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Lower Urinary Tract Pain and Anterior Urethral Stricture Disease: Prevalence and Effects of Urethral Reconstruction

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Abstract

Purpose—Anterior urethral stricture disease most commonly presents as urinary obstruction. Lower urinary tract pain is not commonly reported as a presenting symptom. We prospectively characterized lower urinary tract pain in association with urethral stricture disease and assessed the effects of urethroplasty on this pain.

Materials and Methods—Men (18 years old or older) with anterior urethral stricture disease were prospectively enrolled in a longitudinal, multi-institutional, urethral reconstruction outcomes study from June 2010 to January 2013 as part of TURNS (Trauma and Urologic Reconstruction Network of Surgeons). Preoperative and postoperative lower urinary tract pain was assessed by the validated CLSS. Voiding and sexual function was assessed using validated patient-reported measures, including I-PSS.

Results—Preoperatively 118 of 167 men (71%) reported urethral pain and 68 (41%) reported bladder pain. Age was the only predictor of urethral pain with men 40 years or younger reporting more pain than those 60 years old or older (81% vs 58%, $p = 0.0104$). Lower urinary tract pain was associated with worse quality of life and overall voiding symptoms on CLSS and I-PSS (each $p < 0.01$). Postoperatively lower urinary tract pain completely resolved in 64% of men with urethral pain and in 73.5% with bladder pain. There were no predictive factors for changes in lower urinary tract pain after urethral reconstruction.

Conclusions—Lower urinary tract pain is common in urethral stricture disease, especially in younger men. It is associated with worse quality of life and voiding function. In most men lower urinary tract pain resolves after urethral reconstruction.

Keywords

urethral stricture; lower urinary tract symptoms; pain; quality of life; reconstructive surgical procedures

Anterior USD in men most commonly presents as complaints of a slow or weak urine stream, recurrent urinary tract infections, difficult catheterization and/or acute urinary retention.^{1,2} Pain is described less often as a presenting symptom in USD, although retrospective reports in USD populations mention dysuria rates up to 10%³ and genitourinary pain rates up to 22.9%.⁴ Because conditions that lead to pain are associated with higher patient bother,⁵ health care seeking behavior and health costs,⁶ a study specifically addressing the association of LUTP and USD is warranted. Additionally, with PROMs becoming an increasingly important tool to monitor surgical outcomes the response of LUTP to USD treatment is of particular interest to reconstructive urologists.

The purpose of our study was to 1) describe the prevalence of LUTP in men with anterior USD, 2) determine patient and stricture characteristics associated with LUTP, 3) assess the effect of urethral reconstruction on LUTP in the postoperative period and 4) determine patient and surgical characteristics that predict changes in LUTP after urethroplasty. We hypothesized that 1) using validated questionnaires that assess LUTP with lower urinary tract symptoms we would find LUTP rates in patients with USD that were higher than previously reported in retrospective series, 2) preoperative LUTP rates would differ by stricture location and length, and baseline patient demographics, and 3) successful urethroplasty in patients with complaints of preoperative LUTP would improve their pain.

METHODS

Study Subjects

Between June 2010 and January 2013 men 18 years old or older undergoing anterior urethral reconstruction for USD at a total of 8 institutions participating in TURNS (Trauma and Urologic Reconstruction Network of Surgeons) were offered enrollment in a prospective, longitudinal, institutional review board approved, observational database to study outcomes of anterior urethroplasty. Subjects were excluded from study if they had underlying neurogenic bladder, a suprapubic tube at the time of initial assessment (preventing the ability to assess preoperative voiding pain) or PROM surveys were not obtained preoperatively and postoperatively. For all enrolled subjects a multitude of subjective and objective data, including uroflowmetry, were obtained preoperatively and postoperatively, generally at 3 and 12 months, and yearly thereafter, according to the TURNS specific protocol.⁷ This information along with demographic and clinical data obtained during clinical and operative visits was prospectively recorded in a web based, institutional review board approved database. Stricture characteristics were assessed preoperatively and intraoperatively. However, in the current analysis only intraoperative characteristics such as stricture length were included.

