Tamsulosin Monotherapy Is Effective in Reducing Ureteral Stent-related Symptoms: A Meta-analysis of Randomized Controlled Studies

Yong-bo CHEN†, Liang GAO†, Qing JIANG#, Ke RAN, Run-tian LUO
Department of Urology, the Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China

Summary: This study aimed to evaluate the effectiveness of tamsulosin monotherapy for the treatment of ureteral stent-related symptoms (SRSs) and compare it with that of solifenacin monotherapy and combined therapy of tamsulosin and silifenacin. Randomized controlled trials (RCTs), which evaluated the effectiveness of tamsulosin for the treatment of SRSs, were searched from the databases PubMed, EMBASE and the Cochrane Library published up to November 2018. Eight RCTs involving 1087 participants were finally included in this meta-analysis. The results showed that tamsulosin monotherapy could significantly decrease the urinary symptoms [mean difference (MD) –7.56, 95% confidence interval (CI) (–11.47, –3.65), *P*=0.0001] and body pain [MD –5.25, 95% CI (–8.03, –2.46), *P*=0.0002], and improve the sexual performance [MD –1.06, 95% CI (–1.89, –0.24), *P*=0.01] compared with the control group. Moreover, there was no significant difference between tamsulosin monotherapy and solifenacin monotherapy in all outcomes except for significantly better sexual performance in solifenacin group [MD 0.29, 95% CI (0.06, 0.51), *P*=0.01]. In addition, the effectiveness of combined therapy of tamsulosin and solifenacin was not superior to that of tamsulosin monotherapy. Our study demonstrated that tamsulosin monotherapy was effective for the treatment of patients with SRSs; evident superiority could not be found for therapy of tamsulosin and solifenacin combined.
Key words: tamsulosin; solifenacin; ureteral stent-related symptoms; meta-analysis

Ureteral stents have been widely used in the treatment of obstructive pyelonephritis, intolerable acute renal colic, ureteral edema, ureteral perforation following endoscopic procedures, etc.[1, 2], since they were invented in 1967[3, 4]. However, a great number of patients suffer from stent-related symptoms (SRSs) to various degrees after indwelling of ureteral stents, including lower urinary tract symptoms (LUTS), hematuria, body pain and sexual problems[5, 6], which largely decrease the quality of life of patients.

A variety of medicines have been developed and used to overcome these problems[7]. Studies have demonstrated that tamsulosin and solifenacin could effectively relieve SRSs through relaxing the smooth muscle in the prostate and bladder neck or reducing the sensation of the bladder[8–10]. They have been frequently applied in clinical practice. However, studies exploring the effectiveness of tamsulosin monotherapy for SRSs yielded conflicting results. In the present study, we aimed to examine the effectiveness of tamsulosin monotherapy for SRSs through a meta-analysis.

Yong-bo CHEN, E-mail: 569883194@qq.com; Liang GAO, E-mail: gaoliang3745@163.com
†Both authors contributed equally to this work.
#Corresponding author, E-mail: jiangqiang066@163.com

1 METHODS

1.1 Search Strategy

A comprehensive literature search was performed by two independent reviewers (Yong-bo CHEN, Liang GAO) on the databases PubMed, EMBASE, and the Cochrane Library from inception to November 2018. Search terms in title/abstract were: (alphablocker OR tamsulosin OR α-blockers OR alpha blocker) AND (urinary OR ureteral OR ureteric) AND (stents OR stent OR double J). The references and related articles of potential clinical studies were also reviewed. Studies were selected by two independent authors (Yong-bo CHEN, Liang GAO) according to the inclusion and exclusion criteria. Disagreements were resolved through discussing with a third reviewer (Qing JIANG). When data of included studies were found to be incomplete, we tried to contact the authors through e-mail. The method was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (2009).

1.2 Inclusion and Exclusion Criteria

All published studies investigating the effectiveness

of tamsulosin monotherapy for the treatment of SRSs were considered, with their language limited in English. Studies included were required to be randomized controlled studies (RCTs) which compared the efficacy of tamsulosin monotherapy with that of solifenacin monotherapy or the combined therapy of tamsulosin and solifenacin. All patients underwent urological treatments, such as ureteroscopic lithotripsy (URSL), extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) or endopyelotomy, in which the unilateral ureteral stent was placed. The follow-up in each study must not be less than 1 week.

The studies involving patients who were pregnant or suffering from diseases, such as prostatitis, urinary tract infection, or benign prostatic hyperplasia, might affect the experimental results and were excluded.

1.3 Data Extraction and Outcome Measurement

All data were independently collected by two reviewers (Ke RAN, Run-tian LUO). The Ureteral Stent Symptom Questionnaire (USSQ) was used to assess the effectiveness of each treatment. USSQ was divided into five index areas: urinary symptoms, body pain, general health, work performance and sexual performance. Higher USSQ scores represented lower quality of life.

1.4 Quality assessment

The quality of all RCTs was assessed using the Cochrane collaboration's tools, which included 6 parts: randomization, allocation concealment, blinding to personnel and participants, blinding of outcome measurement, incomplete outcomes, selective reporting and other bias[11]. The quality of each study depended on how many criteria they met. In addition, a modified Jadad scale was also used to assess the quality of included studies, and studies with scores between 4 and 7 were regard as high quality studies.

1.5 Statistical Analysis

The Review manager 5.3 software (The Cochrane Collaboration, Oxford, UK) was used to analyze the data. Mean difference (MD) with 95% CI was used to compare the effectiveness of each treatment, and $P<0.05$ was regarded to be statistically significant between groups. The I^2 and P values were used to assess the heterogeneity among studies. If $P>0.1$ or $I^2<50\%$, a fixed-effect model was used. Otherwise, a randomized-effect model was used. Considering the impact of different follow-up durations among studies, we carried out a subgroup analysis in terms of different follow-up time: at the first week, the second week or the fourth week of follow-up.

2 RESULTS

2.1 Study Characteristics

Eight RCTs[12–19] involving 1087 participants were finally included in our study. The flowchart was shown in fig. 1 and the characteristics of each study are summarized in table 1.

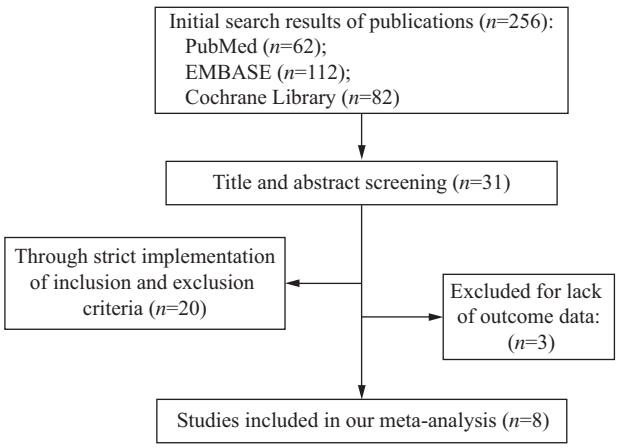


Fig. 1 Flowchart of study selection and inclusion process

Among these studies, patients with renal or ureteric stones were indwelled with the ureteral stent for ESWL in 3 studies[14, 16, 19] and after PCNL in 2 studies[14, 15]. Additionally, patients with ureteral stricture were placed with the ureteral stent after endoscopic endopyelotomy in 1 study[14]. Insignificant differences in sex ratio, average age, stent size and withdrawal rates among groups were reported in these studies. Quality assessment of all studies is demonstrated in fig. 2.

2.2 Tamsulosin *versus* Control

A total of 7 studies[12–18] including 627 participants reported tamsulosin monotherapy for SRSs. Pooled results showed that tamsulosin monotherapy could significantly decrease the urinary symptoms [MD –7.56, 95% CI (–11.47, –3.65), $P=0.0001$] (fig. 3A), body pain [MD –5.25, 95% CI (–8.03, –2.46), $P=0.0002$] (fig. 3B) and improve sexual performance [MD –1.06, 95% CI (–1.89, –0.24), $P=0.01$] (fig. 3E) as compared with the control group. Meanwhile, insignificant differences were found in general health [MD –1.41, 95% CI (–3.04, 0.22), $P=0.09$] (fig. 3C), work performance [MD –0.51, 95% CI (–1.92, 0.90), $P=0.48$] (fig. 3D) and USSQ total score [MD –10.56, 95% CI (–23.59, 2.47), $P=0.11$] (fig. 3F) between tamsulosin monotherapy group and control group.

