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The Effectiveness Between Tamsulosin and Solifenacin Combined with Tamsulosin on Treatment of Ureteral Stent-Related Symptoms

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ABSTRACT

Introduction: *The clinical usage of the ureteral stent caused several stent-related symptoms (SRSs), including lower urinary tract symptoms, pain, general health, work performance, sexual matter and additional problems. This study aims to evaluate the effectiveness between tamsulosin and solifenacin combined with tamsulosin for SRSs.*
Methods: *This double blind randomized controlled trial used 50 patients. Between September 2020 and February 2021, patients underwent double-J stenting after retrograde ureteroscopy were analyzed. All patients would be randomized in a 1:1 ratio in a 1:1 ratio to receive either tamsulosin 0,4 mg (Group A: 25 participants) or tamsulosin 0,4 mg & solifenacin 5 mg combination (group B: 25 participants).We used the Ureteral Symptoms Score Questionnaire (USSQ) as an outcome measure at 1^{s}, 2nd, 3rd and 4th weeks after stent insertion.* ***Results:*** *Group A was found more in women, while in group B was more in men. The highest age in group A and group B was 50-60 years old (36% and 64%). The location of stenting in group A was found more in left (60%), while the group B in the right (52%). Both groups had more patients who were*

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normal nutritional status (60%). There was an improvement in pain and work performance after treatment in both groups, meanwhile group B showed better improvement than group A at all weeks. in addition, there was an improvement in urinary symptoms and sexual matter in group B better than in group A at 2nd to 4th week. Furthermore, group B showed better improvement in general health and additional problem only at 4th week. ***Conclusions:*** *Combination therapy with tamsulosin and solifenacin improved USSQ score more than the monotherapy group. This implied that combination therapy is optimal for improving SRSs.*

1. INTRODUCTION

Ureteral stent placement is very common procedure performed in urologic practice. With the widespread use of indwelling ureteral stents by urologist for urinary diversion, ureteral obstruction relief, and postoperative drainage, issues related to their use have also increased.[1] Despite the wide clinical usage of the ureteral stent, it causes various stent-related symptoms (SRSs), including lower urinary tract symptoms (LUTS), hematuria, body pain, and sexual problems, and ultimately deteriorates the quality of life (QoL) of patients.[2] Up to 80% of patients report on a reduced QoL as a result of the symptoms arising from ureteral stents and the procedure is associated with considerable economic burden.[3]

To reduce the incidence of SRSs, initial efforts have been made to optimize the physical properties of ureteral stents, such as the material, length, design and position. However, as the stent size and designs to reduce SRSs seem limited, optimal stent is still yet to be developed. Nevertheless, oral pharmacologic treatment, has shown beneficial effects of which alpha-blockers and antimuscarinics were mostly adopted.[4] Tamsulosin acts mainly on the urethra, bladder neck and prostate and has a selective blocking effect on smooth muscle in these organs. Tamsolusin can improve LUTS and prevent as well as treat the urinary retention. In addition, tamsulosin can also be used for urinary calculi and adjuvant treatment of male sexual dysfunction. Solifenacin, a muscarinic acetylcholine M3 receptor blocker (M3-blocker), is an anticholinergic drug with high selectivity. It has been suggested that M3 receptors on the bladder detrusor muscle might be the target of this drug. Through inhibiting and blocking the binding of acetylcholine to the M3 receptor, reducing the contractile force of the detrusor, and inhibiting contraction of the detrusor, solifenacin can improve the symptoms of frequent urination and urgency. [5] Solifenacin is the first-line therapy for overactive bladder (OAB) symptoms in LUTS. For all these reasons, antimuscarinics combined with alpha-blockers were recommended for storage symptoms of LUTS.[6]

Lim Kyoung et al reported that combination therapy with tamsulosin and solifenacin improved obstructive and irritative symptoms and quality of life more than in the control group. Therefore, combination therapy with tamsulosin dan solifenacin should be strongly considered for patients who complain of SRSs.[7] Yan et al also reported that the combined use of antimuscarinics and alpha-blockers results in addictive favorable effects in patients with ureteral stent-related symptoms compared with antimuscarinics

monotherapy. The alpha-blockers may enhace the efficacy of the antimuscarinics, which is beneficial for the treatment of SRSs.[8] In the last few decades, many studies have researched effectiveness regarding alpha-blocker and antimuscarinic combined therapy compared with alpha-blocker monotherapy. However, the research included different kinds of alpha-blockers and antimuscarinic, and their results are not completely consistent.[6] Through our research, we aimed to evaluate the effectiveness of tamsulosin and solifenacin combined therapy with tamsulosin monotherapy for SRSs.

2. METHODS

This was a double blind, randomized controlled trial (RCT). According to sample size calculation, 50 patients between September 2020 and February 2021 underwent double-J stenting retrogradely after retrograde ureteroscopy were analyzed. Both male and female, age 20-60 years old, first inserting and unilateral stenting were included in this study. Patients who were diagnosed with hypertension, diabetes mellitus, malignancy, pregnancy and urinary tract infection were excluded from this study.

All participants would be randomized in a 1:1 ratio to receive either tamsulosin 0,4 mg (group A; 25 participants) or tamsulosin 0,4 mg & solifenacin 5 mg combination (group B: 25 participants). We used the Ureteral Symptoms Score Questionnaire (USSQ) to all participants as outcome measure at 1, 2, 3 and 4 weeks after stent inserting.

We hypothesized that medication therapy using tamsulosin and solifenacin combination might be superior to tamsulosin as monotherapy. The *Independent T-test*, *repeated ANOVA test*, and *Friedman test* were used for compassion between groups. All statistical analyses were performed using *SPSS* version 17.0 with $p<0.05$ indicating satirically significant differences.

