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PEYRONIE'S DISEASE

Outcomes of RestoreX Penile Traction Therapy in Men With Peyronie's Disease: Results From Open Label and Follow-up Phases

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ABSTRACT

Background: A randomized, controlled clinical trial evaluating the efficacy of RestoreX traction therapy in men with Peyronie's disease (PD) has been completed, with the 3-month results previously reported. The present study presents outcomes from the open-label and follow-up phases of the original trial.

Aim: To report 6-month (open-label phase) and 9-month (follow-up phase) outcomes from a randomized, controlled trial (NCT03389854).

Methods: A randomized controlled trial was performed from 2017 to 2019 in 110 all-comer men with PD. Men were randomized 3:1 to RestoreX (PTT) or no therapy (control) for 3 months, followed by 3-month open-label and follow-up phases. Key outcomes included adverse events (AEs), changes in penile curvature and length, erectile function, and standardized and nonstandardized assessments of PD.

Outcomes: The primary outcomes are safety, penile length, penile curvature, Peyronie's Disease Questionnaire, International Index of Erectile Function, and satisfaction.

Results: 6-month (n = 64) and 9-month (n = 63) outcomes were reported, with a mean duration of PTT use of 31.1 minutes. No significant AEs were reported, with temporary erythema and discomfort being most common and resolving within minutes. On intent-to-treat analysis, control-to-PTT men experienced significant length (1.7−2.0 cm) and curvature improvements (18−20%). PTT-to-PTT men also achieved additional length (0.6−0.8 cm) without further curvature improvements. An as-treated analysis of PTT use ≥15 minute/day demonstrated 2.0- to 2.3-cm length gains (largest of any PTT to date) and 18−21% curve improvement. All sexual function domains of the International Index of Erectile Function and Peyronie's Disease Questionnaire were significantly improved (except orgasmic domain). 95% of men treated for 6 months experienced length gains (mean 2.0−2.2 cm), and 61% had curve improvements (16.8−21.4° [32.8−35.8%]). RestoreX was preferred 3−4:1 over all other PD treatments, and 100% preferred it over other PTT devices.

Clinical Implications: Use of RestoreX 30 minutes daily results in significant length and curve improvements in PD men without significant AEs.

Strengths & Limitations: Strengths include largest randomized study of PTT, blinded assessments, and inclusion of all-comers with few restrictions; limitations include sample size that precludes comparisons between treatment cohorts and lack of long-duration (>3−9 hours) treatment arm.

Conclusion: PTT with RestoreX results in significant improvements in length, curve, and subjective and objective measures of sexual function without significant AEs. RestoreX PTT represents a safe, conservative, low-cost option for managing men with PD. **Joseph J, Ziegelmann M, Alom M, et al. Outcomes of RestoreX Penile Traction Therapy in Men With Peyronie's Disease: Results From Open Label and Follow-up Phases. J Sex Med 2020;17:2462−2471.**

Key Words: Traction; Peyronie's; Erectile Dysfunction; Hourglass

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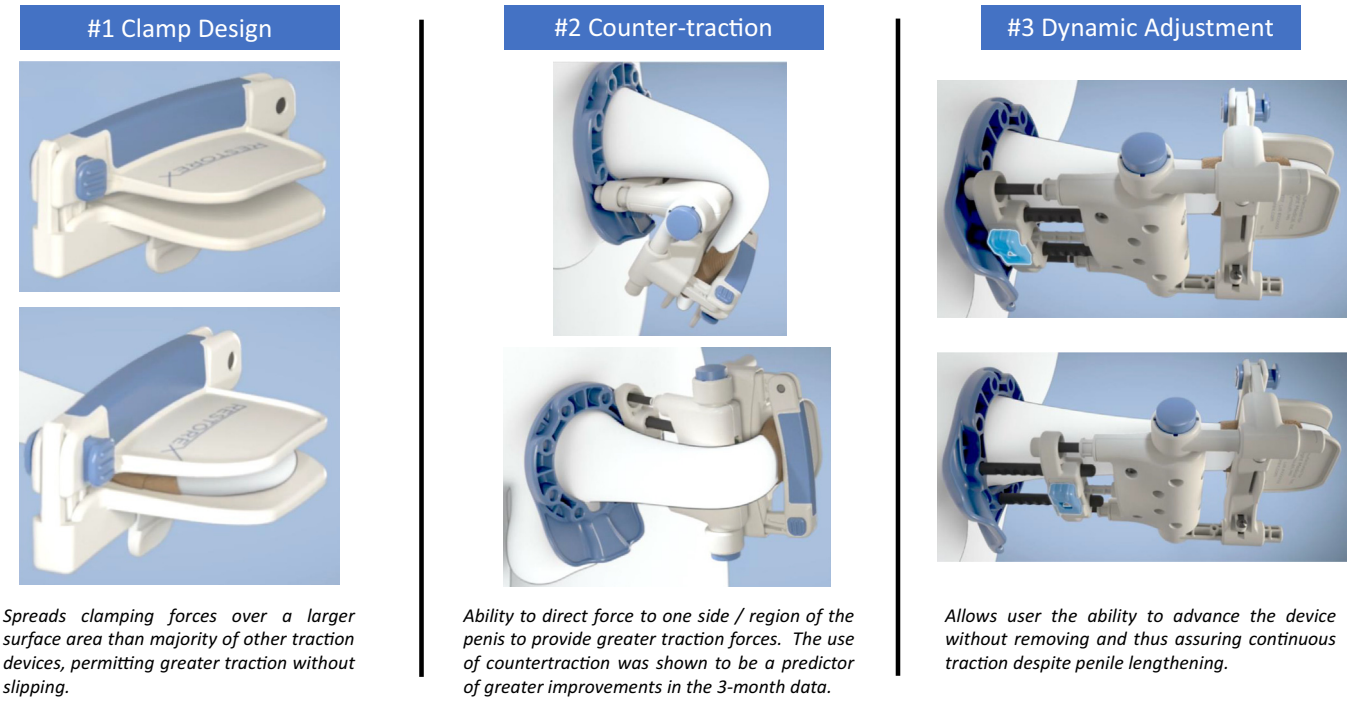

