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EXTRACORPOREAL SHOCK WAVE THERAPY FOR PEYRONIE'S DISEASE: EXPLORATORY META-ANALYSIS OF CLINICAL TRIALS

EKKEHARD W. HAUCK, ULRICH O. MUELLER, THOMAS BSCHLEIPFER, HANS U. SCHMELZ, THORSTEN DIEMER AND WOLFGANG WEIDNER*

From the Department of Urology, Justus Liebig University, Giessen (EWH, HUS, TD, WW), the Institute of Medical Sociology and Social Medicine, Philipps University, Marburg (UOM), and the Department of Urology, Federal Armed Forces Hospital, Ulm (TB, HUS), Germany

ABSTRACT

Purpose: Extracorporeal shock wave therapy (ESWT) for the treatment of Peyronie's disease is still controversial. This exploratory meta-analysis of published studies in the international literature investigates its therapeutic effects.

Materials and Methods: The treatment outcomes from 17 study groups identified by a computerized literature search were compared with natural history outcomes and data from control groups from 2 controlled ESWT studies. An exploratory meta-analysis was performed because a methodologically sound meta-analysis lege artis did not appear appropriate, since treated groups differ considerably in structure, the selection of outcome measures is inconsistent and measurement is not standardized.

Results: ESWT seems to have an effect on penile pain during erection and on the improvement of sexual function. Pain seems to resolve faster after ESWT than during the course of the natural history. The effect on plaque size and penile curvature is less impressive.

Conclusions: ESWT in Peyronie's disease at least seems to be effective in regard to penile pain and sexual function compared to natural history. Deducing from these data the effect on plaque size and curvature remains questionable. However, ESWT is not an evidence based therapy at present. A controlled (preferably pairwise matched), single blind, multicenter study with careful, detailed documentation of disease symptoms before intervention and of outcomes is required to evaluate the real effect of ESWT.

KEY WORDS: penile induration, meta-analysis, lithotripsy

The use of extracorporeal shock wave therapy (ESWT) for the treatment of Peyronie's disease is increasing.[1–17] However, the therapeutic mechanism is unclear. ESWT is successful in the treatment of calcified and noncalcified orthopedic diseases.[7] An improvement in vascularization with consecutive resorption of calcification has been discussed in these terms.[7] A direct disturbance of pain receptors or hyperstimulation analgesia could be the mode of action for pain relief.[7] Peyronie's disease is also an inflammatory disease typified by fibrosis at the initial stage or sometimes typified by calcified plaques later on. Similar mechanisms of ESWT have been hypothesized for treating Peyronie's disease although results from basic and clinical research are hardly available. In patients with Peyronie's disease ESWT seems to decrease packing and clumping of collagen fibers in the plaque.[13] In this study we systematically summarize and analyze the outcomes of all ESWT studies in Peyronie's disease available in international journals using an exploratory meta-analysis.

MATERIALS AND METHODS

Definition of included papers and abstracts. A computerized literature search without language restrictions yielded papers from 15 study groups on ESWT in Peyronie's disease.[1–14] Only the most recent paper was included[2, 10, 12, 13] from 4 study groups with increasing series. At the annual meetings of the American Urological Association and the European Association of Urology 9 abstracts were presented and only 3 were included[15–17] since data from the remaining studies were published elsewhere later. Results from 17 study groups in total contributed to this analysis.

Data extraction. The included publications were analyzed by type of study, patient characteristics, mode of treatment and evaluation following a standardized, predefined procedure. Outcome was measured by alterations in plaque size, curvature, pain and sexual function. Individual data sets for each study were created with as many cases as the original study. No information on individual associations of different outcome variables is available. Thus only bivariate and no multivariate analyses of outcome variables are possible.

Definition of exploratory meta-analysis. Our meta-analysis of the efficacy of ESWT for Peyronie's disease is only exploratory. A rigorous confirmatory meta-analysis lege artis is not possible for many reasons. Study groups differ considerably in regard to subject medical history and symptom severity. The selection of outcome measures is inconsistent and measurement itself is not standardized. Effect size categorization is poorly documented and inconsistent. What constitutes clear success, modest success or no success at all varies from study to study. Thus differences in success frequency among studies may be caused by real differences or differences in success category definitions. In orthopedics even if confined to a well-defined anatomical region, little topological differences lead to with sizeable differences in ESWT outcome. Exact information on plaque size, location and consistency may be critical but, typically, the information is not available. Treatment protocols vary widely and some may be more effective than others. Only 4 of the 17 studies represent prospective controlled studies according to their own defini-