3. RESULTS

Group A (tamsulosin) had more women (52%) that Group B (tamsulosin and solifenacin combined therapy) conversely Group B had more men (56%) than Group A. The highest age of Group A and Group B was 50-60 years old (36% and 64%). The location of stenting in group A was found more in left (60%) while the group B in the right (52%). Both groups had more patients who were normal nutritional status (60%) (Table 1).

Table 1. The Characteristics of Patients.

	Group A		Group B	
	Number	%	Number	%
Sex				
Male	12	48	14	56
Female	13	52	11	44
Ages (years old)				
20-29	2	8	2	8
30-39	6	24	1	4
40-49	8	32	6	24
50-60	9	36	16	64
Stenting				
Right	10	40	13	52

Left	15	60	12	48
Nutritional Status				
Normal	15	60	15	60
Obesity	10	40	10	40

There was improvement of urinary symptoms after treatment in both groups, meanwhile group B showed better improvement than group A at 2nd to 4th week. Also, there was improvement of pain after treatment in both groups, meanwhile group B showed better improvement than group A at 1st to 4th week.

Table 2. Summary of Ureteral Stent Symptom Score

Week	Group	Mean ± SD	p-value[a]	p-value[b]	p-value[c]
Urinary Symptoms					
1ST	A	20.60 ± 4.6	0.40		
	B	21.48 ± 2.3			
2nd	A	14.32 ± 4.9	0.001		
	B	6.56 ± 2.4		0.001*	0.001#
3rd	A	11.56 ± 4.2	0.001		
	B	3.20 ± 1.2			
4th	A	8.92 ± 4.8	0.001		
	B	2.52 ± 1.1			
Pain					
1ST	A	15.36 ± 4.1	0.001		
	B	19.16 ± 2.3			
2nd	A	10.76 ± 4.0	0.001		
	B	6.80 ± 1.6		0.001*	0.001#
3rd	A	8.36 ± 3.4	0.001		
	B	2.04 ± 1.1			
4th	A	5.44 ± 3.9	0.001		
	B	1.32 ± 0.9			
General Health					
1ST	A	6.24 ± 2.5	0.07		
	B	7.28 ± 1.4			
2nd	A	4.24 ± 2.4	0.85		
	B	4.12 ± 2.3		0.001*	0.001#
3rd	A	3.04 ± 2.4	0.12		
	B	2.20 ± 1.0			
4th	A	2.12 ± 2.2	0.001		
	B	0.72 ± 0.9			
Work Performance					
1ST	A	6.40 ± 3.2	0.001		
	B	6.64 ± 0.9			
2nd	A	4.96 ± 3.2	0.001		
	B	2.76 ± 0.6		0.001*	0.001#
3rd	A	3.36 ± 2.8	0.001		
	B	1.68 ± 1.7			
4th	A	2.52 ± 0.5	0.001		
	B	0.20 ± 0.5			
Sexual Matter					
1ST	A	0.72 ± 1.5	0.60		
	B	1.32 ± 1.4			
2nd	A	0.72 ± 1.2	0.03	0.26*	0.001#
	B	0.40 ± 0.7			
3rd	A	0.52 ± 0.9	0.001		
	B	0.00 ± 0.0			

4th	A	0.44 ± 0.8	0.001		
	B	0.00 ± 0.0			
Additional Problems					
1ST	A	7.04 ± 1.3	0.10		
	B	5.52 ± 1.6			
2nd	A	4.32 ± 1.5	0.73		
	B	3.88 ± 1.7			
3rd	A	3.84 ± 1.1	0.90	0.001*	0.001#
	B	1.48 ± 0.9			
4th	A	3.56 ± 1.4	0.02		
	B	0.44 ± 0.6			

[a] Comparation between Group A & B using *Independent T-test*, [b]comparation between week & Group A, comparation between week & Group B*, [c] *Repeated ANOVA test*, and *Friedman test*#.

About general health, there was improvement after treatment in both groups and group B showed better improvement than group A only at 4th week. However, there was improvement of work performance after treatment in both groups and group B showed better improvement than group A from 1st to 4th week. Sexual matter improvement after treatment showed better improvement in group B from 2nd to 4th week. Additional problem improvement after treatment showed better improvement in group B from only in the 4th week. Overall, There was an improvement of USSQ scores from 1st to 4th weeks in both group except sexual matter in group A (table 2).

Table 3. Summary of Independent variables for USSQ

Week	USSQ	Variabel	Mean	*Standardized coefficients (p-value)*
1st	Pain	Treatment	Group A (15.36 ± 4.19) Group B (19.16 ± 2.32)	0.515 (0.001)
	Additional Problems	Treatment	Group A (7.04 ± 0.26) Group B (5.52 ± 1.64)	-0.422 (0.003)
2nd	Urinary Symptoms	Treatment	Group A(14.32 ± 4.95) Group B (6.56 ± 2.43)	-0.700 (0.001)
	Pain	Treatment	Group A (10.76 ± 4.07) Group B (6.80 ± 0.32)	-0.492 (0.001)
	Work Performance	Treatment	Group A (5.17 ± 3.17) Group B (2.76 ± 0.13)	-0.432 (0.004)
3rd	Urinary Symptoms	Treatment	Group A (3.04 ± 0.48) Group B (3.20 ± 1.22)	-0.774 (0.001)
	Pain	Treatment	Group A (8.36 ± 3.50) Group B (2.04 ± 0.23)	-0.790 (0.001)
		Procedure	Right stent (6.00 ± 4.66) Ledt stent (4.33 ± 3.28)	-0.205 (0.025)
	Sexual Matter	Treatment	Group A (0.91 ± 0.37) Group B (0.00 ± 0.00)	-0.429 (0.001)
		Gender	Male (0.42 ± 0.95) Female (0.08 ± 0.28)	-0.278 (0.031)
		Obesity	Normal (0.38 ± 0.18) Obes (0.12 ± 0.09)	0.275 (0.033)