Figure 1. Figure demonstrating key differentiators from other traction devices.

INTRODUCTION

Penile traction therapy (PTT) represents a relatively newer class of treatments to restore length or correct deformities of the penis associated with various disease states, including Peyronie's disease (PD) and diabetes mellitus (DM), or after prostatectomy, among others. Since the initial publication on PTT in 2008, multiple traction devices have been developed that use similar mechanisms, whereby sequential rods are screwed into place to provide elongation of the penis. However, these first generation systems have several notable limitations, including minimal ability to extend when in use, difficulty in applying traction, pain, and other device issues that lessen the amount of force applied to the penis. Possibly due to these limitations, first generation of traction devices require 2−9 hours of daily use to achieve benefits, with available data demonstrating conflicting outcomes.[1−9] Given the extended treatment times required, many have questioned the clinical utility of such therapies, with actual utilization patterns suggesting only 9−56% of compliance with the recommended ≥3 hours of daily use.[6,8]

Given these limitations, a novel, second generation PTT device (RestoreX; PathRight Medical, Plymouth, MN) was developed with 3 notable innovations: (i) modified clamp design to allow for greater force displacement, (ii) counterbending to increase force to diseased segments, and (iii) dynamic adjustment to assure appropriate traction during a treatment session (Figure 1). To evaluate the safety and efficacy of the new device, a randomized controlled trial (RCT; NCT03389854) was performed in 110 men with PD, with the 3-month randomized phase previously reported.[10] Results demonstrated statistically significant improvements in length (94% with mean 1.6-cm gain), curve (77% of PTT men with mean 17.2° improvement), and sexual function (International Index of Erectile Function [IIEF]-erectile function domain, +4.3) among men treated with RestoreX compared with controls. In contrast to prior PTT devices, results were achieved after a mean 43 minutes of daily use, with both the counterbending and white-line indicator being validated as independent factors leading to improved outcomes.

Since the initial publication, additional data have been presented on the efficacy of RestoreX + collagenase clostridium histolyticum (CCH) compared with CCH + other PTT devices or CCH alone.[11] Results demonstrated that men treated with RestoreX + CCH were 3.5x more likely to achieve ≥50% curvature improvements and 10.7x more likely to experience ≥20% length improvements than the other groups, while other PTT + CCH achieved no significant benefits compared with CCH alone. Two additional RCTs are currently ongoing evaluating the efficacy of RestoreX PTT in men with DM and after prostatectomy (NCT03756688, NCT03500419).

The objective of the present study is to report outcomes from the open-label and 9-month follow-up phases of the initial RCT. Key outcomes evaluated during this phase include results of the control arm being newly treated with PTT, impact of 3 additional months of treatment in the original PTT arm, actual utilization during an open-label phase, and adverse events (AEs) at the 6- and 9-month time points.

METHODS

A randomized, single-blinded, controlled study was performed at the Mayo Clinic from October 2017 through May 2019 to

