

In the present study, significant time-course changes in total IPSS score, voiding symptom score, and storage symptom score were not observed in each group (aggravation: non-aggravation of psychological stress group; $p=0.8 : p=0.96$, $p=0.88 : p=0.99$, and $p=0.61 : p=0.83$, respectively) (Figure 2). Additionally, no significant differences were observed in terms of the comparison of total

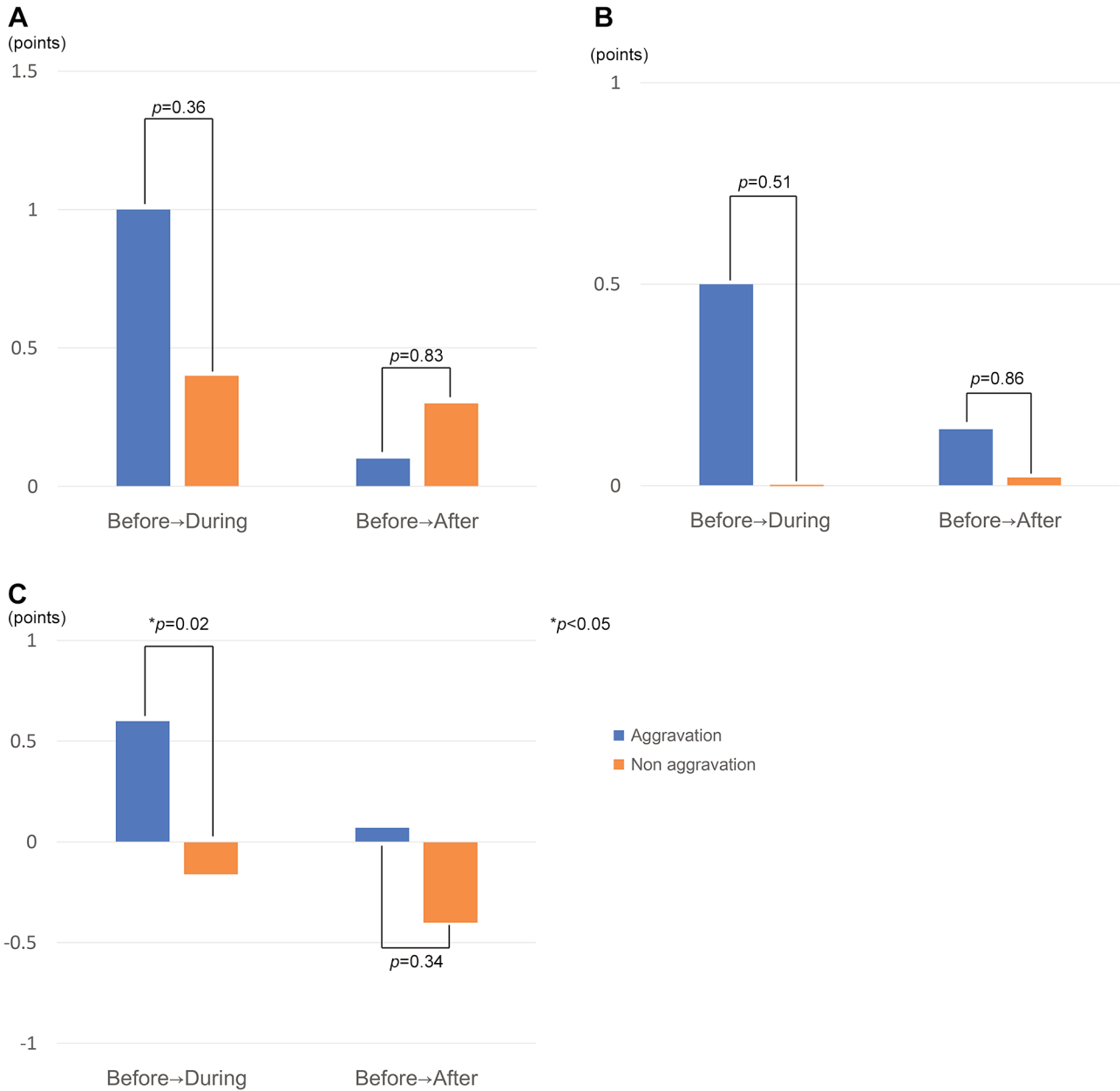


Figure 3. Comparison of changes in the International Prostate Symptom Score (IPSS). A) Comparison of changes in total IPSS score. B) Comparison of changes in IPSS voiding symptom score. C) Comparison of changes in IPSS storage symptom score. Before-During indicates the change in scores from “before the first wave of the COVID-19 pandemic” to “during the first wave of the COVID-19 pandemic”. Before-After indicates the change in scores from “before the first wave of the COVID-19 pandemic” to “after the first wave of the COVID-19 pandemic”. The blue line represents the aggravation of psychological stress group, and the orange line indicates the non-aggravation of psychological stress group.