	Additional Problems	Treatment	Group A (3.84 ± 0.22) Group B (1.48 ± 0.17)	-0.788 (0.001)
4th	Urinary Symptoms	Treatment	Group A (8.92 ± 4.83) Group B (2.52 ± 1.12)	-0.659 (0.001)
		Stenting	Right Stent (6.81 ± 5.95) Left Stent (4.54 ± 2.59)	-0.243 (0.022)
	Pain	Treatment	Group A (5.44 ± 3.93) Group B (1.32 ± 0.20)	-0.564 (0.001)
	General Health	Treatment	Group A (2.12 ± 0.45) Group B (0.72 ± 0.20)	-0.318 (0.022)
		Stenting	Right Stent (1.96 ± 2.12) Left Stent (0.83 ± 1.34)	-0.302 (0.024)
	Work Performance	Treatment	Group A (2.62 ± 0.62) Group B (0.20 ± 0.10)	-0.443 (0.001)
	Sexual Matter	Treatment	Group A (0.73 ± 0.27) Group B (0.00 ± 0.00)	-0.444 (0.001)
		Gender	Male (0.35 ± 0.74) Female (0.08 ± 0.28)	-0.268 (0.037)
		Obesity	Normal (0.31 ± 0.14) Obes (0.12 ± 0.07)	-0.253 (0.049)
	Additional Problem	Treatment	Group A (3.56 ± 0.29) Group B (0.44 ± 0.17)	-0.825 (0.001)

Comparation between Group A & B using *Independent T-test*

Significant differences were found more frequently at the last week (3rd-4th week) than at the beginning of the week (1st-2nd week) for all variables including gender, age, stenting, and nutritional status (appendix 1-4). For all the existing variables, drug administration, which was the main independent variable in this study, had the greatest influence on all domains at all weeks compared to other significant variables (table 3).

4. DISCUSSIONS

Despite of growing number of studies on SRSs, explicit pathophysiology is still matter of debate. SRSs may be the result of ureteric spasm or trigonal irritation. Pain and lower urinary tract symptoms caused be worsened by the increasing pressure transmitted to the renal pelvis during urination, bladder ischemia and lower ureteric bladder spasm. SRSs may also exacerbate pre-existing subclinical detrusor over-activity and induce overactive bladder symptoms.[9]

Our study revealed that tamsulosin & solifenacin combination (group B) was significantly effective for SRSs with comparable results in tamsulosin group (group A) based on USSQ score, which is regarded as the best questionnaire for assessing SRS at present. Jian Zhongyu et al demonstrated that combination of tamsulosin and solifenacin had highest probability to the best intervention for SRSs. This combination might had a synergistic effect, owing to simultaneous inhibition of receptors on smooth muscle located in bladder neck region, lower segment of ureter and detrusor. Alpha-blockers had been proved able to inhibit ureteral contractility in decreased peak ureteral

contraction pressures, which may prevent continuously contracted state of the ureteral smooth muscle caused by the indwelling stent, resulting in ureter dilatation and improvement in drainage. Therefore, alpha-blockers, by reducing muscle spasm and vesicoureteric reflux, can effectively release body pain. With inhibitive effect on Muscarinic-receptors of detrusor smooth muscle cell, solifenacin may be able to handle these symptoms more effectively. Solifenacin had the ability to inhibit abnormal activity of bladder smooth muscle and decreased local contractions of the detrusor.[10]

Regarding USSQ, combination therapy improved urinary symptoms, pain, work performance and sexual matter in almost all weeks. But, general health and additional problem were only improved in 4th week. Yan et al analyzed that alpha-blocker plus antimuscarinics are superior to monotherapy for treatment ureteral stend-related symptoms. Six studies including 483 patients compared the combination therapy of alpha-blockers and antimuscarinics with monotherapy in the treatment of SRSs. Combination therapy improved the pain and work performances score.[8]

There was no reported of side effects both combination and monotherapy in this study. Lim Kyoung et al reported, the side effects of combination therapy were minimal. No patients discontinued the medication because of side effects.[7] Dellis Athanasios et al also showed no patients had to discontinue combination therapy because of side effects or underwent stent removal before the due date.[11]

There are several limitations in our study, although our study was conducted strictly following the methodology of evidence-based medicine. Firstly, number of samples is limited due to COVID-19 pandemic. Secondly, different surgical treatments would also lead to heterogeneity. For example, patients receiving ESWL or ureteroscopic lithotripsy tended to have less trauma, pain and hematuria than those receiving PCNL or open procedures.