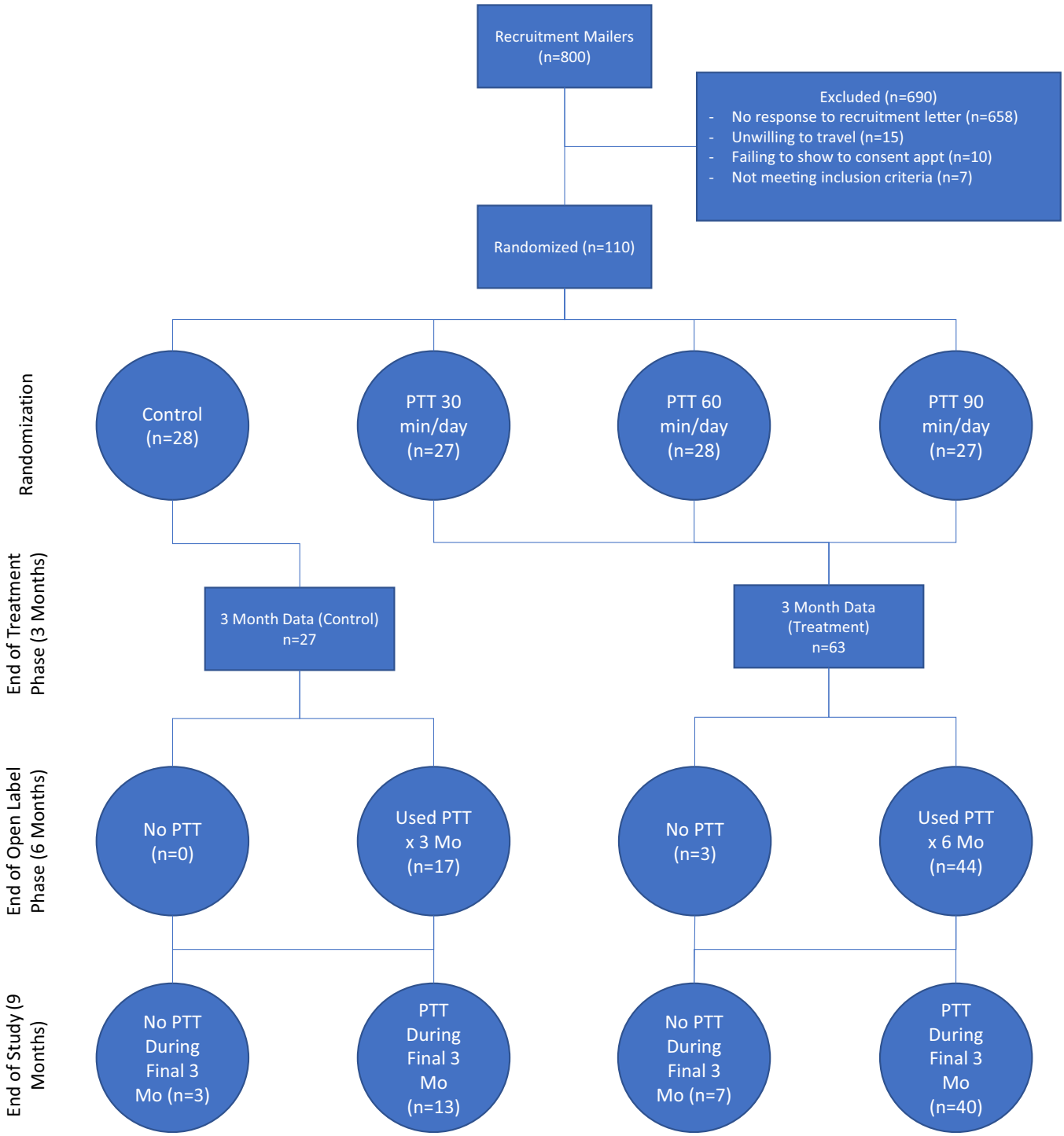

Figure 2. Diagram demonstrating patient flow from study recruitment through the end of 9-month follow-up phase. PTT = penile traction therapy.

evaluate the safety and efficacy of RestoreX in men with PD. All men with PD and aged ≥18 years were considered candidates, while those with <30°, stretched penile length <7 cm, DM with end-organ failure, or ED unresponsive to phosphodiesterase-5 inhibitors or penile injections were excluded. Those with complex deformities, calcification, hourglass deformity, or prior treatments were included to represent a more true-to-life sampling of men with PD. See Figure 2 for an enrollment flow diagram.

After enrollment, men were randomized 3:1 to treatment with RestoreX (30, 60, or 90 minutes daily) or control (no treatment) for a period of 3 months. Data from this phase have been

Table 1. Comparison of key outcomes from objective and standardized questionnaires from 3 to 6 months (open-label phase)

