

Extracorporeal Shockwave Therapy for Peyronie's Disease: Who Benefits?*

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ABSTRACT

Background and Purpose: Extracorporeal shockwave therapy (ESWT) has been reported to improve the symptoms of Peyronie's disease. However, the response rates to this treatment appear to be variable. This study aimed to determine whether any patient or plaque characteristics are associated with a better outcome.

Patients and Methods: A series of 36 patients with Peyronie's disease received ESWT as a primary treatment. Subjective response rates were compared on the basis of patient age, degree of pretreatment penile curvature, predisposing medical factors, duration of disease, and extent of plaque calcification.

Results: Ten men (27.8%) reported subjective improvements in curvature after ESWT. Of the factors considered, only age and pretreatment curvature influenced outcomes: 50% of the men below the mean age reported improvement compared with 5.6% of older men and 62.5% of men with mild curvature reported improvement compared with 8.3% of those with severe curvature.

Conclusion: The response to ESWT is not the same for all men with Peyronie's disease. Younger men and those with milder curvature have the best outcomes.

INTRODUCTION

PEYRONIE'S DISEASE (PD) is a benign affliction of the penis that typically affects middle-aged men. A recent study has suggested a prevalence rate as high as 8.9%.¹ The disease causes localized fibrosis of the tunica albuginea of the corpus cavernosa, leading to the characteristic symptoms of pain, penile curvature, and erectile dysfunction.² The fibrotic plaque is usually easily identifiable on palpation. As the etiology is unknown, current treatments are aimed at symptomatic improvement. Surgical interventions to straighten the penis have been the mainstay.³ However, these procedures have significant risks, such as penile shortening, reduced sensation, and impotence.⁴ Consequently, a wide range of conservative therapies have been proposed, including radiation;⁵ oral drugs such as Potaba,⁶ tamoxifen,⁷ colchicine,⁸ and vitamin E;⁹ and intraleisional injections of verapamil¹⁰ and interferon.¹¹ Extracorporeal shockwave therapy (ESWT) has been used since the 1980s and has shown some promising results.^{12,13}

Although there appears to be an overall benefit from ESWT, some studies have noticed significant variations in response. For example, Hauck and associates¹⁴ found no improvement in their group as a whole but noticed a "remarkable decrease in

curvature" in 30% of their patients. Manikandan and colleagues¹⁵ found that although 14% of their patients reported excellent results and 50% significant improvements, the remainder saw little or no benefit. The reasons for this variable response are not clear. This pilot study was designed to identify any patient or plaque characteristics that may influence treatment response.

PATIENTS AND METHODS

Patients seeking treatment for penile curvature secondary to PD were offered ESWT as a primary treatment of their condition. Men with significant erectile dysfunction not responsive to medical management were excluded. Prior to treatment, patients were asked about disease duration, pain on erection, and the presence of any possible associated or predisposing factors, such as a history of trauma, Dupuytren's contracture, family history, or diabetes.^{16,17} The degree of penile curvature was assessed visually by patients during a normal erection and was categorized as suggested by Kelami¹⁸ into mild (<30°), moderate (30–60°), or severe (>60°).

Treatment consisted of three sessions at monthly intervals.

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TABLE 1. PROPORTIONS OF MEN REPORTING IMPROVEMENT IN PENILE CURVATURE AFTER ESWT IN RELATION TO PRETREATMENT VARIABLES

	No. (%) Improved
Curvature	
<30°	5/8 (62.5) ^a
30–60°	4/16 (25.0)
60°	1/12 (8.2)
Duration of disease (mos)	
<12	3/16 (18.8)
>12	7/20 (35.0)
Predisposing medical history	
Yes	2/7 (28.6)
No	8/28 (28.6)
Age	
<55 years	9/18 (50.0) ^b
>55 years	1/18 (5.6)
Plaque calcification	
Yes	9/27 (33.3)
No	1/9 (11.1)

^aDifference among groups is significant at $P < 0.05$ (χ^2 test).

^bDifference between groups is significant at $P < 0.005$ (χ^2 test).

At each session, 3500 shockwaves were administered at 2 to 4 Hz and power setting 4 or 5 (0.11–0.17 mJ/mm²) using a Storz Minilith SL1 lithotripter. The plaque was localized by ultrasound prior to treatment, and details of the location and shape of the plaque and the presence of calcification were recorded.

A total of 36 patients have completed treatment with the minimum follow-up (mean follow-up 9.8 months). Their mean age was 55 years (range 34–74 years). Sixteen (44%) had had their disease for <12 months, 15 (42%) for 1 to 2 years, and the remaining 5 (14%) for between 2 and 5 years.