LUTP Analysis

To meet the objectives discussed we first analyzed the responses provided by study participants on the CLSS questionnaire⁸ preoperatively and at all postoperative visits. CLSS is a 10-item questionnaire validated to assess a range of lower urinary tract symptoms for a wide range of obstructive and nonobstructive urological diseases. CLSS questions 9 and 10 ask patients to rate the frequency of bladder and urethral/penile pain, respectively, on a Likert scale of 0—never, 1—rarely, 2—sometimes and 3—often. The CLSS QOL question is “If you were to spend the rest of your life with your urinary symptoms just the way it is now, how would you feel about that?” The CLSS PROM does not assess pain severity or the timing of pain in relation to urination.

We also used cumulative data from other questionnaires administered preoperatively and at all postoperative visits to assess the relationship between LUTP and other urological specific conditions. Voiding symptoms and urinary specific QOL were assessed by I-PSS. The total score possible was 35 with 1 to 7 points indicating mild, 8 to 19 indicating moderate and 20 to 35 indicating severe symptoms. The QOL question, “If you had to spend the rest of your life with your symptoms just as they are now, how would you feel about that?” is rated on a scale of 0—delighted to 6—terrible. Ejaculatory function was evaluated using the 4 questions in MSHQ specific to ejaculation. MSHQ includes a total of 25 questions. The 4 questions relating to ejaculation are scored on a range of 5—good to 0—bad. Erectile function was evaluated by SHIM. The total possible score is 25 with 1 to 7 indicating severe, 8 to 11 indicating ED, 12 to 16 indicating mild to moderate and 17 to 21 indicating mild erectile dysfunction.

All subjective and objective data were obtained preoperatively and at each followup appointment. For subjects on whom more than 1 postoperative followup information was available the most recent data were used for analysis.

Statistical Analysis

We first described the presence of urethral/penile and bladder pain in patients with urethral stricture preoperatively using simple statistics. The chi-square test was used to evaluate the association between preoperative patient variables and pain. We then determined how LUTP responded to urethral reconstruction by determining patient specific postoperative changes in pain scores using simple statistics. Changes in pain scores from preoperatively to postoperatively were compared to patient and surgical predictor variables using chi-square analysis for categorical variables and the t-test for continuous variables. In patients who completed more than 1 postoperative CLSS questionnaire we used data only from the most recent questionnaire. Finally, multivariate analysis was done by creating logistic regression models using a stepwise process to predict for preoperative pain and changes in pain postoperatively. All statistical analysis was done with SAS® 9.3 with $p < 0.05$ considered significant.

RESULTS

Demographics and Clinical Factors

Five surgeons provided CLSS questionnaires to their patients at preoperative and postoperative visits between June 2010 and January 2013, resulting in 167 men being included in the current analysis. A total of 97 men who underwent urethroplasty during the study period were excluded because a suprapubic tube was in place at the preoperative evaluation (42), they had neurogenic bladder (13), or there was failure to obtain preoperative or postoperative pain questionnaires (42). Demographic and stricture data did not statistically differ between the included and excluded cohorts.

Mean $\pm$ SD age of men included in study was 45.3 ± 15.4 years and the mean postoperative assessment time was 7.2 ± 4.3 months. Stricture etiology was most commonly idiopathic (87 cases or 52.1%) followed by iatrogenic/traumatic (52 or 31.1%), infection/lichen sclerosus (15 or 8.9%) and pelvic radiation (13 or 7.8%). The urethral stricture location was bulbar in 105 men (62.9%), penile in 25 (15.0%), and penile and bulbar in 37 (22.2%). Mean stricture length assessed intraoperatively was 3.1 ± 2.1 cm. The most common repair was excision with primary anastomosis (95 men or 56.9%). Buccal mucosal grafting using various surgical techniques was done in 47 men (28.1%) while the remaining 25 (15.0%) required a flap with (12) or without (13) a concomitant graft. Table 1 lists demographic and clinical factors.

Preoperative Pain

Preoperatively 118 of the 167 men (70.7%) reported pain in the urethra/penis and 68 (40.7%) reported pain in the bladder. Figure 1 shows the distribution of preoperative urethral/penile pain and bladder pain frequency. Of men who complained of pain in their urethra/penis the highest percent (39%) reported that the pain occurred often.