However, subgroup analysis showed that tamsulosin monotherapy could not significantly decrease the urinary symptoms at the second week and fourth week of follow-up, and the body pain at the first week (fig. 3A, 3B). Moreover, tamsulosin monotherapy could significantly improve the general health at the first week and work performance at the fourth week (fig. 3C, 3D), and decrease USSQ total score at the first week and the fourth week (fig. 3F). In addition, the sexual performance at the second and fourth week could not be significantly improved by

Table 1 Characteristics of included studies

Author	Treatment	Dose	Follow-up	Total subjects	Lost to follow-up	CG[3]	TG[4]	SG[5]	CG[6]	Cochrane collaboration's tools							JADAD
										A	B	C	D	E	F	G	
Park J (2015)	URSL	Tamsulosin 0.4 mg Solifenacin 5 mg Combination	2 weeks	112	31	23	20	20	18	√	√	/	/	√	√	√	6
El-Nahas AR (2015)	URSL	Tamsulosin 0.4 mg Solifenacin 5 mg	1-2 weeks	149	18	44	44	43	/	√	√	√	√	√	√	√	7
Abdelaal AM (2016)	ESWL, URSL, PCNL, others[1]	Tamsulosin 0.4 mg Solifenacin 5 mg Combination	Mean 2.8 weeks	260	26	56	59	58	61	√	?	/	/	√	√	√	3
Damiano R (2008)	URSL	Tamsulosin 0.4 mg	1 weeks	75	0	37	38	/	/	/	/	?	?	√	√	√	2
Dellis AE (2014)	ESWL, URSL	Tamsulosin 0.4 mg	4 weeks	100	0	50	50	/	/	√	√	√	√	√	√	√	6
Wang CJ (2009)	URSL	Tamsulosin 0.4 mg	1 weeks	154	8	71	75	/	/	√	√	√	√	√	√	√	6
Singh I (2014)	URSL, PCNL	Tamsulosin 0.4 mg	4 weeks	60	0	30	30	/	/	√	√	?	?	√	√	√	5
Dellis AE (2017)	ESWL, URSL, others[2]	Tamsulosin 0.4 mg Solifenacin 5 mg Combination	1 weeks	260	0	80	80	80	20	√	√	?	?	√	√	√	4

[1]: stricture ureter, and endoscopic endopyelotomy; [2]: unilateral hydronephrosis of any reason; [3]: control group; [4]: tamsulosin group; [5]: solifenacin group; 6: combination group; A: random sequence generation; B: allocation concealment; C: blinding to participants and personel; D: blinding of outcome assessment; E: incomplete outcome data; F: selective reporting; G: other sources of bias; √: low risk of bias; ?: unclear risk of bias; /: high risk of bias

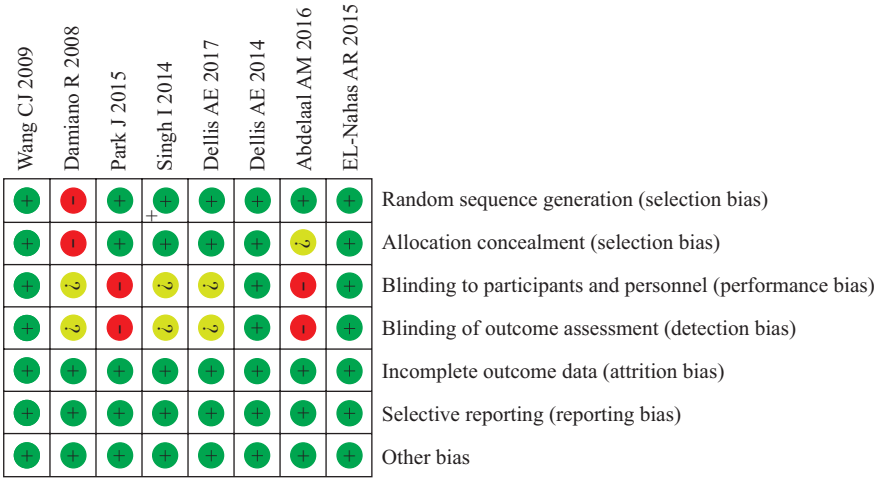


Fig. 2 Quality assessment of all studies
Green, yellow, and red indicates low risk of bias, unclear risk of bias, and high risk of bias, respectively.

tamsulosin monotherapy (fig. 3E). Other outcomes were similar with the totally pooled data.

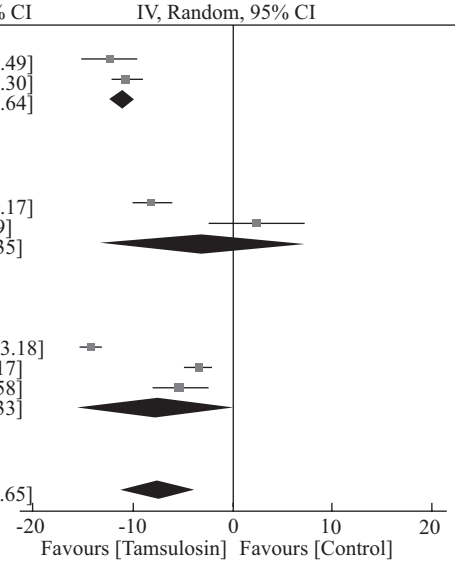
2.3 Tamsulosin *versus* Solifenacin

Four studies[12, 13, 14, 19] including 364 patients compared the effectiveness of tamsulosin monotherapy with that of solifenacin monotherapy. The results showed insignificant differences between the two groups in urinary symptoms [MD 2.44, 95% CI (–0.68, 5.56), *P*=0.13] (fig. 4A), body pain [MD 0.85, 95% CI (–2.07, 3.76), *P*=0.57] (fig. 4B), general health [MD 1.04, 95% CI (–0.62, 2.70), *P*=0.22] (fig. 4C), work performance [MD 0.52, 95% CI (–0.30, 1.34), *P*=0.21] (fig. 4D) and USSQ total score [MD 5.23, 95% CI (–4.77, 15.23), *P*=0.31] (fig. 4F). Furthermore, solifenacin group presented significantly better sexual performance [MD 0.29, 95% CI (0.06, 0.51), *P*=0.01] (fig. 4E).

Subgroup analysis revealed similar results in all outcomes, except for significantly better effectiveness in solifenacin monotherapy group in urinary symptoms, general health, work performance and USSQ total score at the second week of follow-up (fig. 4A, 4C, 4D, 4F). However, the difference of sexual performance between the two groups was not significant at 2 and 4 weeks (fig. 4E).

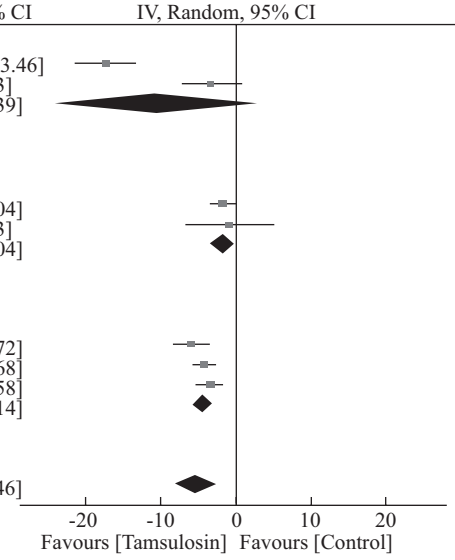
A

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Follow-up after 1 week								
Rocco Damiano 2008	14.1	6.2	38	26.4	6.2	37	14.0%	–12.30 [–15.11, –9.49]
Wang CJ 2009	20.96	3.38	75	31.59	4.69	71	14.9%	–10.63 [–11.96, –9.30]
Subtotal (95% CI)			113			108	28.9%	–10.99 [–12.33, –9.64]
Heterogeneity: Tau²=0.14; Chi²=1.11; df=1 (*P*=0.29); *I*²=10%								
Test for overall effect: *Z*=16.01 (*P*<0.0001)								
1.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	9.6	3.7	44	37.7	5.4	44	14.6%	–8.10 [–10.03, –6.17]
Jinsung Park 2015	31.8	8.1	20	29.3	7.5	23	12.4%	2.50 [–2.19, 7.19]
Subtotal (95% CI)			64			67	27.0%	–3.02 [–13.40, 7.35]
Heterogeneity: Tau²=52.83; Chi²=16.77; df=1 (*P*<0.0001); *I*²=94%								
Test for overall effect: *Z*=0.57 (*P*=0.57)								
1.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	22.9	2.4	59	37.1	3.1	56	15.0%	–14.20 [–15.22, –13.18]
Athanasios E. Dellis 2014	18	3.14	50	21.4	3.14	50	14.9%	–3.40 [–4.63, –2.17]
Iqbal Singh 2014	16.43	5.8	30	21.7	4.78	30	14.1%	–5.27 [–7.96, –2.58]
Subtotal (95% CI)			139			136	44.0%	–7.65 [–15.64, 0.33]
Heterogeneity: Tau²=48.95; Chi²=185.89; df=2 (*P*<0.00001); *I*²=99%								
Test for overall effect: *Z*=1.88 (*P*=0.06)								
Total (95% CI)			316			311	100.0%	–7.56 [–11.47, –3.65]
Heterogeneity: Tau²=26.24; Chi²=219.65; df=6 (*P*<0.00001); *I*²=97%								
Test for overall effect: *Z*=3.79 (*P*=0.0001)								
Test for subgroup differences: Chi²=2.83; df=2 (*P*=0.24); *I*²=29.3%								