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* Correspondence: Department of Urology, Justus Liebig University Giessen, Rudolf-Buchheim-Str. 7, D-35385 Giessen, Germany (telephone: 49-641-9944501; FAX: 49-641-9944509; e-mail: wolfgang.weidner@chiru.med.uni-giessen.de).

tions,[7,8,10,13] and none is single blinded, real vs simulated ESWT, as described in orthopedic studies. Peyronie's disease is known to show divergent natural outcomes.[18,19] Therefore, ESWT effect size in all studies without a proper control group cannot be estimated. Consequently, for an exploratory study we estimated the effect size of ESWT in all study groups compared to the controls of the 2 prospective controlled studies[7,13] and the 2 study groups of on the natural history of the disease[18,19] that provide individual longitudinal data despite its coarseness.

Controls. The patients of Mirone et al were divided into 3 categories, 1 with ESWT alone, 1 receiving perilesional injections of verapamil (101 patients), and 1 with both treatments.[20] The second group was considered the control. Recently the authors had only 2 treatment categories, 1 group (380 patients) with ESWT and perilesional injections of verapamil and 1 (92 patients) with perilesional injections of verapamil alone.[13] From the previous paper[20] it can be concluded that perilesional injections of verapamil are not effective therapy since there were no outcome differences between patients receiving ESWT alone and patients receiving ESWT and verapamil unless we argue that ESWT is specifically suppressing the therapeutic effects of verapamil. However, this argument is implausible. The group in the second paper[13] is a continuation of the series as set up previously,[20] not a new series of cases started later. The slightly smaller number of patients treated with verapamil only (92)[13] may be due to a critical review of the 101 original patients.[20] Thus we chose the 92 patients[13] as the appropriate controls from the Mirone et al series.[13,20]

Hauck et al established a control group of 23 clinically investigated patients similar to the treatment group but who did not receive any therapy.[7] Gelbard et al published the results of 97 retrospective self reports on the history and of self-examinations collected by a mailed survey.[18] Kadioglu et al reported on the clinical data of 307 subjects with a natural history of up to 8 years, but provided little information on individual associations between initial conditions and final outcomes.[19] The control groups of Hauck et al[7] and Mirone et al[20] are used in combination. The data of Gelbard et al[18] and Kadioglu et al[19] also serve as control groups whenever possible.

ESWT. Most study groups (table 1) used the Storz Minilith SL1 lithotriptor (Storz Medical, Kreuzlingen, Switzerland) with differing numbers of sessions (2 to 8), intervals between sessions (1 to 30 days), numbers of shock waves (1,000 to 4,000) per session and energy dosages (mainly between 0.11 and 0.17 mJ/mm^2) per shock wave.[4–8,11–13,15,16] Furthermore, the Wolf Piezolith 2500 (Richard Wolf, Knittlingen, Germany)[2] EDAP LT-02 (EDAP TMS, Vaulx-en-Velin, France)[9] Siemens Lithostar,[1] Siemens Multiline (Siemens AG, Munich, Germany),[10] ReflecTron (High Medical Technologies, Lengwil, Switzerland)[14] and Dornier Epos Ultra Device (Dornier MedTech, Wessling, Germany)[17] lithotriptors were used.

Outcome measures. Most studies used 2 objective measures including change in plaque size and change in penile curvature, and 2 subjective measures, including a decrease in pain during erections and improvement of sexual function. Plaque size has to be measured by caliper, ruler or sonography. Measuring change in penile curvature requires a standardized measurement protocol and the calibration of observers. The curvature degree can be documented with photography from 3 different angles during erection or during an intracavernous injection test. Pain is notoriously difficult to measure whether visual or verbal items are used. Sexual function is measured with the International Index of Erectile Function (IIEF), its shortened version IIEF-5 or with a variety of self-constructed questions.

Because of the different categories of measurement there is little compatibility in outcome variables, especially between different control groups.[7,13,18,19] Also, individual longitudinal information is rarely available that would include a clear definition of the risk group. Individual data on the condition at start and end of observation have to be provided. Population measures such as the mean at the beginning and end of observation are useless for an effect size estimation.

Analysis. First, the 4 groups of controls are compared with each other. Then treatment groups from all studies are compared with each other, followed by a comparison of the treatment groups of every study with the control groups. Finally treatment groups combined with control groups are compared.

RESULTS

Clinical data of the patients are summarized in table 2. Treatment of patients with Peyronie's disease before ESWT varied from series of no treatment to different conservative approaches to a series with patients who had previously undergone surgery.[11] An overview of treatment results is provided in table 3. Severe complications were not reported in any of the studies. Observations included local pain during administration, skin hematoma (seen frequently) and hematuria relating to urethral bleeding (seen rarely).