IPSS score, voiding symptom subscore and storage symptom subscore at each time point between the two groups.

Regarding changes in the score of each parameter from “before the first wave of the pandemic” to “during the first wave of the pandemic”, changes in the total IPSS score ($p=0.36$) and voiding symptom subscore ($p=0.51$) were not

significantly different between the two groups (Figure 3A and B). Only the IPSS storage symptom subscore increased significantly from “before” to “during the first wave of the pandemic” in the aggravation of psychological stress group compared with the non-aggravation of psychological stress group ($p=0.02$) (Figure 3C). On the other hand, in terms of

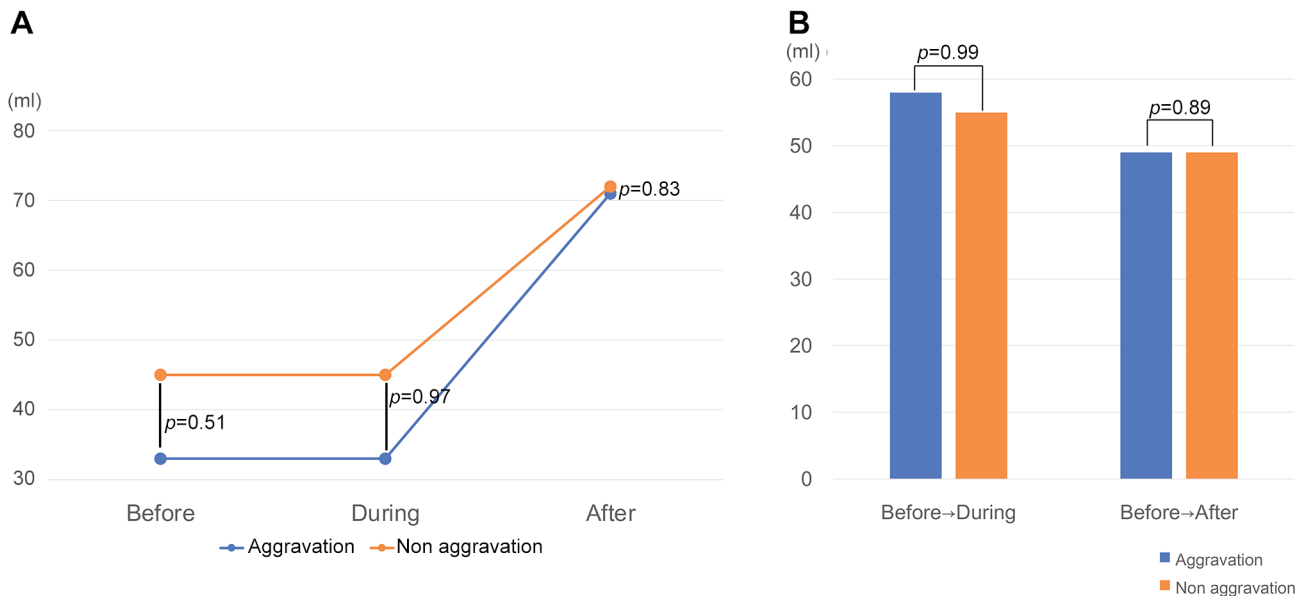


Figure 4. Time-course of changes and group comparison of post-void residual urine volume (PVR) and changes in PVR. A) Time-course of changes and group comparison of PVR. B) Changes in PVR from “before the first wave of COVID-19 pandemic” to “during or after the first wave of COVID-19 pandemic”. The blue line and box represent the aggravation of psychological stress group, and the orange line and box represent the non-aggravation of psychological stress group.

changes in the values of each parameter from “before” to “after the first wave of the pandemic”, no significant differences were observed in changes in total IPSS score, voiding symptom subscore and storage symptom subscore ($p=0.83$, $p=0.86$, $p=0.34$, respectively) between the two groups (Figure 3). PVR and the change in PVR during the observation period were not significantly different between the two groups (Figure 4).