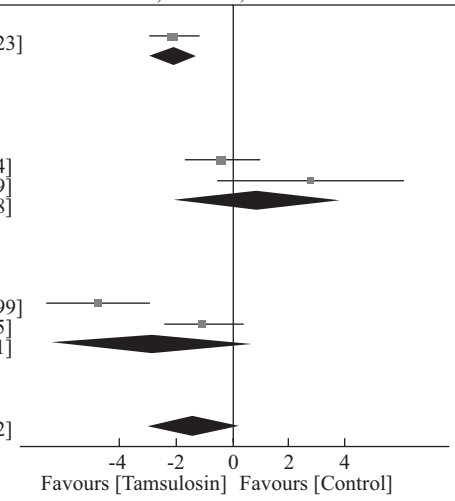
B

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 Follow-up after 1 week								
Rocco Damiano 2008	4.2	8.7	38	21.6	8.7	37	12.9%	–17.40 [–21.34, –13.46]
Wang CJ 2009	9.94	9.65	75	13.3	13.3	71	13.1%	–3.36 [–7.15, 0.43]
Subtotal (95% CI)			113			108	26.0%	–10.37 [–24.13, 3.39]
Heterogeneity: Tau²=94.68; Chi²=25.37; df=1 (*P*<0.00001); *I*²=96%								
Test for overall effect: *Z*=16.01 (*P*<0.0001)								
2.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	17.6	3.5	44	19.4	4.8	44	16.2%	–1.80 [–3.56, –0.04]
Jinsung Park 2015	18.7	10.3	20	19.6	9.4	23	9.7%	–0.90 [–6.83, 5.03]
Subtotal (95% CI)			64			67	25.9%	–1.73 [–3.41, –0.04]
Heterogeneity: Tau²=0.00; Chi²=0.08; df=1 (*P*=0.78); *I*²=0%								
Test for overall effect: *Z*=2.01 (*P*=0.04)								
2.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	15.3	7.3	59	21.3	5	56	15.5%	–6.00 [–8.28, –3.72]
Athanasios E. Dellis 2014	14.1	3.87	50	18.3	3.87	50	16.5%	–4.20 [–5.72, –2.68]
Iqbal Singh 2014	13.16	3.24	30	16.66	4.27	30	16.0%	–3.50 [–5.42, –1.58]
Subtotal (95% CI)			139			136	48.1%	–4.42 [–5.69, –3.14]
Heterogeneity: Tau²=0.37; Chi²=2.81; df=2 (*P*=0.25); *I*²=29%								
Test for overall effect: *Z*=6.80 (*P*<0.00001)								
Total (95% CI)			316			311	100.0%	–5.25 [–8.03, –2.46]
Heterogeneity: Tau²=11.64; Chi²=54.61; df=6 (*P*<0.00001); *I*²=89%								
Test for overall effect: *Z*=3.69 (*P*=0.0002)								
Test for subgroup differences: Chi²=7.22; df=2 (*P*=0.03); *I*²=72.3%								



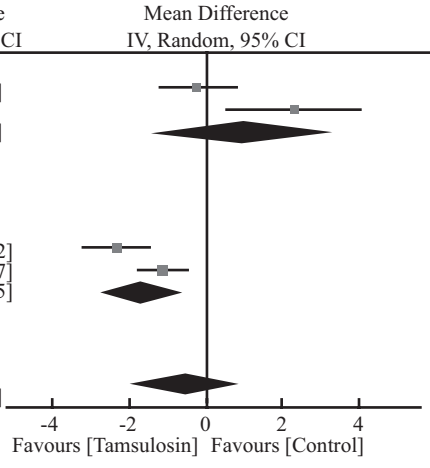
C

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Follow-up after 1 week								
Wang CJ 2009	10.1	2.31	75	12.2	2.99	71	24.1%	–2.10 [–2.97, –1.23]
Subtotal (95% CI)			75			71	24.1%	
Heterogeneity: Not applicable								
Test for overall effect: *Z*=4.73 (*P*<0.00001)								
3.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	16.6	3	44	17	3.4	44	22.0%	–0.40 [–1.74, 0.94]
Jinsung Park 2015	15	6.3	20	12.2	3.4	23	12.6%	2.80 [–0.49, 6.09]
Subtotal (95% CI)			64			67	34.6%	0.83 [–2.22, 3.88]
Heterogeneity: Tau²=3.47; Chi²=3.11; df=1 (*P*=0.08); *I*²=68%								
Test for overall effect: *Z*=0.57 (*P*=0.59)								
3.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	12.5	5.4	59	17.3	4.5	56	19.6%	–4.80 [–6.61, –2.99]
Iqbal Singh 2014	12.46	2.67	30	13.5	2.82	30	21.8%	–1.04 [–2.43, 0.35]
Subtotal (95% CI)			89			86	41.3%	–2.87 [–6.56, 0.81]
Heterogeneity: Tau²=6.39; Chi²=10.41; df=1 (*P*=0.001); *I*²=90%								
Test for overall effect: *Z*=1.53 (*P*=0.13)								
Total (95% CI)			228			224	100.0%	–1.41 [–3.04, 0.22]
Heterogeneity: Tau²=2.66; Chi²=23.69; df=4 (*P*<0.0001); *I*²=83%								
Test for overall effect: *Z*=1.70 (*P*=0.09)								
Test for subgroup differences: Chi²=3.54; df=2 (*P*=0.17); *I*²=43.6%								



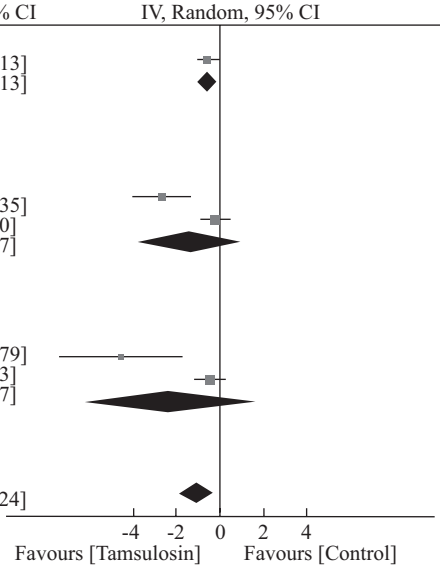
D

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
4.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	9.3	2.4	44	9.5	2.5	44	25.6%	–0.20 [–1.22, 0.82]
Jinsung Park 2015	7.8	3.5	20	5.5	2.1	23	20.2%	2.30 [0.54, 4.06]
Subtotal (95% CI)			64			67	45.8%	0.94 [–1.50, 3.38]
Heterogeneity: Tau²=2.59; Chi²=5.80; df=1 (*P*=0.02); *I*²=83%								
Test for overall effect: *Z*=0.76 (*P*=0.45)								
4.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	10.7	2.3	59	13	2.5	56	26.5%	–2.30 [–3.18, –1.42]
Iqbal Singh 2014	6.86	1.38	30	8	1.28	30	27.7%	–1.14 [–1.81, –0.47]
Subtotal (95% CI)			89			86	54.2%	–1.68 [–2.82, –0.55]
Heterogeneity: Tau²=0.51; Chi²=4.21; df=1 (*P*=0.04); *I*²=76%								
Test for overall effect: *Z*=2.91 (*P*=0.004)								
Total (95% CI)			153			153	100.0%	–0.51 [–0.92, 0.90]
Heterogeneity: Tau²=1.75; Chi²=24.43; df=3 (*P*<0.0001); *I*²=88%								
Test for overall effect: *Z*=0.71 (*P*=0.48)								
Test for subgroup differences: Chi²=3.66; df=1 (*P*=0.06); *I*²=72.7%								