Follow-up was by postal questionnaire a minimum of 6 months after the last session. The questionnaire asked if patients had seen a significant improvement in curvature or pain and whether their sexual function had changed (worse, little worse, same, little better, lot better). Partners were also asked to rate the sexual function using the same scale. Overall levels of satisfaction with sex life were recorded.

Non-parametric statistical tests (chi-square, Spearman's rank correlation) were performed using SPSS for Windows V. 10.1. Patient age and sexual function were dichotomized for statistical analysis.

RESULTS

Only seven men gave a history of possible predisposing factors (one each of diabetes, trauma, and Dupuytren's contracture; two each of previous surgery or multiple factors). Plaque location was mainly dorsal (78%) and in the proximal two-thirds of the penis (83%). Eight had curvature <30°, 16 had curvature between 31 and 60°, and 12 had curvature >60°. Twenty-seven men (75%) had calcified plaques.

Overall, 10 of the 36 men (27.8%) reported an improvement in penile curvature after treatment. Improvement in curvature and an improvement in sex life were strongly correlated ($r =$

0.766; $P < 0.001$). There was good agreement between patients and their partners regarding change in sexual function ($r = 0.803$; $P < 0.001$).

Of the factors considered, only age and degree of pretreatment curvature influenced the outcome (Table 1). Men below the mean age of the group had a significantly better response rates than men older than this (50% v 5.6%; $P = 0.003$). Those with initial curvature <30° had a response rate more than seven times that of men with curvature >60° (62.5% compared with 8.3%). Mean age did not differ between these groups. All men who had an initial curvature <30° and were younger than 56 reported improvement. In contrast, none of the men who had curvature >30° and were 56 or older reported an improvement (Table 2). The effect of changing the age cut-off on the proportion of treatment responders is shown in Figure 1, which indicates that the greatest chance of success was seen in those under the age of 50.

DISCUSSION

Most prior studies of ESWT in PD have reported reduction in curvature. The effect on sexual function is less clear and often is poorly described. The few studies that have reported on the effects of ESWT on penile rigidity have failed to find a difference.^{14,19,20} Given the availability and efficacy²¹ of medical therapies for ED, it is our practice to offer these methods to men with combined PD and erectile dysfunction prior to considering ESWT. Those who show a good response and achieve near-normal penile rigidity are offered ESWT. Those who fail medical therapy are offered a penile prosthesis as a first-choice treatment.²² As a consequence, penile curvature was the main complaint of men entering this study and also our main outcome measure. Although we collected data relating to improvements in sexual function, this correlated strongly with improvements in curvature and so is not reported separately. This correlation is not surprising, as any residual sexual dysfunction in the study group was secondary to penile curvature.

There has been no uniform means of assessing penile curvature in trials of ESWT. Techniques have included artificial erection, photographs, and questionnaires. It has been suggested that pretreatment and post-treatment measurements of an artificial erection provide the best objective measure of changing curvature.¹⁹ Although we acknowledge the value of objective assessments in a trial setting, we have taken a more pragmatic approach. For a treatment to be clinically useful, it is essential that the patient regard it as a success. Although objective measures may demonstrate statistically significant changes, they are irrelevant unless accompanied by a patient's subjective feeling

TABLE 2. INTERACTION BETWEEN AGE AND DEGREE OF PRETREATMENT CURVATURE

	Amount of curvature (no. [%] of patients)		
	≤30	>30	Total
≤55 years	4/4 (100)	5/15 (35.7)	9/18 (50)
>55 years	1/4 (25)	0/14	1/18 (5.6)
Total	5/8 (62.5)	5/28 (17.9)	10/36 (27.8)

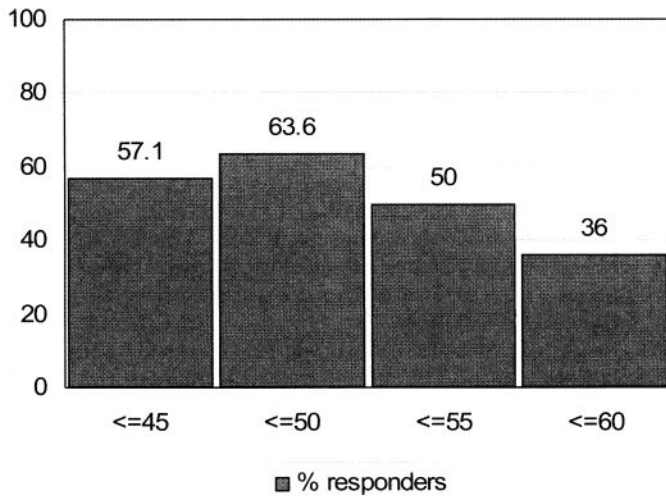


FIG. 1. Effect of age on proportion of men responding to ESWT for PD. Graph shows number of men under each age limit who reported improvement after treatment.

of improvement. We have chosen, therefore, to concentrate on the patients' subjective feeling of improvement, as we feel this best reflects the real-world efficacy of the treatment. Similarly, the degree of curvature was assessed by the patient under normal circumstances rather than using artificial erection. It is possible that these men may not normally achieve the degree of tumescence created with an artificial erection, so the latter type of assessment may not reflect their normal situation.