5. CONCLUSION

Combination therapy with tamsulosin and solifenacin improved USSQ score more than in monotherapy group. It is implied that combination therapy is optimal to improve SRSs. However, further large-scale & prospective study are needed to get more accurate information.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Appendix 1. USSQ Score by Gender

USSQ		1st week			2nd week			3rd week			4th week		
		Group A	Group B	p-value	Group A	Group B	p-value	Group A	Group B	p-value	Group A	Group B	p-value
Urinary Symptoms	Overall	20.60± 4.65	21.48 ± 2.31	0.400	**14.32 ± 4.95**	**6.56 ± 2.43**	**0.000**	**11.56 ± 4.28**	**3.20 ± 1.22**	**0.000**	**8.92 ± 4.83**	**2.52 ± 1.12**	**0.000**
	Male	20.25 ± 4.99	21.29 ± 1.82	0.510	**15.08 ± 5.48**	**7.00 ± 2.45**	**0.000**	**12.58 ± 4.34**	**3.50 ± 1.10**	**0.000**	**9.17 ± 5.11**	**2.71 ± 0.99**	**0.000**
	Female	20.92 ± 4.50	21.73 ± 2.90	0.600	**13.61 ± 4.50**	**6.00 ± 2.41**	**0.000**	**10.61 ± 4.17**	**2.82 ± 1.33**	**0.000**	**8.70 ± 4.75**	**2.27 ± 1.27**	**0.000**
	p-value	0.730	0.660		0.494	0.230		0.273	0.210		0.547	0.290	
Pain	**Overall**	**15.36 ± 4.19**	**19.16 ± 2.32**	**0.00**	**10.76 ± 4.07**	**6.80 ± 0.32**	**0.000**	**8.36 ± 3.50**	**2.04 ± 0.23**	**0.000**	**5.44 ± 3.93**	**1.32 ± 0.20**	**0.000**
	Male	**14.50 ± 5.14**	**18.50 ± 2.10**	**0.046**	**10.33 ± 4.73**	**6.64 ± 0.41**	**0.009**	**8.50 ± 4.06**	**1.93 ± 1.27**	**0.000**	**5.58 ± 3.96**	**1.07 ± 0.29**	**0.002**
	Female	**16.15 ± 3.08**	**20.00 ± 2.41**	**0.003**	**11.15 ± 0.97**	**7.00 ± 1.73**	**0.002**	**8.23 ± 3.06**	**2.18 ± 1.08**	**0.000**	**5.30 ± 4.07**	**1.64 ± 0.81**	**0.007**
	p-value	0.299	0.173		0.784	0.608		0.854	0.688		0.865	0.172	
General Health	Overall	6.24 ± 2.50	7.28 ± 0.29	0.103	4.24 ± 0.47	4.12 ± 0.47	0.774	3.04 ± 0.48	2.20 ± 0.22	0.237	**2.12 ± 0.45**	**0.72 ± 0.20**	**0.012**
	Male	6.08 ± 2.43	7.21 ± 0.38	0.417	4.33 ± 2.53	5.07 ± 0.68	0.529	3.17 ± 1.90	2.28 ± 0.30	0.185	**2.08 ± 1.83**	**0.71 ± 0.19**	**0.037**
	Female	6.38 ± 2.66	7.63 ± 0.47	0.185	4.15 ± 0.65	2.90 ± 0.41	0.162	2.92 ± 0.81	2.09 ± 0.31	0.637	2.15 ± 0.74	0.73 ± 0.38	0.097
	p-value	0.770	0.955		0.781	0.022		0.455	0.862		0.739	0.508	
Work Performance	Overall	6.67 ± 0.61	6.64 ± 0.18	0.334	**5.17 ± 3.17**	**2.76 ± 0.13**	**0.004**	3.50 ± 0.59	1.68 ± 0.09	0.060	**2.62 ± 0.62**	**0.20 ± 0.10**	**0.000**
	Male	6.67 ± 3.26	6.50 ± 0.23	0.386	**5.33 ± 3.20**	**2.86 ± 0.18**	**0.045**	**4.42 ± 3.15**	**1.50 ± 0.14**	**0.009**	**3.67 ± 3.65**	**0.29 ± 0.16**	**0.001**

	Female	6.67 ± 0.81	6.82 ± 0.98	0.617	**5.00 ± 3.27**	**2.64 ± 0.20**	**0.049**	2.58 ± 0.68	1.91 ± 0.91	0.844	**1.58 ± 0.53**	**0.09 ± 0.09**	**0.005**
	p-value	0.953	0.400		0.803	0.395		0.121	0.033		0.122	0.390	
Sexual Matter	Overall	1.64 ± 0.58	2.06 ± 1.18	0.334	1.27 ± 1.35	0.62 ± 0.20	0.103	**0.91 ± 0.37**	**0.00**	**0.000**	**0.73 ± 0.27**	**0.00**	**0.000**
	Male	1.28 ± 1.50	2.09 ± 1.04	0.152	1.71 ± 1.50	0.64 ± 0.24	0.051	**1.14 ± 1.46**	**0.00**	**0.000**	**0.85 ± 0.40**	**0.00**	**0.000**
	Female	2.25 ± 2.63	2.00 ± 1.58	0.874	0.50 ± 0.28	0.60 ± 0.40	1.000	**0.50 ± 0.28**	**0.00**	**0.000**	**0.50 ± 0.28**	**0.00**	**0.000**
	p-value	0.536	0.905		0.111	0.899		0.326			0.402		
Additonal symptoms	**Overall**	**7.04 ± 0.26**	**5.52 ± 1.64**	**0.000**	4.32 ± 0.31	3.88 ± 1.76	0.296	**3.84 ± 0.22**	**1.48 ± 0.17**	**0.000**	**3.56 ± 0.29**	**0.44 ± 0.17**	**0.000**
	Male	**6.83 ± 0.49**	**5.00 ± 1.36**	**0.003**	4.25 ± 1.96	4.14 ± 2.11	0.894	**3.92 ± 1.44**	**1.35 ± 1.01**	**0.000**	**3.17 ± 0.49**	**0.43 ± 0.14**	**0.001**
	Female	**7.23 ± 0.23**	**6.18 ± 1.78**	**0.024**	4.38 ± 0.31	3.54 ± 1.21	0.171	**3.77 ± 0.20**	**1.64 ± 0.20**	**0.000**	**3.92 ± 0.31**	**0.45 ± 0.21**	**0.000**
	p-value	0.931	0.045		0.552	0.757		0.706	0.361		0.419	0.889	