E

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.1.1 Follow-up after 1 week								
Wang CJ 2009	3.65	1.2	75	4.23	1.56	71	27.3%	–0.58 [–1.03, –0.13]
Subtotal (95% CI)			75			71	27.3%	–0.58 [–1.03, –0.13]
Heterogeneity: Not applicable								
Test for overall effect: *Z*=2.51 (*P*=0.01)								
5.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	2.4	2.7	44	5.1	3.7	44	16.5%	–2.70 [–4.05, –1.35]
Jinsung Park 2015	3	1	20	3.2	1	23	25.7%	–0.20 [–0.80, 0.40]
Subtotal (95% CI)			64			67	42.2%	–1.37 [–3.82, 1.07]
Heterogeneity: Tau²=2.84; Chi²=10.96; df=1 (*P*=0.0009); *I*²=91%								
Test for overall effect: *Z*=1.10 (*P*=0.27)								
5.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	5.2	7.2	59	9.8	8.1	56	6.7%	–4.60 [–7.41, –1.79]
Iqbal Singh 2014	0.43	1.33	30	0.86	1.65	30	23.8%	–0.43 [–1.19, 0.33]
Subtotal (95% CI)			89			86	30.4%	–2.29 [–6.35, 1.77]
Heterogeneity: Tau²=7.59; Chi²=7.90; df=1 (*P*=0.005); *I*²=87%								
Test for overall effect: *Z*=1.10 (*P*=0.27)								
Total (95% CI)			228			224	100.0%	–1.06 [–1.89, –0.24]
Heterogeneity: Tau²=0.59; Chi²=18.96; df=4 (*P*=0.0008); *I*²=79%								
Test for overall effect: *Z*=2.54 (*P*=0.01)								
Test for subgroup differences: Chi²=1.04; df=2 (*P*=0.59); *I*²=0%								



F

Study of Subgroup	Tamsulosin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
6.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	49.7	15.5	60	55.7	13.3	60	26.9%	–6.00 [–11.17, –0.83]
Subtotal (95% CI)			60			60	26.9%	–6.00 [–11.17, –0.83]
Heterogeneity: Not applicable								
Test for overall effect: *Z*=2.28 (*P*=0.02)								
6.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	76	8	44	8.3	12.6	44	27.2%	–7.00 [–11.41, –2.59]
Jinsung Park 2015	76.3	28.2	20	69.8	24.4	23	19.8%	6.50 [–9.38, 22.38]
Subtotal (95% CI)			64			67	47.0%	–2.49 [–14.97, 9.98]
Heterogeneity: Tau²=55.77; Chi²=2.58; df=1 (*P*=0.11); *I*²=61%								
Test for overall effect: *Z*=0.39 (*P*=0.70)								
6.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	66.7	19.6	59	98.6	17.1	56	26.1%	–31.90 [–38.61, –25.19]
Subtotal (95% CI)			59			56	26.1%	–31.90 [–38.61, –25.19]
Heterogeneity: Not applicable								
Test for overall effect: *Z*=0.39 (*P*<0.00001)								
Total (95% CI)			183			183	100.0%	–10.56 [–23.59, 2.47]
Heterogeneity: Tau²=157.57; Chi²=48.65; df=3 (*P*<0.00001); *I*²=94%								
Test for overall effect: *Z*=1.59 (*P*=0.11)								
Test for subgroup differences: Chi²=39.75; df=2 (*P*<0.00001); *I*²=95.0%								

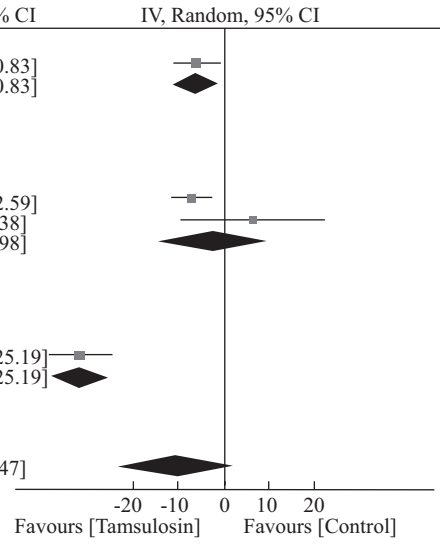
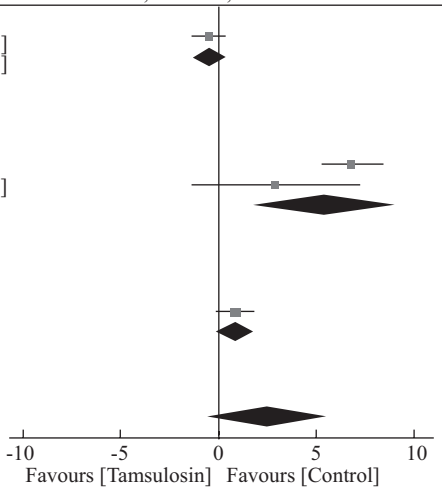


Fig. 3 Comparison of the effectiveness of tamsulosin monotherapy with that of control
A: urinary symptoms; B: body pain; C: general health; D: work performance; E: sexual performance; F: USSQ total score

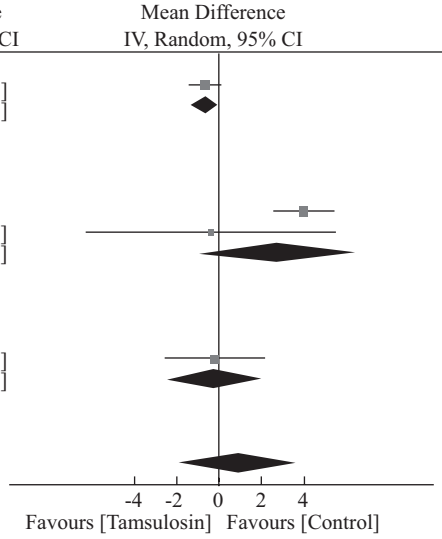
A

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
7.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	17.2	2.4	60	17.7	2.5	60	27.7%	–0.50 [–1.38, 0.38]
Subtotal (95% CI)			60			60	27.7%	–0.50 [–1.38, 0.38]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.12 (P=0.26)								
7.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	29.6	3.7	44	22.8	3.7	43	26.4%	6.80 [5.24, 8.36]
Jinsung Park 2015	31.8	8.1	20	28.9	5.7	20	18.3%	2.90 [–1.44, 7.24]
Subtotal (95% CI)			64			63	44.7%	5.40 [1.73, 9.07]
Heterogeneity: Tau^2=4.84; Chi^2=2.75; df=1 (P=0.10); I^2=64%								
Test for overall effect: Z=2.88 (P=0.004)								
7.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	22.9	2.4	59	22	2.8	58	27.6%	0.90 [–0.05, 1.85]
Subtotal (95% CI)			59			58	27.6%	0.90 [–0.05, 1.85]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.87 (P=0.06)								
Total (95% CI)			183			181	100.0%	2.44 [–0.68, 5.56]
Heterogeneity: Tau^2=8.97; Chi^2=65.20; df=3 (P<0.00001); I^2=95%								
Test for overall effect: Z=1.53 (P=0.13)								
Test for subgroup differences: Chi^2=12.17; df=2 (P=0.002); I^2=83.6%								



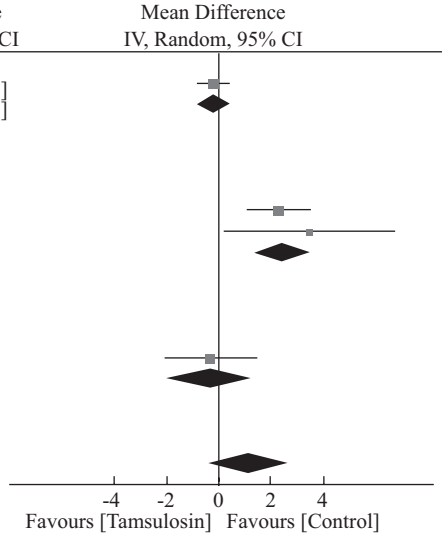
B

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
8.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	14.1	2	60	14.8	2.1	60	30.9%	–0.70 [–1.43, 0.03]
Subtotal (95% CI)			60			60	30.9%	–0.70 [–1.43, 0.03]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.87 (P=0.06)								
8.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	17.6	3.5	44	13.6	3.4	43	29.2%	4.00 [2.55, 5.45]
Jinsung Park 2015	18.7	10.3	20	19.1	8.8	20	13.7%	–0.40 [–6.34, 5.54]
Subtotal (95% CI)			64			63	42.9%	2.78 [–1.08, 6.64]
Heterogeneity: Tau^2=4.82; Chi^2=1.99; df=1 (P=0.16); I^2=50%								
Test for overall effect: Z=1.41 (P=0.16)								
8.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	15.3	7.3	59	15.5	5.5	58	26.2%	–0.20 [–2.54, 2.14]
Subtotal (95% CI)			59			58	26.2%	–0.20 [–2.54, 2.14]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.17 (P=0.87)								
Total (95% CI)			183			181	100.0%	0.85 [–2.07, 3.76]
Heterogeneity: Tau^2=7.03; Chi^2=32.31; df=3 (P<0.00001); I^2=91%								
Test for overall effect: Z=0.57 (P=0.57)								
Test for subgroup differences: Chi^2=3.11; df=2 (P=0.21); I^2=35.6%								