Overall, 28% of the men in our study reported a significant improvement in penile curvature. The response rate was not influenced by the presence of plaque calcification, duration of disease, or predisposing medical conditions. However, both age and the degree of initial curvature had an effect on outcome. A greater proportion of younger men and those with lesser curvature reported improvement compared with older men and men with more severe curvature.

The proportion of men in our study reporting an improvement in curvature is within the range seen in other studies, which is 21% to 74%.²³ Patient selection, treatment regimens, outcome assessments, and follow-up periods differed in nearly all of these studies. As such, any direct comparisons are difficult, and the differences may explain some of the significant variation in reported success rates.

Few studies have attempted to assess outcomes within patient subcategories. It has been suggested that ESWT is ineffective in reducing curvature for those in the acute phase of PD.²⁴ In our series, 18.8% of those with disease duration <12 months reported improvement compared with 35% of those with disease duration >12 months. This difference was not statistically significant. Husain and associates²⁵ also compared outcomes for those with disease durations of greater or less than 12 months. As with our study, the level of improvement was greater in those with PD for >12 months, but the difference did not reach statistical significance. Despite this, there does appear to be a trend for those in the acute phase to do less well with ESWT. This finding contrasts with the effect of most other conservative treatments for PD, which are usually recommended in the acute phase.²⁶ However, no study so far has been

sufficiently powered to permit any definitive statement about the effect of disease duration.

Hauck et al.¹⁴ considered pretreatment curvature in their results. Although they found no improvement in their overall study population, there was a statistically significant decrease in curvature, from 45.7° to 38.5°, in those whose initial curvature was between 31° and 60°. Those authors raise the issue of whether this would be a clinically appreciable improvement but do not record any subjective assessments. In contrast, we found milder degrees of curvature to be associated with better outcome by subjective assessment. This effect was independent of any other patient characteristics. No other report of ESWT has considered the effect of curvature on response, but Kadioglu and colleagues⁸ also found better response rates in those with curvature <30° when using oral colchicine. It is possible that some of this is perceptual rather than a true difference in response, as a given amount of improvement in curvature is likely to be more noticeable, and have a greater impact, in those with mild curvature than in those with severe curvature.

To date, no other studies have considered the effect of patient age on treatment response, yet we found this factor to be the most significant influence on the outcome, with rates of improvement around 10-fold greater in younger patients. Despite our relatively small numbers, retrospective power calculations show an 88% chance that this is a true difference at the 5% significance level. Although the actual mechanism of action of ESWT remains unclear, there is some evidence that it stimulates vascularization and improves healing.²⁷ These processes may be impaired with increasing age, leading to the difference in response. Also, recent evidence indicates that older men have lower latent collagenase levels within the tunica albuginea,²⁸ suggesting impaired ability to break down the fibrous plaque. Studies of the natural history of PD provide some support for this idea. Kadioglu et al found that among 307 men with a mean age of 53, 30.2% worsened, 66.7% remained stable, and only 3.2% improved.² In contrast, Tefekli and coworkers²⁹ found an improvement in 36.8% of men under 40, with only 21% showing deterioration and 42.1% remaining stable. The better response rates in younger men may simply be a reflection of the greater tendency to resolution in this group. It may be that the factors that bring about a greater likelihood of spontaneous improvement are also involved in the better response to treatment.

As with the majority of studies looking at ESWT for PD, our study may be criticized for the absence of a separate control group. This is largely because of the difficulties in recruiting to such a group. However, this lack is less significant in a comparative study, such as this, than in one attempting to establish absolute response rates. As the groups being compared are well matched except for the factor under consideration, they effectively act as controls for each other.

This pilot study is the first to consider the effect of patient characteristics on the response to ESWT in men with PD. Our results suggest that younger men with milder disease appear to be the best candidates for this treatment. However, the numbers in this initial study are still quite small, and further work will be required to clarify the exact nature of these variations in response. It is likely that this question will need to be investigated in the setting of a large-scale controlled trial before any definitive comments can be made on the exact role of ESWT in PD.

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