Variable	PTT to PTT, n = 63	*P* value[†]	Control to PTT, n = 27	*P* value[†]
Objective Measures				
Change in length	n = 47		n = 17	
To tip, mean cm (SE)	0.8 (0.2)	**<.0001**	1.7 (0.4)	**<.001**
To tip, mean %	5.0		11.1	
To corona, mean cm (SE)	0.6 (0.2)	**<.001**	2.0 (0.3)	**<.0001**
To corona, mean %	4.7		17.1	
Change in curvature	n = 47		n = 17	
Primary, mean degree (SE)	0.7 (1.6)	.54	−8.4 (2.9)	**.02**
Primary, mean %	1.9		18.4	
Composite, mean degree (SE)[‡]	−1.7 (2.0)	.51	−12.5 (4.6)	**.01**
Composite, mean %	−3.7		19.7	
Composite responder @ 6 months, %[§]	27.9, n = 43		17.6, n = 17	
Standardized questionnaires				
IIEF, positive denotes improvement, mean change from baseline (SE)	n = 59		n = 15	
EFD (all-comers)	+0.0 (1.0)	.67	+1.1 (0.8)	.21
EFD (baseline ED: IIEF-EFD ≤ 25)	+0.3 (1.7)	.76	+1.7 (1.3)	.22
OFD	+0.6 (0.3)	.05	+0.4 (0.4)	.50
SDD	+0.2 (0.2)	.41	+0.5 (0.3)	.17
ISD	−0.4 (0.4)	.54	+1.4 (1.0)	.13
OSD	+0.2 (0.2)	.44	+0.6 (0.4)	.16
SEP 2 (3 mo no, 6-month yes), %	0, n = 3		0, n = 2	NA[*,‖]
SEP 3 (3 mo no, 6-month yes), %	33.3, n = 3		0, n = 1	NA[*,‖]
PDQ	n = 40	.96	n = 16	
No. of vaginal intercourse in past 3 months	+0.2 (0.7)	.78	+3.2 (1.5)	**.03**
Psychological and physical domain, mean (SE)[¶]	−0.3 (0.5)	.99	−3.4 (1.5)	**<.05**
Penile pain, mean (SE)[¶]	+0.3 (0.4)	.52	−2.0 (0.9)	**.03**
Symptom bother, mean (SE)[¶]	−0.3 (0.5)		−1.9 (1.0)	.08
Q12, vaginal intercourse difficult/impossible, % that were "yes" at 3 mo and changed to "no" at 6 mo	60.0, n = 10		16.7, n = 6	.08[*,‖]
Q14, less frequent vaginal intercourse, % that were "yes" at 3 mo and changed to "no" at 6 mo	26.7, n = 15		14.3, n = 7	.51[*,‖]

Analyses performed using an intent-to-treat model.
Bolded *P*-values represent statistically significant results (<.05).
ED = erectile dysfunction; EFD = erectile function domain; IIEF = International Index of Erectile Function; ISD = intercourse satisfaction domain; OFD = orgasmic function domain; OSD = overall satisfaction domain; PDQ = Peyronie's Disease Questionnaire; PTT = penile traction therapy; SE = standard error; SDD = sexual desire domain; SEP = sexual encounter profile.
*Comparing between groups.
[†]Wilcoxon tests used for all statistical analyses unless otherwise indicated due to nonparametric nature of data; tests performed using matched pairs analysis.
[‡]Composite includes the summation of primary and secondary curvatures (if applicable).
[§]Composite responder defined as ≥20.0% improvement in penile curvature plus an improvement in the PDQ bother score of ≥1 or a change from reporting no sexual activity at screening to reporting sexual activity (consistent with phase III collagenase trials).
[‖]Likelihood ratio used to assess for significance.
[¶]Negative denotes an improvement.

reported previously, and greater detail on study methodology is reported therein.[10] Study participants then underwent an open-label phase for 3 months, where all groups were allowed to use the RestoreX device as much or as little as desired for 3 months. The treatment phase was then concluded, and men were then queried 3 months later (9 months since onset) for additional follow-up. Men were not requested to continue therapy during those final 3 months; however, they were also not prohibited from doing so. See Supplemental Figure 1 for an overview of study design.

Objective assessments were obtained at baseline and after the 3- and 6-month periods. All men underwent stretched penile length measurements (pubic symphysis to corona and tip of the glans penis) by the same provider (where possible) who was blinded to prior results and device usage. Curvature assessments were performed after repeated dosing of erectogenic medication (Trimix) to achieve a penetration-quality erection. Photographs were obtained by professional, surgical photographers in 2 planes, and measurements were then performed using a goniometer in a blinded manner. In cases where patients refused office photography, curvature assessments were performed by 2 care providers who were blinded to prior results and who had obtained measurements on the patient previously. If 2 directions of curvature were observed (eg, dorsal and lateral), the 2 were summed together and reported as the "composite" curvature as has previously been reported.[12]

Questionnaires included the IIEF, Peyronie's Disease Questionnaire (PDQ), Sexual Encounter Profile (SEP) questions 2 and 3, AEs, and other nonvalidated subjective preference questions using Likert scales.

The primary outcome of the study was safety, and secondary outcomes included changes in penile curvature and length, differences in IIEF and PDQ subdomains, overall satisfaction, satisfaction comparison to other devices, ability to penetrate, and avoidance of surgery and other therapies. Data from the 3-month phase were reported using an intent-to-treat analysis, while data from the 6-month and 9-month time points are presented using both intent-to-treat and as-treated analyses.

Statistical comparisons were performed using JMP 14.2.0 (SAS Institute, Minneapolis, MN). Parametric data were reported as means and standard deviations, while nonparametric data were reported as medians and ranges. Statistical tests included Student's *t*-test, Wilcoxon Rank Sum, Fisher's Exact, Pearson, and Likelihood ratios, where appropriate. Two-tailed *P* values of $<.05$ were considered statistically significant.

RESULTS

A total of 110 men were randomized to control (n = 28) or PTT (n = 82), with 3-month data available on 90 (control 27, PTT 63), 6-month data on 64 (original controls 17, original PTT 47), and 9-month data on 63 (original controls 16, original PTT 47). Detailed demographic data and 3-month outcomes have been presented previously.[10] Of note, 3 of 110 (3%) men were within the first 3 months of disease onset (acute phase), while the remainder would be classified as chronic phase. The average duration of device use at 6 months was 31.1 minutes per day (standard deviation 16.3).