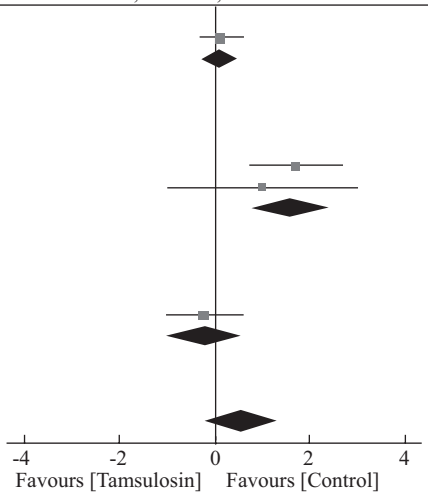
C

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
9.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	7.8	1.7	60	8	1.8	60	32.0%	–0.20 [–0.83, 0.43]
Subtotal (95% CI)			60			60	32.0%	–0.20 [–0.83, 0.43]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.63 (P=0.53)								
9.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	16.6	3	44	14.3	2.7	43	28.6%	2.30 [1.10, 3.50]
Jinsung Park 2015	15	6.3	20	11.5	3.8	20	14.8%	3.50 [0.28, 6.72]
Subtotal (95% CI)			64			63	43.4%	2.45 [1.32, 3.57]
Heterogeneity: Tau^2=0.00; Chi^2=0.47; df=1 (P=0.49); I^2=0%								
Test for overall effect: Z=4.27 (P<0.0001)								
9.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	12.5	5.4	59	12.8	4.1	58	24.6%	–0.30 [–2.04, 1.44]
Subtotal (95% CI)			59			58	24.6%	–0.30 [–2.04, 1.44]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.34 (P=0.73)								
Total (95% CI)			183			181	100.0%	1.04 [–0.62, 2.70]
Heterogeneity: Tau^2=2.14; Chi^2=17.33; df=3 (P=0.0006); I^2=83%								
Test for overall effect: Z=1.22 (P=0.22)								
Test for subgroup differences: Chi^2=16.86; df=2 (P=0.0002); I^2=88.1%								



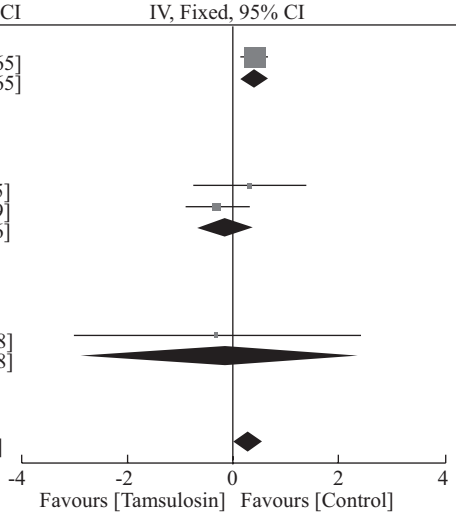
D

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
10.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	7.2	1.1	60	7.1	1.1	60	35.1%	0.10 [–0.29, 0.49]
Subtotal (95% CI)			60			60	35.1%	0.10 [–0.29, 0.49]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.50 (P=0.62)								
10.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	9.3	2.4	44	7.6	2.2	43	25.0%	1.70 [0.73, 2.67]
Jinsung Park 2015	7.8	3.5	20	6.8	2.9	20	11.8%	1.00 [–0.99, 2.99]
Subtotal (95% CI)			64			63	36.8%	1.57 [0.70, 2.44]
Heterogeneity: Tau^2=0.00; Chi^2=0.38; df=1 (P=0.54); I^2=0%								
Test for overall effect: Z=3.53 (P=0.0004)								
10.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	10.7	2.3	59	10.9	2.1	58	28.1%	–0.20 [–1.00, 0.60]
Subtotal (95% CI)			59			58	28.1%	–0.20 [–1.00, 0.60]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.49 (P=0.62)								
Total (95% CI)			183			181	100.0%	0.52 [–0.30, 1.34]
Heterogeneity: Tau^2=0.46; Chi^2=10.96; df=3 (P=0.01); I^2=73%								
Test for overall effect: Z=1.24 (P=0.21)								
Test for subgroup differences: Chi^2=10.57; df=2 (P=0.005); I^2=81.1%								



E

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
11.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	3.4	0.8	60	3	0.6	60	79.9%	0.40 [–0.15, 0.65]
Subtotal (95% CI)			60			60	79.9%	0.40 [–0.15, 0.65]
Heterogeneity: Not applicable								
Test for overall effect: Z=3.10 (P=0.002)								
11.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	2.4	2.7	44	2.1	2.3	43	4.6%	0.30 [–0.75, 1.35]
Jinsung Park 2015	3	1	20	3.3	0.9	20	14.7%	–0.30 [–0.89, 0.29]
Subtotal (95% CI)			64			63	19.3%	–0.16 [–0.67, 0.36]
Heterogeneity: Chi^2=0.95; df=1 (P=0.33); I^2=0%								
Test for overall effect: Z=0.60 (P=0.55)								
11.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	5.2	7.2	59	5.5	7.6	58	0.7%	–0.30 [–2.98, 2.38]
Subtotal (95% CI)			59			58	0.7%	–0.30 [–2.98, 2.38]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.22 (P=0.83)								
Total (95% CI)			183			181	100.0%	0.29 [0.06, 0.51]
Heterogeneity: Tau^2=4.76; df=3 (P=0.19); I^2=37%								
Test for overall effect: Z=2.49 (P=0.01)								
Test for subgroup differences: Chi^2=3.81; df=2 (P=0.15); I^2=47.5%								



F

Study of Subgroup	Tamsulosin Mean	SD	Total	Solifenacin Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
12.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	49.7	15.5	60	50.6	12.8	60	27.6%	–0.90 [–5.99, 4.19]
Subtotal (95% CI)			60			60	27.6%	–0.90 [–5.99, 4.19]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.35 (P=0.73)								
12.1.2 Follow-up after 2 weeks								
Ahmed R. EL-Nahas 2015	76	8	44	61	8.8	43	28.7%	15.00 [11.46, 18.54]
Jinsung Park 2015	76.3	28.2	20	69.3	22.2	20	17.1%	7.00 [–8.73, 22.73]
Subtotal (95% CI)			64			63	45.8%	14.62 [11.16, 18.07]
Heterogeneity: Chi^2=0.00; Chi^2=0.95; df=1 (P=0.33); I^2=0%								
Test for overall effect: Z=8.30 (P<0.00001)								
12.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	66.7	19.6	59	66.8	15.6	58	26.5%	–0.10 [–6.51, 6.31]
Subtotal (95% CI)			59			58	26.5%	–0.10 [–6.51, 6.31]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.03 (P=0.98)								
Total (95% CI)			183			181	100.0%	5.23 [–4.77, 15.23]
Heterogeneity: Tau^2=87.44; Chi^2=32.95; df=3 (P<0.00001); I^2=91%								
Test for overall effect: Z=1.03 (P=0.31)								
Test for subgroup differences: Chi^2=32.00; df=2 (P<0.00001); I^2=93.8%								

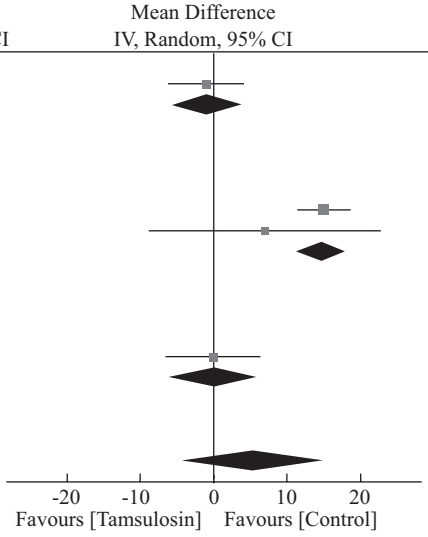


Fig. 4 Comparison of the effectiveness of tamsulosin monotherapy with that of solifenacin monotherapy
A: urinary symptoms; B: body pain; C: general health; D: work performance; E: sexual performance; F: USSQ total score

2.4 Tamsulosin *versus* the Combined Therapy

Totally, 3 studies[12, 14, 19] including 238 participants reported the effectiveness of tamsulosin monotherapy for SRSs compared with that of the combined therapy with tamsulosin and solifenacin. Pooled data showed that there was no significant difference between the two groups in urinary symptoms [MD 3.65, 95% CI (–0.82, 8.11), *P*=0.11] (fig. 5A), body pain [MD 1.70, 95% CI (–3.80, 7.20), *P*=0.54] (fig. 5B), general health [MD 1.04, 95% CI (–0.61, 2.69), *P*=0.22] (fig. 5C), work performance [MD 0.49, 95% CI (–0.02, 1.00), *P*=0.06] (fig. 5D), sexual performance [MD 0.24, 95% CI (–0.63, 1.11), *P*=0.59] (fig. 5E) and USSQ total score [MD 8.60, 95%CI (–5.19, 22.39), *P*=0.22] (fig. 5F).