On univariate analysis age was the only significant predictor of urethral/penile pain. Younger patients (age 40 years or less) were significantly more likely to report pain than older patients (age 60 years or greater) ($p = 0.0104$, table 1). No other preoperative demographic or clinical factor was predictive of penile/urethral pain, including stricture location or etiology, the maximum flow rate preoperatively or the change in the maximum flow rate postoperatively (table 1). Therefore, multivariate analysis was not done.

No baseline patient demographics predicted bladder pain, although bladder pain was more common in the presence of urethral/penile pain ($p < 0.0001$, data not shown). Men with preoperative bladder pain had a lower urinary flow rate than those without bladder pain (7.30 vs 9.33 ml per second, $p = 0.043$).

LUTP Association with Other Patient Reported Measures

On I-PSS and CLSS patients with preoperative LUTP reported worse overall voiding scores and lower voiding QOL than those without pain (each $p < 0.01$, table 2). Erectile (SHIM) and ejaculatory (MSHQ-ejaculation) function scores were similar between the groups but there were worse ejaculatory scores in men who reported bladder pain ($p = 0.0014$).

Postoperative LUTP Changes

In most patients with preoperative LUTP the pain resolved postoperatively (figs. 2 and 3). Of 118 men who initially reported urethral/penile pain 75 (64%) achieved complete resolution of pain after urethral reconstruction. Another 17 men (14%) reported improvement in pain postoperatively and only 8 (5%) had a worsening frequency of pain (fig. 2). Bladder pain also resolved in 50 of 68 men (74%) and improved in 3 (4%). Only 7 men (4%) reported an increased frequency of bladder pain (fig. 3).

Univariate and multivariate analysis showed no predictive value of demographic and clinical variables in regard to LUTP resolution or improvement after surgical repair in men who had pain preoperatively (data not shown). Men with penile urethral stricture had a greater decrease in the postoperative pain frequency score compared to those with bulbar stricture (1.78 vs 1.44, $p = 0.02$). In 11 men (6.6%) cystoscopy revealed recurrent stricture at followup, of whom 9 reported LUTP preoperatively. Pain had resolved in only 2 the 9 men (22%) at the time that stricture recurrence was noted. The 2 men without preoperative pain remained pain free at the time of recurrence.

DISCUSSION

In this longitudinal multi-institutional study of 167 men with anterior USD LUTP was much more common than previously described.^{3,4} Importantly in most of these patients LUTP completely resolved or improved after urethral reconstruction. There were few predictors of preoperative pain or pain resolution in our cohort, likely due to the unexpectedly high preoperative prevalence rates and the correspondingly high resolution rates, although preoperative urethral pain appeared to be more common in younger men.

Traditional outcome measures used to evaluate the effectiveness of urethroplasty have focused on objective indicators of successful repair such as cystoscopy, retrograde urethrography or uroflowmetry.^{9,10} These measures may not always agree with the patient perception of a successful procedure.¹¹ In more recent years PROMs have become an increasingly important tool after surgery in all disciplines with a major emphasis on improving patient reported satisfaction.^{12,13} Only a few urethral reconstructive studies that used PROMs to assess outcomes looked at patient satisfaction.^{14,15} Although these studies generally showed favorable outcomes,^{16,17} most focused on postoperative voiding and sexual function.¹⁸⁻²⁰

To our knowledge the relationship between LUTP and USD has never been directly assessed in a prospective manner. In the recently developed urethroplasty specific PROM by Jackson et al pain is included in the questionnaire but only in the setting of overall patient health determined by EQ-5D™.²¹ EQ-5D is a generic QOL measure, which precludes the ability to assess urethral stricture specific QOL. Despite this limitation the findings of Jackson et al suggest that voiding pain assessment should become a standard part of initial evaluation and preoperative evaluation in men with USD and it should be included when developing any future PROM. This is emphasized in our study by the worse urological QOL reported by our patients who had LUTP.

Findings in the current study support our initial hypothesis that LUTP rates would be higher than previously reported when assessing LUTP prospectively in a validated questionnaire format. Interestingly the results do not support our hypothesis that specific stricture characteristics would predict for pain. However, this may be related to the high prevalence of pain in our patients, which made it more difficult to find statistical associations. Followup studies that assess pain on a more granular level, including the exact pain location and pain severity, may help us better understand the etiology of LUTP in the stricture population and help increase our likelihood of improving LUTP postoperatively.