Key outcomes from the 3- to 6-month open-label phase are presented in Table 1 using an intent-to-treat (all-comers, regardless of device use) analysis. Results demonstrated that among men who previously were in the PTT randomized group, the additional 3 months of treatment led to further significant length gains (+0.6 to +0.8 cm), while those who were previously in the control group achieved a +1.7- to +2.0-cm length gain. In contrast, those who were previously treated with PTT for 3 months did not achieve further statistically significant curvature improvements from 3 to 6 months, while those in the control group achieved similar improvements to those observed in the PTT group during the 0- to 3-month time point (primary curve −8.4° [18%], composite curve −12.5° [19.7%]). Outcomes from questionnaires demonstrated nonstatistically significant improvements in most IIEF subdomains, although the number of men in the original control arm was small (n = 15). Similarly, the number of men who originally responded "no" to the SEP-2 and SEP-3 questions were too small to provide reliable data (n = 1−3). Among men who were originally controls, results from the open-label phase PDQ domains demonstrated a statistically significant increase in number of vaginal intercourse attempts at 3 months and improvements in the psychological and penile pain domains, with nonstatistically significant improvements in the bother domain ($P = .08$). For those who were previously in the PTT group, no additional improvements were identified beyond those achieved at 3 months in any of the PDQ domain scores.

Data were also analyzed using an as-treated analysis, with men who performed an average of at least 15 minutes of PTT daily during the most recent 3 months included for analysis (Table 2). Results demonstrated stretched length improvements (corona) of +2.0 to +2.3 cm and composite curve improvements of −12.5 to −14.9 (18−21%). The percentage of "composite" responders ranged from 21 to 34% and was defined as a ≥20% curvature improvement along with a ≥1 point improvement in bother or return of sexual activity. All domains of the IIEF were statistically improved, with the exception of the orgasmic function domain which was not significant when analyzed using an as-treated model but was significant when additional patients were all-comers and were included at 6 months (Table 2, Supplemental Figure 2). The percentage of men responding yes to SEP-2 and SEP-3 after an initial "no" at baseline was 38% and 44%, respectively. All PDQ domains were also significantly improved compared to baseline, and a total of 45% and 42% of men indicated that vaginal intercourse was no longer difficult/impossible or that the PD resulted in less frequent vaginal intercourse than baseline, respectively.

Among men who used traction for ≥15 minutes daily for 6 months (original PTT, n = 37, as-treated analysis), 95% experienced length gains and 61% curvature improvements. Those with improvements had an average length gain of +2.2 cm to the tip or +2.0 cm to the corona and −16.8° (35.8%, primary curvature) or −21.4° (32.8%, composite curvature).

Subjective responses to nonvalidated questionnaires are presented in Table 3 and demonstrate that most men felt that PTT resulted in a meaningful improvement (84%), improved erectile

function (78%), and improved ability to penetrate (86%). Other key measures included 50% who reported restored or facilitated penetration, 84% who continued to use at 9 months, 59% with improvements in indentation/hourglass deformity, and 63% who felt that ongoing use led to further curve and length improvements at 9 months.

Table 4 highlights reported AEs at 6 and 9 months. The most commonly reported symptoms included temporary penile erythema or discoloration (35% at 6 months, 4% at 9 months) and mild, temporary penile discomfort (27% at 6 months, 4% at 9 months). Although 30% of men reported loss of or abnormal penile sensation at baseline, an additional 5% noted transient decreased sensation at

Table 2. Comparison of key outcomes from objective and standardized questionnaires from 0 to 6 months using an as-treated analysis