Appendix 2. USSQ Score by Age

USSQ		1st week			2nd week			3rd week			4th week		
		Group A	Group B	p-value	Group A	Group B	p-value[a]	Group A	Group B	p-value	Group A	Group B	p-value
Urinary Symptoms	Overall	20.60 ± 4.65	21.48 ± 2.31	0.400	**14.32 ± 4.95**	**6.56 ± 2.43**	**0.000**	**11.56 ± 4.28**	**3.20 ± 1.22**	**0.000**	**8.92 ± 4.83**	**2.52 ± 1.12**	**0.000**
	20-29 y.o	19.00 ± 1.00	24.00 ± 2.00	0.121	14.00 ± 3.00	4.50 ± 0.50	0.121	11.00 ± 6.00	3.40 ± 0.50	0.121	7.00 ± 7.00	3.50 ± 0.50	1.000
	30-39 y.o	20.67 ± 3.98	19.00	0.801	13.33 ± 2.42	5.00	0.130	11.83 ± 3.06	2.00	0.130	9.50 ± 2.14	2.00	0.130
	40-49 yo	22.62 ± 4.21	21.17 ± 1.33	0.382	**17.25 ± 5.12**	**8.83 ± 2.14**	**0.002**	14.12 ± 3.94	4.00 ± 1.41	0.000	**10.25 ± 5.52**	**2.33 ± 1.03**	**0.005**
	50-60 y.o	19.11 ± 1.89	21.44 ± 2.47	0.153	**12.44 ± 5.60**	**6.06 ± 0.55**	**0.001**	9.22 ± 1.23	2.94 ± 1.12	0.000	**7.78 ± 1.02**	**2.50 ± 1.21**	**0.000**
	p-value	0.330	0.359		0.211	0.040		0.121	0.283		0.890	0.594	
Pain	Overall	**15.36 ± 4.19**	**19.16 ± 2.32**	**0.00**	**10.76 ± 4.07**	**6.80 ± 0.32**	**0.000**	**8.36 ± 3.50**	**2.04 ± 0.23**	**0.000**	**5.44 ± 3.93**	**1.32 ± 0.20**	**0.000**
	20-29 y.o	15.50 ± 1.50	18.50 ± 1.50	0.221	10.00 ± 0.00	7.00 ± 1.00	0.102	4.50 ± 4.50	0.00 ± 0.00	0.317	3.50 ± 3.50	0.00 ± 0.00	0.317
	30-39 y.o	14.33 ± 1.15	18.00 ± 0.00	0.203	11.33 ± 1.23	10.00 ± 0.00	0.799	8.50 ± 0.85	2.00 ± 00	0.127	6.50 ± 0.88	1.00 ± 0.00	0.130
	40-49 yo	16.50 ± 5.01	18.67 ± 0.80	0.513	**11.62 ± 5.12**	**6.83 ± 0.70**	**0.038**	**10.25 ± 2.96**	**2.50 ± 0.22**	**0.002**	**7.25 ± 4.40**	**2.00 ± 0.63**	**0.022**
	50-60 y.o	15.00 ± 4.82	19.50 ± 0.64	0.018	**9.78 ± 1.45**	**6.56 ± 0.38**	**0.015**	**7.44 ± 3.61**	**2.12 ± 1.20**	**0.000**	3.56 ± 1.27	1.25 ± 0.25	0.244
	p-value	0.768	0.735		0.373	0.382		0.240	0.140		0.257	0.091	
General Health	Overall	6.24 ± 2.50	7.28 ± 0.29	0.103	4.24 ± 0.47	4.12 ± 0.47	0.774	3.04 ± 0.48	2.20 ± 0.22	0.237	**2.12 ± 0.45**	**0.72 ± 0.20**	**0.012**