The only patient demographic variable that was predictive of preoperative urethral/penile pain was younger patient age (40 years or less). This finding was surprising, considering that epidemiological studies generally show that reported pain rates for given disease processes are higher as patients age.^{22–24} However, the findings are consistent with a recent study by Lubahn et al, which showed higher pain rates and poorer QOL in younger than in older men who performed self-dilation.²⁵ A post hoc hypothesis that we explored when trying to explain this age difference was that differences in preoperative urine flow dynamics may lead to differences in pain. To test this hypothesis we looked at preoperative and postoperative maximum flow rates in men with vs without preoperative pain, assuming that those with a higher flow rate and a greater change in the flow rate may generate higher pressure proximal to the stricture, leading to more urethral dilatation and, therefore, more urethral pain. However, none of these uroflowmetry parameters was predictive of pain.

Pain resolved or improved in most of the patients who underwent urethroplasty in this cohort. Pain resolution was not predicted by any of the collected variables but again this may be related to the high resolution rates. The reasons for pain improvement are unclear and could not be answered in this study, although potential mechanisms include altered intraurethral flow dynamics and pressures, decreased intraurethral inflammation and/or denervation of the area around the urethra due to urethroplasty. Given the high success rate of urethroplasty, it may not be surprising that pain improves after repair. An interesting followup study may be to examine the rates of pain resolution after other procedures such as urethral dilation or internal urethrotomy with their lower success rates. This cohort could serve as a control group to help determine whether persistent pain after intervention is indicative of stricture recurrence. Because of the strong association of pain and patient satisfaction, further investigation of the mechanism is certainly warranted.

Certain study limitations must be addressed. Our followup was less than 1 year and, therefore, it is unknown whether the observed improvement in LUTP would remain and for how long. Additionally, while we found no statistical difference in pain resolution in men with recurrent stricture, this study was underpowered (only 11 recurrences) to determine whether the report of pain could be a reliable marker of stricture recurrence. Finally, only the frequency of pain was assessed in this population. Future studies that address pain severity may allow researchers to better determine patient and stricture factors related to LUTP and its resolution postoperatively.

CONCLUSIONS

In this longitudinal observational study LUTP in men with anterior urethral stricture disease was much more common than previously described. Younger age was a significant predictor in these men with LUTP. Because pain can have significant effects on QOL and health care spending, assessing the LUTP prevalence before and after urethral reconstruction will become increasingly important in our changing health system, especially to determine the best treatment algorithms for patients with USD. Moreover, the finding of pain resolution/improvement after urethral reconstruction in most but not all patients has important implications for preoperative counseling.

Acknowledgments

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Abbreviations and Acronyms

CLSS	Core Lower Urinary Tract Symptoms Score
I-PSS	International Prostate Symptom Score
LUTP	lower urinary tract pain
MSHQ	Male Sexual Health Questionnaire
PROM	patient reported outcomes measure
QOL	quality of life
SHIM	Sexual Health Inventory for Men
USD	urethral stricture disease

REFERENCES

1. Mundy AR, Andrich DE. Urethral strictures. *BJU Int*. 2011; 107:6. [PubMed: 21176068]
2. Romero Pérez P, Mira Llinares A. Male urethral stenosis: review of complications. *Arch Esp Urol*. 2004; 57:485. [PubMed: 15382567]
3. Nuss GR, Granieri MA, Zhao LC, et al. Presenting symptoms of anterior urethral stricture disease: a disease specific, patient reported questionnaire to measure outcomes. *J Urol*. 2012; 187:559. [PubMed: 22177165]
4. Rourke K, Hickie J. The clinical spectrum of the presenting signs and symptoms of anterior urethral stricture: detailed analysis of a single institutional cohort. *Urology*. 2012; 79:1163. [PubMed: 22446349]
5. Lapane KL, Quilliam BJ, Benson C, et al. Impact of noncancer pain on health-related quality of life. *Pain Pract*. 2014 Epub ahead of print.
6. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. National Academies Press; Washington, D.C.: 2011.
7. Erickson BA, Elliott SP, Volelzke BB, et al. Multi-institutional 1-year bulbar urethroplasty outcomes using a standardized prospective cystoscopic follow-up protocol. *Urology*. 2014; 84:213. [PubMed: 24837453]
8. Homma Y, Yoshida M, Yamanishi T, et al. Core Lower Urinary Tract Symptom score (CLSS) questionnaire: a reliable tool in the overall assessment of lower urinary tract symptoms. *Int J Urol*. 2008; 15:816. [PubMed: 18657204]