Variable	Total cohort, n = 51	*P* value[†]	Original PTT, n = 37	Original control, n = 14	*P* value*
Objective measures					
Change in length					
To tip, mean cm (SE or SD)	1.8 (0.2)	**<.0001**	1.9 (1.3)	1.6 (1.2)	.40
To tip, mean %	12.1		13.2	10.7	
To corona, mean cm (SE or SD)	2.0 (0.2)	**<.0001**	2.0 (1.1)	2.3 (2.0)	.90
To corona, mean %	17.2		17.7	19.5	
Change in curvature					
Primary, mean degree (SE or SD)	−9.0 (1.8)	**<.0001**	−8.9 (14.5)	−9.3 (7.9)	.76
Primary, mean %	−20.0		18	22	
Composite, mean degree (SE or SD)[‡]	−14.3 (2.6)	**<.0001**	−14.9 (18.1)	−12.5 (18.6)	.64
Composite, mean %	−23.6		21.4	18.2	
Composite responder @ 6 months, %[§]	30.4, n = 46		34.4	21.4	.37[‖]
Standardized questionnaires					
IIEF, positive denotes improvement, mean change from baseline (SE or SD)					
EFD (all-comers)	+3.8 (1.0)	**.0001**	+4.4 (7.4)	+1.8 (4.4)	.66
EFD (baseline ED: IIEF-EFD ≤ 25)	+6.4 (1.4)	**.0001**	+7.7 (7.8)	+2.4 (5.2)	.20
OFD	+0.7 (0.4)	.11	+0.7 (3.0)	+0.7 (2.1)	.93
SDD	+0.7 (0.2)	**<.01**	+0.8 (1.6)	+0.4 (2.1)	.38
ISD	+1.6 (0.4)	**<.0001**	+1.9 (2.8)	+0.6 (2.7)	.40
OSD	+0.6 (0.3)	**<.05**	+0.8 (1.9)	+0.3 (2.7)	.69
SEP 2 (baseline no, 6-month yes), %	37.5, n = 8		50.0, n = 6	0, n = 2	.13*,[‖]
SEP 3 (baseline no, 6-month yes), %	44.4, n = 9		42.9, n = 7	50.0, n = 2	.86*,[‖]
PDQ		.36			
No. vaginal intercourse in past 3 months	+1.0 (1.0)	**<.01**	+0.6 (5.5)	+2.3 (8.6)	.66
Psychological and physical domain, mean (SE or SD)[¶]	−2.9 (1.0)	**<.01**	−2.4 (5.2)	−4.0 (7.6)	.72
Penile pain, mean (SE or SD)[¶]	−2.2 (0.6)	**.0001**	−2.0 (3.3)	−2.7 (5.3)	.94
Symptom bother, mean (SE or SD)[¶]	−2.7 (0.6)		−3.0 (3.7)	−2.0 (4.6)	.58
Q12, vaginal intercourse difficult/impossible, % "yes" at baseline and changed to "no" at 6 mo	45.0, n = 20		57.1, n = 14	16.7, n = 6	.08*,[‖]
Q14, less frequent vaginal intercourse, % "yes" at baseline and changed to "no" at 6 mo	42.3, n = 26		43.8, n = 16	40.0, n = 10	.85*,[‖]

Analyses performed using an as-treated model of men using device an average of 15 min/d or more during final 3 mo.
Bolded *P*-values represent statistically significant results (<.05).
ED = erectile dysfunction; EFD = erectile function domain; IIEF = International Index of Erectile Function; ISD = intercourse satisfaction domain; OFD = orgasmic function domain; OSD = overall satisfaction domain; PDQ = Peyronie's Disease Questionnaire; PTT = penile traction therapy; SDD = sexual desire domain; SE = standard error; SEP = sexual encounter profile.
*Comparing between groups.
[†]Wilcoxon tests used for all statistical analyses unless otherwise indicated because of nonparametric nature of data; tests performed using matched pairs analysis.
[‡]Composite includes the summation of primary and secondary curvatures (if applicable).
[§]Composite responder defined as ≥20.0% improvement in penile curvature plus an improvement in the PDQ bother score of ≥1 or a change from reporting no sexual activity at screening to reporting sexual activity (consistent with phase III collagenase trials).
[‖]Likelihood ratio used to assess for significance.
[¶]Negative denotes an improvement.

Table 3. Subjective outcomes of men at 6 and 9 months

Variable, % unless otherwise indicated	Total cohort
6-month outcomes, n = 64	
Has the therapy resulted in a meaningful improvement for you?	
Yes	84
No	16
Did the therapy restore your ability to penetrate?	
Yes or easier now	50
No	13
Always could penetrate	37
Did the therapy prevent you from needing surgery?	
Yes	20
No	6
Would never have done surgery	47
Not sure	27
Did the therapy prevent you from needing additional treatments?	
Yes	36
No	11
Not sure	53
9-month outcomes, n = 63	
Continued to use device at 9 mo	84
Median ongoing daily use, min	21.4
Improvement in penile deformity (indentation, hourglass)	59
Mild improvement	25
Moderate improvement	33
Significant improvement	42
Additional benefits noted from 6 to 9 mo	
Curve	15
Length	10
Curve and length	63
Neither curve nor length	12
Improved erectile function	78
Improved ability to penetrate	86
SEP 2, restored ability to penetrate (no at baseline, yes at 9 months)	44
SEP 3, restored erection duration (no at baseline, yes at 9 months)	44

Analyses performed using all data points with no exclusions.
SEP = sexual encounter profile question.

the 6-month time point and 0% at 9 months. Notably, no patients discontinued therapy because of AEs.

Subset analyses were performed of men with varying baseline erectile function using both intent-to-treat (all-comers) and as-treated analyses and demonstrated statistically significant improvements among all categories of baseline ED, with the exception of the intent-to-treat group with moderate ED (Supplemental Figure 3). Clinically meaningful improvements in the IIEF-erectile function domain were also assessed based on the widely accepted criteria of 4-point improvement overall, 2 points among men with mild ED, 5 points with moderate ED, and 7 points with severe ED.[13] Results showed that most men overall achieved clinically meaningful improvements (61% [intent-to-treat] or 67% [as-treated]), with moderate ED exhibiting the largest improvement (71% [intent-to-treat] and 100% [as-treated]) and severe ED the lowest (40% [intent-to-treat] or 56% [as-treated]). When analyzing differences between intent-to-treat and as-treated analyses, only moderate ED demonstrated statistical significance, although comparisons are of limited value given the small overall numbers assessed.