	20-29 y.o	6.50 ± 2.50	8.00 ± 0.00	1.000	6.50 ± 2.50	5.00 ± 0.00	1.000	3.00 ± 1.00	2.50 ± 0.50	0.683	1.50 ± 1.50	0.50 ± 0.50	0.683
	30-39 y.o	6.33 ± 3.23	18.00 ± 0.00	0.317	4.33 ± 3.77	10.00 ± 0.00	0.445	3.50 ± 3.94	2.00 ± 0.00	0.207	3.50 ± 3.56	1.00 ± 0.00	0.799
	40-49 yo	6.00 ± 2.20	7.83 ± 1.72	0.189	4.12 ± 1.46	4.50 ± 0.81	0.946	**2.87 ± 1.96**	**2.67 ± 1.21**	**0.000**	**1.87 ± 1.73**	**1.00 ± 0.89**	**0.012**
	50-60 y.o	6.33 ± 2.45	6.81 ± 0.30	0.433	3.78 ± 1.79	4.00 ± 0.66	0.953	2.89 ± 2.08	2.12 ± 0.96	0.405	**1.56 ± 0.50**	**0.44 ± 0.16**	**0.029**
	p-value	0.993	0.103		0.641	0.264		0.989	0.279		0.779	0.146	
Working Performance	Overall	6.67 ± 0.61	6.64 ± 0.18	0.334	**5.17 ± 3.17**	**2.76 ± 0.13**	**0.004**	3.50 ± 0.59	1.68 ± 0.09	0.060	**2.62 ± 0.62**	**0.20 ± 0.10**	**0.000**
	20-29 y.o	3.00 ± 3.00	7.00 ± 1.00	0.221	6.00 ± 1.00	2.50 ± 0.50	0.121	6.50 ± 3.50	1.50 ± 0.50	0.121	6.00 ± 6.00	0.00 ± 0.00	0.317
	30-39 y.o	6.17 ± 3.82	6.00 ± 0.00	0.604	4.00 ± 4.15	4.00 ± 0.00	0.797	2.00 ± 2.28	2.00 ± 0.00	0.799	1.88 ± 1.33	0.00 ± 0.00	0.186
	40-49 yo	7.37 ± 2.06	6.83 ± 0.75	0.511	**5.75 ± 2.50**	**2.83 ± 0.75**	**0.013**	4.25 ± 2.60	1.83 ± 0.17	0.084	**3.37 ± 2.97**	**0.00 ± 0.00**	**0.010**
	50-60 y.o	6.44 ± 3.43	6.56 ± 0.24	0.506	4.67 ± 3.74	2.68 ± 0.15	0.289	2.78 ± 0.94	1.62 ± 0.12	0.952	**1.44 ± 0.65**	**0.31 ± 0.15**	**0.038**
	p-value	0.557	0.753		0.791	0.357		0.196	0.665		0.577	0.465	
Sexual Matter	Overall	1.64 ± 0.58	2.06 ± 1.18	0.334	1.27 ± 1.35	0.62 ± 0.20	0.103	**0.91 ± 0.37**	**0.00 ± 0.00**	**0.000**	**0.73 ± 0.27**	**0.00 ± 0.00**	**0.000**
	20-29 y.o	0.00 ± 0.00	0.00 ± 0.00	1.000	0.00 ± 0.00	0.00 ± 0.00	1.000	0.00 ± 0.00	0.00 ± 0.00	1.000	0.00 ± 0.00	0.00 ± 0.00	1.000
	30-39 y.o	2.00 ± 2.10	4.00 ± 0.00	0.445	0.83 ± 0.75	2.00 ± 0.00	0.186	0.67 ± 0.21	0.00 ± 0.00	0.248	0.67 ± 0.21	0.00 ± 0.00	0.258
	40-49 yo	.0.50 ± 0.50	2.17 ± 1.33	0.031	1.37 ± 0.60	1.00 ± 0.63	0.892	0.87 ± 1.46	0.00 ± 0.00	0.106	0.75 ± 0.41	0.00 ± 0.00	0.106

	50-60 y.o	0.22 ± 0.22	1.00 ± 0.28	0.064	0.22 ± 0.22	0.125 ± 0.125	0.673	0.22 ± 0.22	0.00 ± 0.00	0.182	0.11 ± 0.11	0.00 ± 0.00	0.182
	p-value	0.459	0.093		0.099	0.009		0.469	1.000		0.284	1.000	
Additional Problems	Overall	**7.04 ± 0.26**	**5.52 ± 1.64**	**0.000**	4.32 ± 0.31	3.88 ± 1.76	0.296	**3.84 ± 0.22**	**1.48 ± 0.17**	**0.000**	**3.56 ± 0.29**	**0.44 ± 0.17**	**0.000**
	20-29 y.o	8.00 ± 0.00	6.00 ± 0.00	0.083	6.00 ± 2.00	3.50 ± 0.50	0.221	3.50 ± 0.50	2.00 ± 0.00	0.102	2.00 ± 2.00	1.00 ± 1.00	0.683
	30-39 y.o	7.00 ± 0.89	10.00 ± 0.00	0.123	4.00 ± 0.63	2.00 ± 0.00	0.116	3.67 ± 0.82	2.00 ± 0.00	0.116	3.67 ± 0.49	0.00 ± 0.00	0.098
	40-49 yo	**6.50 ± 2.07**	**4.17 ± 1.33**	**0.026**	3.87 ± 1.46	3.17 ± 2.40	0.430	**3.75 ± 0.45**	**1.33 ± 0.82**	**0.008**	**3.37 ± 0.53**	**0.67 ± 0.21**	**0.012**
	50-60 y.o	**7.33 ± 0..17**	**5.69 ± 0.31**	**0.001**	4.56 ± 1.33	4.31 ± 0.38	0.552	**4.11 ± 0.42**	**1.44 ± 0.24**	**0.000**	**4.00 ± 0.41**	**0.31 ± 0.48**	**0.000**
	p-value	0.302	0.044		0.442	0.259		0.834	0.676		0.776	0.360	