9. Erickson BA, Breyer BN, McAninch JW. Changes in uroflowmetry maximum flow rates after urethral reconstructive surgery as a means to predict for stricture recurrence. *J Urol.* 2011; 186:1934. [PubMed: 21944128]
10. Wong SS, Aboumarzouk OM, Narahari R, et al. Simple urethral dilatation, endoscopic urethrotomy, and urethroplasty for urethral stricture disease in adult men. *Cochrane Database Syst Rev.* 2012; 12:CD006934. [PubMed: 23235635]
11. Kessler TM, Fisch M, Heitz M, et al. Patient satisfaction with the outcome of surgery for urethral stricture. *J Urol.* 2002; 167:2507. [PubMed: 11992068]
12. Black N. Patient reported outcome measures could help transform healthcare. *BMJ.* 2013; 346:f167. [PubMed: 23358487]
13. Dawson J, Doll H, Fitzpatrick R, et al. The routine use of patient reported outcome measures in healthcare settings. *BMJ.* 2010; 340:c186. [PubMed: 20083546]
14. Voelzke BB. Critical review of existing patient reported outcome measures after male anterior urethroplasty. *J Urol.* 2013; 189:182. [PubMed: 23174257]
15. Warren GJ, Erickson BA. The role of noninvasive testing and questionnaires in urethroplasty follow-up. *Transl Androl Urol.* 2014; 3:221.
16. DeLong J, Buckley J. Patient-reported outcomes combined with objective data to evaluate outcomes after urethral reconstruction. *Urology.* 2013; 81:432. [PubMed: 23374824]
17. Jackson MJ, Chaudhury I, Mangera A, et al. A prospective patient-centred evaluation of urethroplasty for anterior urethral stricture using a validated patient-reported outcome measure. *Eur Urol.* 2013; 64:777. [PubMed: 23664422]
18. Erickson BA, Granieri MA, Meeks JJ, et al. Prospective analysis of erectile dysfunction after anterior urethroplasty: incidence and recovery of function. *J Urol.* 2010; 183:657. [PubMed: 20018319]
19. Johnson EK, Latini JM. The impact of urethroplasty on voiding symptoms and sexual function. *Urology.* 2011; 78:198. [PubMed: 21458033]
20. Morey AF, McAninch JW, Duckett CP, et al. American Urological Association symptom index in the assessment of urethroplasty outcomes. *J Urol.* 1998; 159:1192. [PubMed: 9507830]
21. Jackson MJ, Sciberras J, Mangera A, et al. Defining a patient-reported outcome measure for urethral stricture surgery. *Eur Urol.* 2011; 60:60. [PubMed: 21419566]
22. Ferrell BA. Pain evaluation and management in the nursing home. *Ann Intern Med.* 1995; 123:681. [PubMed: 7574224]
23. Roy R, Thomas M: A survey of chronic pain in an elderly population. *Can Fam Physician.* 1986; 32:513. [PubMed: 21267146]
24. Tracy B, Morrison SR. Pain management in older adults. *Clin Ther.* 2013; 35:1659. [PubMed: 24148553]
25. Lubahn JD, Zhao LC, Scott JF, et al. Poor quality of life in patients with urethral stricture treated with intermittent self-dilation. *J Urol.* 2014; 191:143. [PubMed: 23820057]

Figure 1. Preoperative LUTP frequency. Blue indicates never. Orange indicates rarely. Green indicates sometimes. Purple indicates often.

Figure 2.

Postoperative urethral/penile pain frequency stratified by preoperative pain cohort. Blue bars indicate never. Orange bars indicate rarely. Green bars indicate sometimes. Purple bars indicate often.

Figure 3.

Postoperative bladder pain frequency stratified by preoperative pain cohort. Blue bars indicate never. Orange bars indicate rarely. Green bars indicate sometimes. Purple bars indicate often.