Discussion

The present study demonstrated that aggravation of psychological stress induced by the first year of the COVID-19 pandemic worsened the storage symptom of lower urinary tract dysfunction, as evaluated by the IPSS. The present results were consistent with the results reported by Schiavi *et al.*, who investigated LUTS and quality of life (QOL) using several questionnaires in female overactive bladder (OAB) patients during the COVID-19 outbreak (2). They demonstrated that micturition frequency, nocturia, OAB symptoms and QOL were significantly worsened during the COVID-19 outbreak (2). However, they did not demonstrate the rationale why LUTS worsened during the COVID-19 outbreak. Also, Barone *et al.* demonstrated that the association between the LUTS and psychological stress during the COVID-19 outbreak (12). However, this study was conducted by an anonymous cross-sectional web-based survey. Therefore, the cohort in the study conducted by Barone *et al.* included the healthy subjects. On the other

hand, our present study was conducted only by the patients with LUTS. Thus, this study is the first to show that psychological stress regarding the COVID-19 pandemic might have induced LUTS during the first wave of the COVID-19 outbreak in the patients with LUTS who visited our outpatient clinic.

The present results also demonstrated that aggravation of storage symptoms during the COVID-19 pandemic was transient, and there was an improvement in storage symptoms by the end of the first wave of the pandemic. Thus, if a similar situation occurs in the future, physicians might be able to anticipate that the aggravation of LUTS is likely to be transient, and can temporarily prescribe additional drugs for patients complaining of aggravation of LUTS during abnormal circumstances.

In the present study, PVR did not significantly increase in patients with aggravation of psychological stress. In addition, significant differences in voiding symptoms were not observed between patients with and without aggravation of psychological stress. Also, in the entire cohort, psychological stress was not significantly aggravated during the first wave of the COVID-19 pandemic. Thus, because psychological stress was not that severe in the early part of the pandemic, its effect on voiding symptoms and lower urinary tract function might have been minimal even in patients with aggravation of psychological stress.

Several limitations must be considered in the present study. First, the statistical power was weak due to the small sample

size. However, it was difficult to accumulate more patients during the emergency situation of the pandemic. Second, lower urinary tract function was only evaluated by PVR. Performance of urodynamic studies, *e.g.*, by uroflowmetry, would have better revealed lower urinary tract dysfunction during the pandemic. Third, there might be a recall bias regarding the psychological stress before the first wave of the COVID-19 pandemic. Finally, it is possible that patients with COVID-19 were not completely excluded from the present cohort. RT-PCR was not performed in afebrile patients or patients without respiratory symptoms. Since another study demonstrated that COVID-19 infected patients with BPH had aggravation of LUTS and worsening of lower urinary tract function (5), we could not completely exclude the possibility that not just psychological stress, but also COVID-19 infection itself might have affected the LUTS in patients with aggravation of psychological stress in the present study.

In conclusion, psychological stress during the COVID-19 pandemic might have transiently aggravated storage symptoms in patients with LUTS. In a similar situation as in the present study, physicians should anticipate that aggravation of LUTS is not likely to persist for a long time, and that transient additional medication for LUTS might be effective in patients with psychological stress during future pandemics.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

Nobuhiro Haga contributed to the conception and design. Takeshi Miyazaki contributed to the drafting of the manuscript. Kosuke Tominaga contributed to the acquisition of the data. Yu Okabe provided administrative, technical or material support. Naotaka Gunge contributed to the acquisition of the data. Wataru Matsuoka contributed to the analysis and interpretation of the data. Hiroshi Matsuzaki provided administrative, technical or material support. hintaro Aso contributed to the acquisition of the data. Masahiro Tachibana contributed to the acquisition of the data. Chizuru Nakagawa contributed to the analysis and interpretation of the data. Aiko Fujikawa contributed to the analysis and interpretation of the data. Kazuna Tsubouchi performed the statistical analysis. Nobuyuki Nakamura performed the statistical analysis. Hirofumi Matsuoka contributed to the supervision.

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