Appendix 3. USSQ Score by Stenting

USSQ		1st week			2nd week			3rd week			4th week		
		Group A	Group B	p-value	Group A	Group B	p-value[a]	Group A	Group B	p-value	Group A	Group B	p-value
Urinary Symptoms	Overall	20.60± 4.65	21.48 ± 2.31	0.400	14.32 ± 4.95	**6.56 ± 2.43**	**0.000**	**11.56 ± 4.28**	**3.20 ± 1.22**	**0.000**	**8.92 ± 4.83**	**2.52 ± 1.12**	**0.000**
	Right stenting	21.69 ± 4.82	21.69 ± 2.21	1.000	14.54 ± 4.45	**6.38 ± 0.58**	**0.000**	**12.92 ± 3.88**	**2.77 ± 1.09**	**0.000**	**11.54 ± 4.94**	**2.08 ± 0.24**	**0.000**
	Left stenting	19.42 ± 4.36	21.25 ± 2.49	0.222	14.08 ± 5.63	**6.75 ± 0.82**	**0.001**	**10.08 ± 4.36**	**3.67 ± 0.35**	**0.000**	**6.08 ± 2.71**	**3.00 ± 0.35**	**0.001**
	p-value	0.228	0.644		0.848	0.912		0.100	0.047		0.003	0.047	
Pain	Overall	**15.36 ± 4.19**	**19.16 ± 2.32**	**0.00**	**10.76 ± 4.07**	**6.80 ± 0.32**	**0.000**	**8.36 ± 3.50**	**2.04 ± 0.23**	**0.000**	**5.44 ± 3.93**	**1.32 ± 0.20**	**0.000**
	Right stenting	16.85 ± 4.08	18.54 ± 2.87	0.225	**12.00 ± 3.98**	**6.46 ± 0.53**	**0.000**	**10.08 ± 2.75**	**1.92 ± 1.32**	**0.000**	**7.08 ± 4.27**	**1.23 ± 1.09**	**0.000**
	Left stenting	**13.75 ± 3.84**	**19.83 ± 1.34**	**0.000**	**9.42 ± 3.89**	**7.17 ± 0.34**	**0.017**	**6.50 ± 3.34**	**2.17 ± 1.03**	**0.002**	**3.67 ± 2.71**	**1.42 ± 0.26**	**0.044**
	p-value	0.063	0.041		0.119	0.085		0.008	0.754		0.026	0.563	
General Health	Overall	6.24 ± 2.50	7.28 ± 0.29	0.103	4.24 ± 0.47	4.12 ± 0.47	0.774	3.04 ± 0.48	2.20 ± 0.22	0.237	**2.12 ± 0.45**	**0.72 ± 0.20**	**0.012**
	Right stenting	6.85 ± 2.73	6.92 ± 1.32	0.928	4.54 ± 0.63	4.00 ± 0.56	0.329	**3.85 ± 0.70**	**2.00 ± 1.22**	**0.009**	**3.00 ± 2.38**	**0.92 ± 0.33**	**0.009**
	Left stenting	**5.58 ± 2.15**	**7.67 ± 1.56**	**0.024**	3.92 ± 2.57	4.25 ± 2.73	0.618	2.17 ± 0.61	2.42 ± 0.26	0.195	1.17 ± 0.50	0.50 ± 0.19	0.356
	p-value	0.063	0.205		0.330	0.718		0.049	0.491		0.021	0.402	
Work Performance	Overall	6.67 ± 0.61	6.64 ± 0.18	0.334	**5.17 ± 3.17**	**2.76 ± 0.13**	**0.004**	3.50 ± 0.59	1.68 ± 0.09	0.060	**2.62 ± 0.62**	**0.20 ± 0.10**	**0.000**

	Right stenting	6.23 ± 0.86	6.92 ± 0.21	0.895	4.69 ± 3.40	2.85 ± 0.19	0.113	3.54 ± 0.78	1.85 ± 0.10	0.356	**2.38 ± 0.70**	**0.31 ± 0.17**	**0.009**
	Left stenting	6.58 ± 3.42	6.33 ± 0.98	0.812	**5.25 ± 3.25**	**2.67 ± 0.18**	**0.045**	3.17 ± 0.89	1.50 ± 0.15	0.209	**2.67 ± 1.02**	**0.08 ± 0.08**	**0.001**
	p-value	0.639	0.141		0.662	0.507		0.741	0.069		0.955	0.306	
Sexual Matter	Overall	1.64 ± 0.58	2.06 ± 1.18	0.334	1.27 ± 1.35	0.62 ± 0.20	0.103	**0.91 ± 0.37**	**0.00**	**0.000**	**0.73 ± 0.27**	**0.00**	**0.000**
	Right stenting	0.69 ± 0.47	1.31 ± 0.36	0.064	0.38 ± 0.24	0.38 ± 0.21	0.972	0.15 ± 0.10	0.00 ± 0.00	0.149	0.12 ± 0.10	0.00 ± 0.00	0.149
	Left stenting	0.75 ± 0.37	1.33 ± 0.43	0.315	1.08 ± 0.39	0.42 ± 0.19	0.243	**0.92 ± 0.36**	**0.00 ± 0.00**	**0.006**	**0.75 ± 0.28**	**0.00 ± 0.00**	**0.006**
	p-value	0.618	0.099		0.406	0.304		0.120	1.000		0.153	1.000	
Additional Problems	**Overall**	**7.04 ± 0.26**	**5.52 ± 1.64**	**0.000**	4.32 ± 0.31	3.88 ± 1.76	0.296	**3.84 ± 0.22**	**1.48 ± 0.17**	**0.000**	**3.56 ± 0.29**	**0.44 ± 0.17**	**0.000**
	Right stenting	**7.15 ± 0.22**	**5.46 ± 1.76**	**0.002**	4.23 ± 0.34	3.54 ± 1.85	0.272	**3.92 ± 0.21**	**1.31 ± 0.29**	**0.000**	**4.00 ± 0.27**	**0.31 ± 0.17**	**0.000**
	Left stenting	**6.92 ± 0.50**	**5.58 ± 1.56**	**0.015**	4.42 ± 1,88	4.25 ± 1.66	0.820	**3.75 ± 1.42**	**1.67 ± 0.18**	**0.000**	**3.08 ± 1.73**	**0.58 ± 0.15**	**0.002**
	p-value	0.954	0.538		0.755	0.417		0.542	0.430		0.106	0.129	