Patient preference outcomes between PD therapies are displayed in Supplemental Figure 5. To assess preferences, participants were asked, "knowing what you know now about Peyronie's Disease, if you were being treated for the first time, which therapy would be your preferred treatment?" (Supplemental Figure 5A). Results demonstrated that at baseline, most men would select traction (45%), followed by CCH (21%) and oral treatments (17%). At the 3-month, posttreatment time point, the numbers changed to RestoreX (74%), CCH (24%), and oral therapies (15%), with 6% choosing a vacuum device, 2% surgery, and 0% another device for PTT. Findings continued to increase at 6 months, where 81% preferred RestoreX, followed by CCH (17%) and oral therapies (12%), with other PTT devices remaining 0%. Similarly, when queried on level of satisfaction (Supplemental Figure 5B), 77% were very or somewhat satisfied with RestoreX, while 20% were neutral and 3% dissatisfied. To assess comparative device preferences, men who had previously used other devices were asked which device they preferred. Results demonstrated that 100% of men preferred RestoreX to the other devices (Supplemental Figure 5C), which included Andropenis (Madrid, Spain), X4 labs (Vaudreuil-Dorion, Canada), Phallosan Forte (Lichtenstein), Penimaster (Berlin, Germany), Hydromax (West Yorkshire, UK), and Size Genetics (Lyngby, Denmark).

DISCUSSION

The present study demonstrates several notable findings with the RestoreX PTT device and further supports results from the 3-month randomized phase. Specifically, PD men who were originally controls (control to PTT) exhibited statistically significant improvements in penile length, curvature, psychological and pain aspects of PD, and an increase in the number of vaginal intercourse attempts. When combined with men in the PTT arm using an intent-to-treat analysis, significant improvements were noted in all IIEF domains, including erectile function, sexual desire, intercourse satisfaction, overall sexual satisfaction, and orgasmic function. Erectile function improvements met the criteria for being clinically significant in most men, and length improvements were larger than any previously reported ones with any mechanical device.[1,2,7,9,14] These findings are particularly notable given that RestoreX is the only mechanical device shown to achieve improvements with an average of 30 minutes of daily use compared with the 2 to 9 hours daily required with alternatives.[1,2,7,9] Although the exact mechanism for the more efficient improvements is not well studied, results may be

Table 4. Adverse events reported at baseline, 6 mo, and 9 mo among men treated with traction therapy

Adverse event, %	Baseline, n = 81	6 months, n = 63	9 months, n = 57
Penile erythema or discoloration, transient	9	35	4
Loss or abnormal penile sensation (new onset and transient for 6- and 9-mo cohorts)	30	5	0
New cold glans, transient	NA	0	0
New penile discomfort, transient	NA		
Mild		27	4
Moderate		0	0
Severe		0	0
New bump	NA	0	0
New penile swelling	NA	0	0
New penile curvature		0	0

All de-novo symptoms were mild and resolved within minutes of completion of daily therapy. No adverse effects led to study withdrawal or therapy discontinuation.

attributable to the novel device changes that permit greater and more sustained traction forces than other designs (Figure 1).

Subjective outcomes also support the objective and standardized assessments, as 84% of men felt that improvements were meaningful and continued to use the device at 9 months despite an end to the treatment phase at 6 months. Most men also felt that the treatment improved their erectile function (78%) and ability to penetrate (86%).

Other notable findings included an ongoing improvement in penile length from 3 to 6 months among men who were originally in the PTT arm, although the rate of increase was slower than that achieved during the initial 3 months of treatment. These findings are also consistent with 9-month surveys, during which 73% of men who continued to use the device felt that it resulted in additional length improvements during the 6- to 9-month time point. In contrast, the impact of ongoing traction on further curvature improvements is equivocal. The 3- to 6-month objective length data among men originally in the PTT arm failed to demonstrate any additional statistically significant improvements beyond what had already been achieved by 3 months. However, subjectively, 78% of men who continued to use the device at 9 months reported further curvature improvements during the 6- to 9-month time point. These data overall suggest that ongoing use of the RestoreX device results in continued improvements in length over time, while the benefits on curvature are unclear.

To our knowledge, the present study is one of the few to report outcomes of any mechanical therapy on penile indentation or hourglass deformity.[1] These impairments can be particularly impactful for men with PD, as they often exacerbate penile instability, decrease girth, and can further impair erectile function. Of those with subjectively reported baseline indentation or hourglass, 59% felt that traction therapy improved outcomes, with 25% noting mild, 33% moderate, and 42% significant improvements. These findings are notable, in that there are currently no conservative therapies that have demonstrated consistent improvements in this difficult-to-treat subset. The mechanism for improvements on hourglass deformity may be similar to those suggested for traction on penile curvature, including mechanotransduction on the extracellular matrix, apoptosis, and cellular proliferation.[15,16] Limited data on the impact of traction therapy on Dupuytren's contracture (similar disease process to PD) demonstrate improvements in fibrous nodules via remodeling of collagen.[17] Similarly, in vitro data of PD plaques show reduced myofibroblast activity and increased matrix metalloproteinases, both of which provide a potential mechanism for observed improvements clinically.[18–21]