Table 1

Patient demographic and clinical characteristics by preoperative urethral/penile pain

	Overall	Urethral/Penile Pain		p Value
		Yes	No	
No. age (%):				
40 or Less	72 (43.1)	58 (80.6)	14 (19.4)	0.0104
41–59	65 (38.9)	46 (70.8)	19 (29.2)	
60 or Greater	30 (18.0)	17 (56.7)	13 (43.3)	
No. obesity (%):				
Body mass index less than 30 kg/m ²	95 (56.9)	68 (71.6)	27 (28.4)	0.1361
Body mass index 30 kg/m ² or greater	72 (43.1)	55 (76.4)	17 (23.6)	
No. diabetes (%):				
No	145 (86.8)	113 (77.9)	32 (22.1)	0.6800
Yes	22 (13.2)	18 (81.8)	4 (18.2)	
No. active smoking (%):				
No	140 (83.8)	98 (70)	42 (30)	0.1963
Yes	27 (16.2)	22 (81.5)	5 (18.5)	
No. comorbidity (%): *				
0	68 (40.7)	50 (73.5)	18 (26.5)	0.9885
1–2	78 (46.7)	58 (74.4)	20 (25.6)	
Greater than 2	21 (12.6)	16 (76.2)	5 (23.8)	
No. stricture etiology (%):				
Idiopathic	87 (52.1)	62 (71.3)	25 (28.7)	0.1089
Iatrogenic/trauma	52 (31.1)	37 (71.2)	15 (28.8)	
Infection/lichen sclerosis	15 (8.9)	14 (93.3)	1 (6.7)	
Hypospadias	10 (6.0)	6 (60.0)	4 (40.0)	
Radiation	3 (1.8)	1 (33.3)	2 (66.7)	
No. stricture location (%):				
Bulbar	105 (62.9)	79 (75.2)	26 (24.8)	0.6983
Penile	25 (15.0)	19 (76.0)	6 (24.0)	
Bulbar + penile	18 (10.8)	12 (66.7)	6 (33.3)	
Multiple strictures	19 (11.4)	14 (73.7)	5 (26.3)	
No. cm stricture length at urethroplasty (%):				
Less than 2	115 (63.5)	86 (74.8)	29 (25.2)	0.7150
2–5	34 (15.0)	26 (76.5)	8 (23.5)	
Greater than 5	18 (10.8)	15 (83.3)	3 (16.7)	
No. previous urethroplasty (%):				
No	110 (65.9)	81 (73.6)	29 (26.4)	0.8082
Yes	57 (34.1)	46 (80.7)	11 (19.3)	
No. previous procedures (%):				
0	54 (32.3)	41 (75.9)	13 (24.1)	0.5218
1–5	89 (53.3)	60 (67.4)	29 (32.6)	

	Urethral/Penile Pain			p Value
	Overall	Yes	No	
Greater than 5	24 (14.4)	18 (75.0)	6 (25.0)	
Mean $\pm$ SD max flow (ml/sec):	–			
Preop		8.46 $\pm$ 6.77	8.41 $\pm$ 6.78	0.9678
Change		14.9 $\pm$ 12.6	14.8 $\pm$ 14.6	0.85

* Including hypertension, diabetes, coronary artery disease, peripheral vascular disease and chronic obstructive pulmonary disease.

Table 2

LUTP associations with other urological PROMs

	<u>Mean ± SD Urethral Pain</u>			<u>Mean ± SD Bladder Pain</u>		
	No	Yes	p Value	No	Yes	p Value
I-PSS:						
QOL	3.8 (1.28)	4.45 (1.24)	0.0001	4.09 (1.30)	4.49 (1.23)	0.0108
Total	14.9 (8.39)	20.61 (8.07)	<0.0001	16.07 (8.37)	22.91 (7.16)	<0.0001
MSHQ total	13.14 (5.89)	11.98 (5.61)	0.1394	13.29 (5.51)	11.06 (5.71)	0.0014
SHIM total	18.71 (7.39)	18.80 (6.57)	0.9271	19.07 (6.88)	18.47 (6.66)	0.4723
CLSS:						
QOL	4.04 (1.50)	4.90 (1.28)	<0.0001	4.37 (1.46)	5.02 (1.22)	<0.0001
Total	9.79 (5.04)	15.95 (5.52)	<0.0001	11.41 (4.96)	17.89 (5.37)	<0.0001