Subgroup analysis showed that all outcomes were similar with the totally pooled data at 1 and 2 weeks of follow-up, except that tamsulosin monotherapy had a better effectiveness in body pain at 1 week (fig. 5B). However, the combined therapy had significantly better effectiveness in all outcomes at 4 weeks (fig. 5A–E).

2.5 Sensitivity Analysis

According to our assessment, studies by Damiano *et al*[18] and Abdelaal *et al*[14] were regarded to had a low quality. To avoid the impact of these two studies, a sensitivity analysis was carried out, which showed similar results. Furthermore, considering that studies on patients experiencing PCNL and ESWL might affect the accuracy of our study, we also carried out a sensitivity analysis by excluding those studies, respectively. When studies involving PCNL were excluded, similar results were demonstrated in all outcomes except a significant decrease in total USSQ score in tamsulosin group compared with the control group [MD –5.75, 95%CI (–9.77, –1.73), *P*=0.005]. With studies on ESWL excluded, we also obtained a similar result in all outcomes, which meant our results were stable.

3 DISCUSSION

Although a number of studies showed that drug therapy is helpful to relieve SRSs, the underlying mechanism remains unknown. It is speculated that SRSs may be caused by mechanical irritation of stents to the ureter and trigonal region of the bladder, disruption of ureteral peristalsis, detrusor spasm, bladder mucosal inflammation, or reflux of urine into the kidney[20]. According to these theories, tamsulosin, a highly selective α1-receptor blocker, is used for treatment of SRSs[21, 22]. Similarly, solifenacin, a competitive antagonist of muscarinic receptor, is also effective for SRSs[23, 24].

Our study revealed that tamsulosin monotherapy was significantly effective for SRSs with comparable results in solifenacin monotherapy group (except for worse sexual performance in tamsulosin group) and the combined therapy of tamsulosin and solifenacin group based on the USSQ score, which is regarded as the best questionnaire for assessing SRSs at present[25]. In order to ensure the quality of our meta-analysis, studies using other scales such as, international prostate symptom score (IPSS), visual analogue pain score (VAPS) and quality of life (QOL), were not included for pooling.

In previous studies, Damiano *et al*[18] firstly reported that tamsulosin is effective for the treatment of SRSs, with a significant improvement in the USSQ, QOL and VAPS. Further, Navanimitkul *et al*[26] in their RCT showed that tamsulosin 0.4 mg/day could obviously decrease both IPSS and QOL scores with less side-effects compared with the control. However, only 42 patients were analyzed in this study. Afterwards, Lee *et al*[23] found that solifenacin significantly improved SRSs with less adverse events compared with the control.

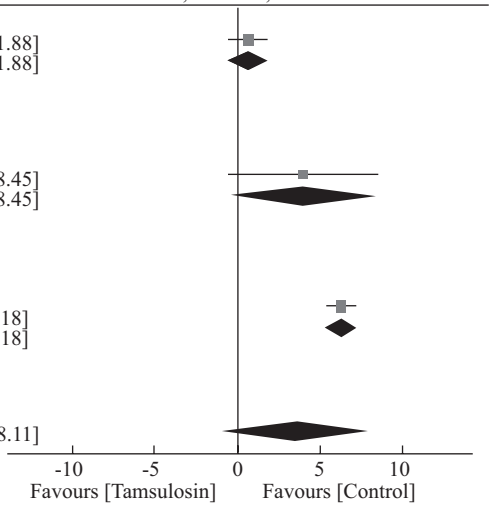
The effectiveness of combined therapy of tamsulosin and solifenacin was also explored. Yan *et al*[24] proposed that solifenacin monotherapy and therapy with solifenacin and tamsulosin combined were both effective in reducing SRSs. They also demonstrated the superiority of combined therapy in their meta-analysis. Shalaby *et al*[27] conducted a study based on 338 patients from four institutions after strict selection, which verified the effectiveness of combined therapy in its good performance in IPSS, QOL and VAPS scores. However, in their study, the effectiveness of tamsulosin or solifenacin monotherapy was not satisfactory. In another study, no significant difference between tamsulosin monotherapy and control groups in the score of IPSS and USSQ was found[28], in which phloroglucinol was used as the control. Furthermore, Lim *et al*[29] evaluated the effectiveness of tamsulosin and solifenacin using IPSS, VAPS and QOL questionnaires, and found that neither tamsulosin nor solifenacin monotherapy had obvious advantage in ameliorating most SRSs while the combined therapy showed a great superiority.

A recent study by Liu *et al*[30] found that combined therapy took effect faster than monotherapy in the first few days, especially on the symptoms of bladder pain and urgency. Based on this study, the combined therapy was recommended for patients who had relatively severe SRSs at the beginning or who were eager to release their symptoms. However, increased risks of drug side effects and complications should also be cautioned[30]. In our study, the subgroup analysis showed the effectiveness of combined therapy of tamsulosin and solifenacin would be superior to that of tamsulosin monotherapy at 4 weeks of follow-up in all outcomes, which indicated that combined therapy holds promises for the long-term treatment for SRSs. However, this result should be further confirmed.

On the other hand, adverse events were only

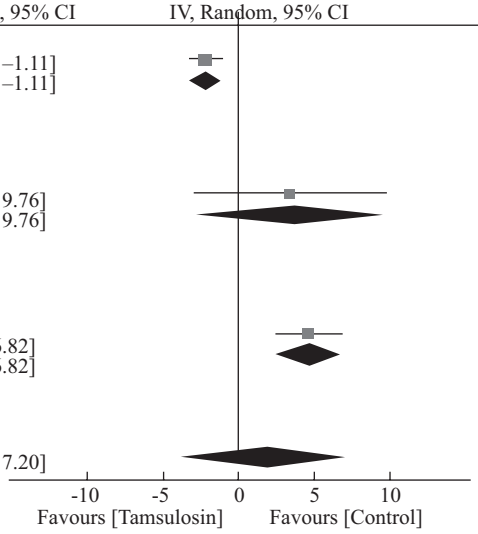
A

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
13.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	17.2	2.4	60	16.5	2.3	20	36.2%	0.70 [–0.48, 1.88]
Subtotal (95% CI)			60			20	36.2%	0.70 [–0.48, 1.88]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.17 (P=0.24)								
13.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	31.8	8.1	20	27.8	5.8	18	27.2%	4.00 [–0.45, 8.45]
Subtotal (95% CI)			20			18	27.2%	4.00 [–0.45, 8.45]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.76 (P=0.08)								
13.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	22.9	2.4	59	16.6	2.5	61	36.6%	6.30 [5.42, 7.18]
Subtotal (95% CI)			59			61	36.6%	6.30 [5.42, 7.18]
Heterogeneity: Not applicable								
Test for overall effect: Z=14.08 (P<0.00001)								
Total (95% CI)			139			99	100.0%	3.65 [–0.82, 8.11]
Heterogeneity: Tau²=13.98; Chi²=55.96; df=2 (P<0.00001); I^2=96%								
Test for overall effect: Z=1.60 (P=0.11)								
Test for subgroup differences: Chi²=55.96; df=2 (P<0.00001); I^2=96.4%								