The overall study findings of improved erectile function are surprising and consistent with those observed during the 3-month randomized phase.[10] Statistically significant improvements were noted among all categories of men with ED, including mild, moderate, and severe, and findings achieved the minimal clinically significant threshold in 61% (intent-to-treat) to 67% (as-treated) of men overall. Although the underlying mechanism for these findings is unclear, it may relate to increased release of nitric oxide from penile endothelial cells exposed to mechanical shear forces, as demonstrated in animal models and human vascular studies.[22,23] Improvements noted in the other IIEF domains were also notable and may relate to curvature correction, length increases, or other aspects of improved PD. However, without an appropriate sham device, it is not possible to know if these improvements can be wholly attributed to device use vs psychological effects. Further follow-up studies are required to better evaluate these findings.

Several other studies have evaluated the efficacy of other, first generation PTT systems (X4 labs, Andropenis, Penimaster Pro) with mixed results. Two early studies of PTT (n = 25 combined) each demonstrated minor improvements in length (+0.8 to +1.0 cm) without any improvements in curvature despite a mean 5–6 hours of daily use.[1,2] A larger, prospective, open-labeled study demonstrated improvements in curve and length in PD men in the acute phase of disease; however, no significant benefits were

noted among those >3 months out from disease onset.[7] More recently, a randomized, controlled trial was reported and demonstrated both length and curvature improvements, with AEs reported in 43% of cases (6% required study discontinuation).[9] The study has several notable limitations, including a lack of trial registration, lack of intent-to-treat analyses, missing key outcome data (eg, control group outcomes), lack of comparison between groups (only comparing to baseline), and multiple exclusions (eg, hourglass, curvature < 45°, multiplanar curvatures, prior intralesional therapies, noncompliance with ≥3 hours daily use). These exclusions are particularly notable as they would have resulted in exclusion of 90% of the present study cohort and are not reflective of contemporary practice. Similarly, compliance with ≥3 hours daily use was reported at 96%, which is in contrast to other reported series of 9−56%.[6,8]

Relatively limited data are available comparing outcomes between first generation devices and RestoreX. In the only relevant study published to date, outcomes were compared among those doing CCH alone, CCH + first generation traction devices, and CCH + RestoreX.[11] Results demonstrated no added benefits of CCH + first generation traction devices compared with CCH alone (even among subset analyses of those using ≥3 hours daily), while CCH + RestoreX men were 10.7x more likely to achieve ≥20% length gain and 3.5x more likely to have ≥50% curve improvements.

From a clinical standpoint, results from the present study would suggest that the greatest improvements occur during the first 3 months, with additional length gains achievable with ongoing use. In contrast, no additional curvature improvements were noted beyond 3 months. Although further study is required to determine benefits with longer term use on penile curvature, data from the present study suggest that additional changes would likely be very slow, if at all. Based on the preliminary nature of the current data, the use of RestoreX as a primary therapy for hourglass deformity or erectile dysfunction requires further study and validation before routine implementation.

The present study has a few limitations, including a limited sample size which does not allow for comparisons among subgroups, single center, inclusion of only men with PD, and lack of a ≥3−9 hours daily treatment arm. Although providers who assessed penile curvature using photographs were blinded to patient classification (PTT vs control), they were not blinded to time point. This may have introduced some degree of bias at the 6-month (post open label) time point but would not have expected to impact 3-month results (blinded to grouping). Similarly, as patients had received a RestoreX device at no charge in the study, this may have potentially impacted their overall comparative preference for RestoreX over other units. The percentage of patients who reported ongoing length and curvature improvements in the 6- to 9-month period may also be biased, as only men who elected to continue to use the device responded to the question. Other subjective questions, such as preferred first-line therapy, are also limited by their nonstandardized nature and lack of experience with all available treatments. However, the study has several strengths, including being the largest randomized, controlled trial on PTT to date, use of both photography and blinded curvature assessments for key outcomes, use of standardized instruments and questionnaires, and inclusion of all-comer PD men.

CONCLUSIONS

PTT with RestoreX results in significant subjective and objective improvements in penile length, curvature, and standardized assessments of erectile and sexual function. Patients in the present study preferred RestoreX PTT to all other PD treatment by 4:1. In contrast to other PTT devices that require 2−9 hours of daily use and are therefore of limited clinical utility, RestoreX achieves improvements in approximately 30 minutes per day. Although not all men who use RestoreX experience benefits, given the low cost and lack of significant AEs, these findings represent a notable paradigm shift in the role for PTT in managing men with PD.

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Conflict of Interest: Landon Trost is the inventor of the RestoreX device. This conflict has been reviewed with the Mayo Clinic Conflict of Interest Board. Landon Trost was given the option of either investing in the company or doing research on the device, and he elected to pursue research. This was felt to be an acceptable level of conflict by the board.

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STATEMENT OF AUTHORSHIP

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jsxm.2020.10.003.