Appendix 4. USSQ Score by Nutritional Status

USSQ		1st week			2nd week			3rd week			4th week		
		Group A	Group B	p-value	Group A	Group B	p-value	Group A	Group B	p-value	Group A	Group B	p-value
Urinary Symptoms	Overall	20.60± 4.65	21.48 ± 2.31	0.400	**14.32 ± 4.95**	**6.56 ± 2.43**	**0.000**	**11.56 ± 4.28**	**3.20 ± 1.22**	**0.000**	**8.92 ± 4.83**	**2.52 ± 1.12**	**0.000**
	Normal	19.54 ± 5.86	21.47 ± 2.39	0.248	**13.54 ± 4.88**	**6.07 ± 0.60**	**0.000**	**10.18 ± 3.68**	**3.00 ± 1.41**	**0.000**	**7.91 ± 2.98**	**2.13 ± 0.26**	**0.000**
	Obes	21.43 ± 4.48	21.50 ± 2.32	0.960	**14.93 ± 5.09**	**7.30 ± 0.79**	**0.000**	**12.64 ± 4.53**	**3.50 ± 0.37**	**0.000**	**9.71 ± 5.89**	**3.10 ± 0.35**	**0.001**
	p-value	0.332	0.973		0.498	0.135		0.148	0.212		0.331	0.037	
Pain	Overall	**15.36 ± 4.19**	**19.16 ± 2.32**	**0.00**	**10.76 ± 4.07**	**6.80 ± 0.32**	**0.000**	**8.36 ± 3.50**	**2.04 ± 0.23**	**0.000**	**5.44 ± 3.93**	**1.32 ± 0.20**	**0.000**
	Normal	**14.36 ± 4.61**	**19.40 ± 2.41**	**0.006**	**9.54 ± 4.41**	**6.87 ± 0.46**	**0.033**	**7.54 ± 3.36**	**2.07 ± 0.27**	**0.000**	**4.73 ± 3.16**	**1.40 ± 0.27**	**0.006**
	Obes	16.14 ± 3.82	18.80 ± 2.25	0.052	**11.71 ± 3.67**	**6.70 ± 0.45**	**0.001**	**9.00 ± 3.59**	**2.00 ± 1.41**	**0.000**	**6.00 ± 4.49**	**1.20 ± 0.29**	**0.022**
	p-value	0.315	0.714		0.137	0.908		0.309	0.907		0.415	0.637	
General Health	Overall	6.24 ± 2.50	7.28 ± 0.29	0.103	4.24 ± 0.47	4.12 ± 0.47	0.774	3.04 ± 0.48	2.20 ± 0.22	0.237	**2.12 ± 0.45**	**0.72 ± 0.20**	**0.012**
	Normal	6.18 ± 2.18	7.27 ± 0.36	0.167	3.82 ± 0.60	3.87 ± 0.66	0.937	2.82 ± 2.14	1.73 ± 0.25	0.262	1.64 ± 0.62	0.80 ± 0.30	0.331
	Obes	6.28 ± 2.81	7.30 ± 1.64	0.497	4.57 ± 0.72	4.50 ± 2.07	0.784	3.21 ± 0.73	2.90 ± 0.28	0.952	**2.50 ± 0.64**	**0.60 ± 0.22**	**0.016**
	p-value	0.918	0.931		0.314	0.336		0.824	0.009		0.345	0.903	
Work Performance	Overall	6.67 ± 0.61	6.64 ± 0.18	0.334	**5.17 ± 3.17**	**2.76 ± 0.13**	**0.004**	3.50 ± 0.59	1.68 ± 0.09	0.060	**2.62 ± 0.62**	**0.20 ± 0.10**	**0.000**

	Normal	6.73 ± 3.58	6.53 ± 0.29	0.331	4.54 ± 3.84	3.00 ± 0.17	0.469	2.54 ± 2.42	1.73 ± 0.12	0.532	**1.45 ± 0.39**	**0.20 ± 0.11**	**0.004**
	Obes	6.14 ± 0.79	6.80 ± 0.13	0.759	**5.28 ± 2.89**	**2.40 ± 0.16**	**0.010**	4.00 ± 3.16	1.60 ± 0.16	0.131	**3.36 ± 0.98**	**0.20 ± 0.20**	**0.004**
	p-value	0.259	0.480		0.841	0.027		0.302	0.493		0.470	0.602	
Sexual Matter	Overall	1.64 ± 0.58	2.06 ± 1.18	0.334	1.27 ± 1.35	0.62 ± 0.20	0.103	**0.91 ± 0.37**	**0.00**	**0.000**	**0.73 ± 0.27**	**0.00**	**0.000**
	Normal	0.73 ± 0.41	1.33 ± 0.40	0.235	1.09 ± 0.43	0.40 ± 0.19	0.209	**0.91 ± 0.39**	**0.00 ± 0.00**	**0.005**	**0.73 ± 0.30**	**0.00 ± 0.00**	**0.005**
	Obes	0.71 ± 0.43	1.30 ± 0.37	0.104	0.43 ± 0.23	0.40 ± 0.22	0.941	0.21 ± 0.11	0.00 ± 0.00	0.126	0.21 ± 0.11	0.00 ± 0.00	0.126
	p-value[b]	0.630	0.578		0.377	0.859		1.720	1.000		0.245	1.000	
Additional Problems	Overall	**7.04 ± 0.26**	**5.52 ± 1.64**	**0.000**	4.32 ± 0.31	3.88 ± 1.76	0.296	**3.84 ± 0.22**	**1.48 ± 0.17**	**0.000**	**3.56 ± 0.29**	**0.44 ± 0.17**	**0.000**
	Normal	**6.91 ± 0.51**	**5.67 ± 0.43**	**0.004**	4.09 ± 1.58	3.53 ± 1.68	0.347	**3.82 ± 1.47**	**1.73 ± 0.21**	**0.000**	**3.54 ± 1.63**	**0.40 ± 0.16**	**0.000**
	Obes	**7.14 ± 0.95**	**5.30 ± 1.64**	**0.007**	4.50 ± 0.41	4.40 ± 1.84	0.808	**3.86 ± 0.20**	**1.10 ± 0.28**	**0.000**	**3.57 ± 0.36**	**0.50 ± 0.17**	**0.000**
	p-value[b]	0.726	0.627		0.711	0.278		0.861	0.089		0.772	0.519	