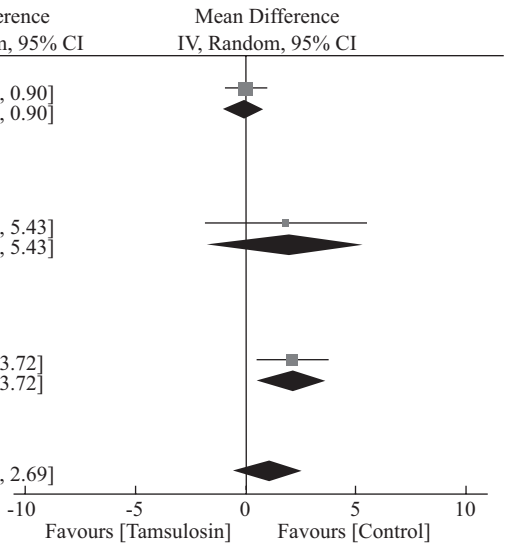
B

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
14.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	14.1	2	60	16.3	2.2	20	38.1%	–2.20 [–3.29, –1.11]
Subtotal (95% CI)			60			20	38.1%	–2.20 [–3.29, –1.11]
Heterogeneity: Not applicable								
Test for overall effect: Z=3.96 (P<0.0001)								
14.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	18.7	10.3	20	15.3	9.7	18	25.5%	3.40 [–2.96, 9.76]
Subtotal (95% CI)			20			18	25.5%	3.40 [–2.96, 9.76]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.05 (P=0.29)								
14.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	15.3	7.3	59	10.7	4.8	61	36.4%	4.60 [2.38, 6.82]
Subtotal (95% CI)			59			61	36.4%	4.60 [2.38, 6.82]
Heterogeneity: Not applicable								
Test for overall effect: Z=4.06 (P<0.0001)								
Total (95% CI)			139			99	100.0%	1.70 [–3.80, 7.20]
Heterogeneity: Tau²=20.35; Chi²=30.79; df=2 (P<0.00001); I^2=94%								
Test for overall effect: Z=0.61 (P=0.54)								
Test for subgroup differences: Chi²=30.79; df=2 (P<0.00001); I^2=93.5%								



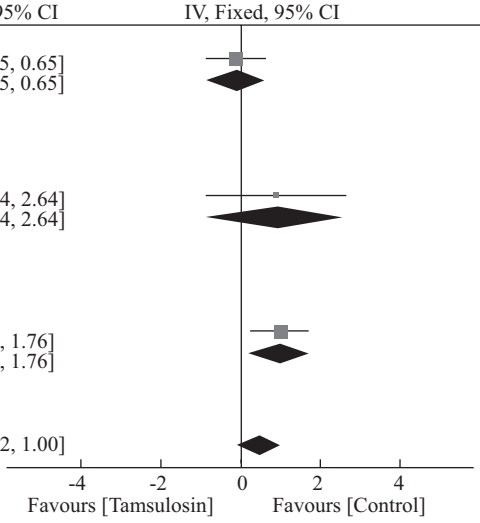
C

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
15.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	7.8	1.7	60	7.8	1.8	20	48.3%	0.00 [–0.90, 0.90]
Subtotal (95% CI)			60			20	48.3%	0.00 [–0.90, 0.90]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.00 (P=1.00)								
15.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	15	6.3	20	13.2	5.1	18	15.2%	1.80 [–1.83, 5.43]
Subtotal (95% CI)			20			18	15.2%	1.80 [–1.83, 5.43]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.97 (P=0.33)								
15.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	12.5	2.4	59	10.4	3.4	61	36.5%	2.10 [0.48, 3.72]
Subtotal (95% CI)			59			61	36.5%	2.10 [0.48, 3.72]
Heterogeneity: Not applicable								
Test for overall effect: Z=2.54 (P=0.01)								
Total (95% CI)			139			99	100.0%	1.04 [–0.61, 2.69]
Heterogeneity: Tau²=1.27; Chi²=5.41; df=2 (P=0.07); I^2=63%								
Test for overall effect: Z=1.23 (P=0.22)								
Test for subgroup differences: Chi²=5.41; df=2 (P=0.07); I^2=63.0%								



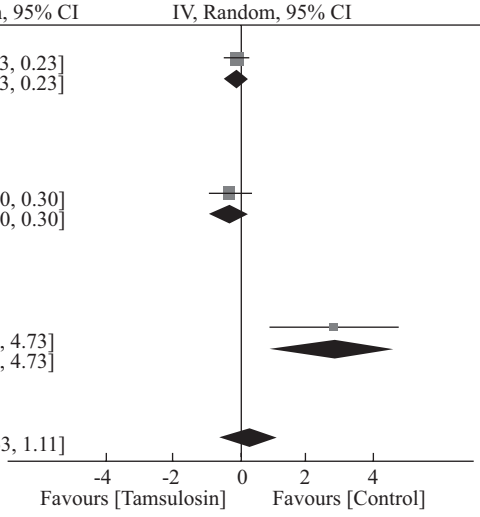
D

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
16.1.1 Follow-up after 1 week								
Athanasios E.Dellis 2017	7.2	1.1	60	7.3	1.6	20	45.8%	–0.10 [–0.85, 0.65]
Subtotal (95% CI)			60			20	45.8%	–0.10 [–0.85, 0.65]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.26 (P=0.80)								
16.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	7.8	3.5	20	6.9	1.8	18	8.6%	0.90 [–0.84, 2.64]
Subtotal (95% CI)			20			18	8.6%	0.90 [–0.84, 2.64]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.01 (P=0.31)								
16.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	10.7	2.3	59	9.7	1.9	61	45.6%	1.00 [0.24, 1.76]
Subtotal (95% CI)			59			61	45.6%	1.00 [0.24, 1.76]
Heterogeneity: Not applicable								
Test for overall effect: Z=2.59 (P=0.010)								
Total (95% CI)			139			99	100.0%	0.49 [–0.02, 1.00]
Heterogeneity: Chi^2=4.31; df=2 (P=0.12); I^2=54%								
Test for overall effect: Z=1.87 (P=0.06)								
Test for subgroup differences: Chi^2=4.31; df=2 (P=0.12); I^2=53.6%								



E

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
17.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	3.4	0.8	60	3.5	0.6	20	45.9%	–0.10 [–0.43, 0.23]
Subtotal (95% CI)			60			20	45.9%	–0.10 [–0.43, 0.23]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.59 (P=0.55)								
17.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	3	1	20	3.3	0.9	18	39.7%	–0.30 [–0.90, 0.30]
Subtotal (95% CI)			20			18	39.7%	–0.30 [–0.90, 0.30]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.97 (P=0.33)								
17.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	5.2	7.2	59	2.4	2.3	61	14.4%	2.80 [0.87, 4.73]
Subtotal (95% CI)			59			61	14.4%	2.80 [0.87, 4.73]
Heterogeneity: Not applicable								
Test for overall effect: Z=2.85 (P=0.004)								
Total (95% CI)			139			99	100.0%	0.24 [–0.63, 1.11]
Heterogeneity: Tau^2=0.40; Chi^2=9.12; df=2 (P=0.01); I^2=78%								
Test for overall effect: Z=0.54 (P=0.59)								
Test for subgroup differences: Chi^2=9.12; df=2 (P=0.01); I^2=78.1%								



F

Study of Subgroup	Tamsulosin Mean	SD	Total	Conmbination Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
18.1.1 Follow-up after 1 week								
Athanasios E. Dellis 2017	49.7	15.5	60	51.4	14.6	20	36.2%	–1.70 [–9.20, 5.80]
Subtotal (95% CI)			60			20	36.2%	–1.70 [–9.20, 5.80]
Heterogeneity: Not applicable								
Test for overall effect: Z=0.44 (P=0.66)								
18.1.2 Follow-up after 2 weeks								
Jinsung Park 2015	76.3	28.2	20	65.5	23.3	18	25.8%	10.80 [–5.59, 27.19]
Subtotal (95% CI)			20			18	25.8%	10.80 [–5.59, 27.19]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.29 (P=0.20)								
18.1.3 Follow-up after 4 weeks								
Ashraf M. Abdelaal 2016	66.7	19.6	59	49.8	9	61	38.1%	16.90 [11.41, 22.39]
Subtotal (95% CI)			59			61	38.1%	16.90 [11.41, 22.39]
Heterogeneity: Not applicable								
Test for overall effect: Z=6.04 (P<0.00001)								
Total (95% CI)			139			99	100.0%	8.60 [–5.19, 22.39]
Heterogeneity: Tau^2=122.18; Chi^2=15.38; df=2 (P=0.0005); I^2=87%								
Test for overall effect: Z=1.22 (P=0.22)								
Test for subgroup differences: Chi^2=15.38; df=2 (P=0.0005); I^2=87.0%								

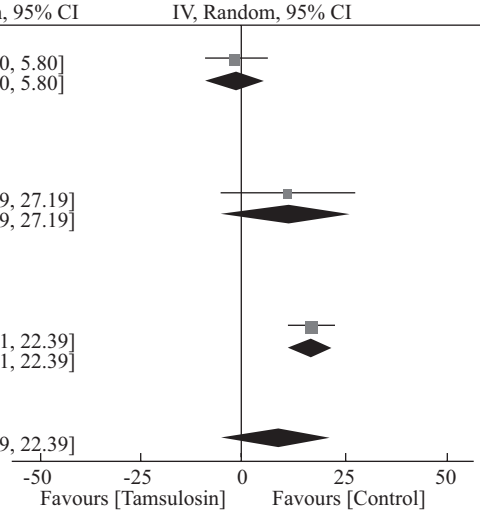


Fig. 5 Comparison of the effectiveness of tamsulosin monotherapy with that of combined therapy of tamsulosin and solifenacin
A: urinary symptoms; B: body pain; C: general health; D: work performance; E: sexual performance; F: USSQ total score

reported in the study by Abdelaal *et al*[14], in which a significantly higher incidence of dry mouth happening during solifenacin monotherapy (6/58) and combined therapy (7/61) was demonstrated. Meanwhile, 5 patients in this study suffered from a retrograde ejaculation, in which, 2 were in tamsulosin group (n=33) and 3 in combined therapy group (n=37). Based on these results, it was concluded that these treatments were safe, although adverse events sporadically occurred.

There are several limitations in our study, although our study was conducted strictly following the methodology of evidence-based medicine. Firstly, the implementation of blind method was still absent in some studies. Secondly, some conflicting results were presented at different follow-up time in the subgroup analysis, which would affect the reliability of our study. Meanwhile, possible heterogeneities among studies could not be avoided, such as different stent sizes, regional differences, etc. Thirdly, 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. As Lee *et al*[31] reported, the position of the stent might be more important than medical treatment for SRSs. In studies included in the meta-analysis, different stents were used and these stents were indwelled by different operators, which would also cause biases to our results. At last, some data in the included studies were missing or could not be collected, which compromised the accurate assessment of drug effectiveness and would even increase the heterogeneities.

In conclusion, our study showed that tamsulosin monotherapy was effective for treatment of SRSs, especially for urinary symptoms, body pain and sexual performance. In addition, solifenacin monotherapy showed insignificant superiority over tamsulosin monotherapy in all outcomes except sexual performance. Therapy of tamsulosin and solifenacin combined was not recommended for the treatment of SRSs. Given possible biases in our study, more high quality trials are necessary to be included to further verify the outcomes of our meta-analysis in the future.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

REFERENCES

1 Chew BH, Knudsen BE, Denstedt JD. The use of stents in contemporary urology. Curr Opin Urol, 2004,14(2):111-115

2 Jeong H, Kwak C, Lee SE. Ureteric stenting after ureteroscopy for ureteric stones: a prospective randomized study assessing symptoms and complications. BJU Int, 2004,93(7):1032-1034; discussion 1034-1035

3 Zimskind PD, Fetter TR, Wilkerson JL. Clinical use of long-term indwelling silicone rubber ureteral splints inserted cystoscopically. J Urol, 1967,97(5):840-844

4 Fiuk J, Bao Y, Calleary JG, *et al*. The use of internal stents in chronic ureteral obstruction. J Urol, 2015,193(4):1092-1100

5 Joshi HB, Okeke A, Newns N, *et al*. Characterization of urinary symptoms in patients with ureteral stents. Urology, 2002,59(4):511-516

6 El-Nahas AR, El-Assmy AM, Shoma AM, *et al*. Self-retaining ureteral stents: analysis of factors responsible for patients'discomfort. J Endourol, 2006,20(1):33-37

7 Chew BH, Seitz C. Impact of ureteral stenting in ureteroscopy. Curr Opin Urol, 2016,26(1):76-80

8 Zhou L, Cai X, Li H, *et al*. Effects of alpha-Blockers, Antimuscarinics, or Combination Therapy in Relieving Ureteral Stent-Related Symptoms: A Meta-Analysis. J Endourol, 2015,29(6):650-656

9 Wang J, Zhang X, Zhang T, *et al*. The role of solifenacin, as monotherapy or combination with tamsulosin in ureteral stent-related symptoms: a systematic review and meta-analysis. World J Urol, 2017,35(11):1669-1680

10 Zhang YM, Chu P, Wang WJ. PRISMA-combined alpha-blockers and antimuscarinics for ureteral stent-related symptoms: A meta-analysis. Medicine, 2017, 96(7):e6098

11 Higgins JP, Altman DG, Gotzsche PC, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj, 2011,343:d5928

12 Park J, Yoo C, Han DH, *et al*. A critical assessment of the effects of tamsulosin and solifenacin as monotherapies and as a combination therapy for the treatment of ureteral stent-related symptoms: a 2 x 2 factorial randomized trial. World J Urol, 2015,33(11):1833-1840

13 El-Nahas AR, Tharwat M, Elsaadany M, *et al*. A randomized controlled trial comparing alpha blocker (tamsulosin) and anticholinergic (solifenacin) in treatment of ureteral stent-related symptoms. World J Urol, 2016,34(7):963-968

14 Abdelaal AM, Al-Adl AM, Abdelbaki SA, *et al*. Efficacy and safety of tamsulosin oral-controlled absorption system, solifenacin, and combined therapy for the management of ureteric stent-related symptoms. Arab J Urol, 2016,14(2):115-122

15 Singh I, Tripathy S, Agrawal V. Efficacy of tamsulosin hydrochloride in relieving "double-J ureteral stent-related morbidity": a randomized placebo controlled clinical study. Int Urol Nephrol, 2014, 46(12):2279-2283

16 Dellis AE, Keeley FX, Jr, Manolas V, *et al*. Role of alpha-blockers in the treatment of stent-related symptoms: a prospective randomized control study. Urology, 2014,83(1):56-61

17 Wang CJ, Huang SW, Chang CH. Effects of specific alpha-1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study. Urol Res, 2009,37(3):147-152

18 Damiano R, Autorino R, De Sio M, *et al*. Effect of tamsulosin in preventing ureteral stent-related morbidity: a prospective study. J Endourol, 2008,22(4):651-656

19 Dellis AE, Papatsoris AG, Keeley FX, Jr, *et al*. Tamsulosin, Solifenacin, and Their Combination for the

Treatment of Stent-Related Symptoms: A Randomized Controlled Study. J Endourol, 2017,31(1):100-109
20 Koprowski C, Kim C, Modi PK, *et al*. Ureteral Stent-Associated Pain: A Review. J Endourol, 2016, 30(7):744-753
21 Lamb AD, Vowler SL, Johnston R, *et al*. Meta-analysis showing the beneficial effect of alpha-blockers on ureteric stent discomfort. BJU Int, 2011,108(11):1894-1902
22 He F, Man LB, Li GZ, *et al*. Efficacy of alpha-blocker in improving ureteral stent-related symptoms: a meta-analysis of both direct and indirect comparison. Drug Des Devel Ther, 2016,10:1783-1793
23 Lee YJ, Huang KH, Yang HJ, *et al*. Solifenacin improves double-J stent-related symptoms in both genders following uncomplicated ureteroscopic lithotripsy. Urolithiasis, 2013,41(3):247-252
24 Yan H, Wang Y, Sun R, *et al*. The Efficacy of Antimuscarinics Alone or in Combination with Alpha-Blockers for the Treatment of Ureteral Stent-Related Symptoms: A Systematic Review and Meta-Analysis. Urol Int, 2017,99(1):6-13
25 Joshi HB, Newns N, Stainthorpe A, *et al*. Ureteral stent symptom questionnaire: development and validation of a multidimensional quality of life measure. J Urol, 2003,169(3):1060-1064
26 Navanimitkul N, Lojanapiwat B. Efficacy of tamsulosin 0.4 mg/day in relieving double-J stent-related symptoms: a randomized controlled study. J Int Med Res, 2010, 38(4):1436-1441
27 Shalaby E, Ahmed AF, Maarouf A, *et al*. Randomized controlled trial to compare the safety and efficacy of tamsulosin, solifenacin, and combination of both in treatment of double-j stent-related lower urinary symptoms. Adv Urol, 2013,2013:752382
28 Valiere Vialeix M, Puichaud A, Irani J. Role of tamsulosin in improving double-J ureteric stent-related symptoms. A prospective multi-center, randomized study. Prog Urol, 2014,24(10): 620-627
29 Lim KT, Kim YT, Lee TY, *et al*. Effects of tamsulosin, solifenacin, and combination therapy for the treatment of ureteral stent related discomforts. Korean J Urol, 2011,52(7):485-488
30 Liu Q, Liao B, Zhang R, *et al*. Combination therapy only shows short-term superiority over monotherapy on ureteral stent-related symptoms - outcome from a randomized controlled trial. BMC Urol, 2016,16(1):66
31 Lee SJ, Yoo C, Oh CY, *et al*. Stent Position Is More Important than alpha-Blockers or Anticholinergics for Stent-Related Lower Urinary Tract Symptoms after Ureteroscopic Ureterolithotomy: A Prospective Randomized Study. Korean J Urol, 2010,51(9):636-641

(Received Jan. 4, 2019; revised April 17, 2019)