TABLE 1. *Technical parameters*

References	ESWT Technique	No. Settings	Days Between Settings	No. Shock Waves/Setting	Energy/Shock Wave (mJ/mm^2)
Abdel-Salam et al[1]	Siemens Lithostar	5 (range 4–10)	Unknown	4,000	15–21 kV
Awogu et al[15]	Storz Minilith SL1	3 (repeat 6)	30	3,000	4–5 (0.11–0.15)*
Baumann et al[2]	Wolf Piezolith 2500	6	14–28	2,500	3
Bellorofonte et al[3]	Wolf Piezolith 2300	6	7	800	40–100 Mpa
Butz[4]	Storz Minilith SL1	3–5	1–7	3,000	Unknown (0.09–0.14)
Colombo and Nicola[5]	Storz Minilith SL1	4	2	3,000	4 (0.11)
Gianneo et al[16]	Storz Minilith SL1	6–8	Unknown	3,000–4,000	3–4 (0.07–0.11)*
Hamm et al[6]	Storz Minilith SL1	4 (range 1–5)	Unknown	3,000	2–5 (0.04–0.17)
Hauck et al[7]	Storz Minilith SL1	2	3	2,000	1–7 (0.03–0.35)
Husain et al[8]	Storz Minilith SL1	3	Unknown	3,000	4–5 (0.11–0.17)
Kiyota et al[9]	EDAP LT-02	3–5	Unknown	Unknown	450–960 Bar
Lebret et al[10]	Siemens Multiline	2 (range 1–3)	90	3,000	(0.3)
Manikandan et al[11]	Storz Minilith SL1	3–6	2 Groups (1 vs 30)	3,000	4–5 (0.11–0.17)
Michel et al[12]	Storz Minilith SL1	5	7	1,000	3–5 (0.07–0.17)
Mirone et al[13]	Storz Minilith SL1	3	2	Unknown	Unknown
Oeynhausen et al[14]	Reflec Tron	5 (range 3–6)	30	2,000–4,000	(0.13–0.15)
Sautter et al[17]	Dornier Epos Ultra Device	1–3	30	3,000	Unknown

* Awogu[15] and Gianneo[16] et al provided J/mm^2 as unit in their studies but it must be mJ/mm^2 according to manufacturer instructions.

TABLE 2. *Basic patient data in 17 studies on ESWT for Peyronie's disease*

References	No. Pts*	Mean Pt Age (range)	Mean Mos History (range)	No. Plaque Calcification (%)	Mean Degree Penile Curvature (range)	Stable Disease	Treatment Before ESWT
Abdel-Salam et al[1]	24	55 (36–67)	26 (6–240)	Unknown	Unknown	Yes	Unknown
Awogu et al[15]	31	Unknown	Greater than 12	Unknown	30–80	Unknown	Yes
Baumann et al[2]	74	54 (29–70)	19 (12–72)	Unknown	Unknown	(Yes)	Yes
Bellorofonte et al[3]	9	41 (32–65)	Unknown	Unknown	Unknown	Unknown	Unknown
Butz[4]	72	55 (26–74)	17 (3–96)	Unknown	Unknown	Unknown	Unknown
Colombo and Nicola[5]	82	54 (44–74)	23 (3–120)	36/82 (44)	Unknown	Unknown	Unknown
Gianneo et al[16]	153	31–76	Unknown	136/153 (89)	20–Greater than 40	Unknown	Unknown
Hamm et al[6]	28	57 (34–72)	Greater than 12	Unknown	Unknown	Yes	Unknown
Hauck et al[7]	20	51 (38–59)	12 (3–93)	12/20 (60)	42 (10–90)	No	Yes
Husain et al[8]	34	56 (24–69)	19 (4–60)	Unknown	51 (20–90)	Unknown	Unknown
Kiyota et al[9]	4	52 (35–65)	Unknown	Unknown	20–40	Unknown	Yes
Lebret et al[10]	54	56 (29–76)	16 (3–60)	Unknown	48 (20–110)	Unknown	No
Manikandan et al[11]	42	55 (32–72)	17 (3–60)	Unknown	20–75	Unknown	Yes
Michel et al[12]	35	58	34	Unknown	50	Yes	Unknown
Mirone et al[13]	380	47 (32–71)	Greater than 6	Unknown	Unknown	Unknown	Yes
Oeynhausen et al[14]	30	55 (28–72)	25 (4–96)	19/30 (63)	Greater than 30–greater than 60	Unknown	Yes
Sautter et al[17]	15	57 (42–72)	Unknown	Unknown	Unknown	Unknown	Unknown

* Available at followup.

TABLE 3. *Results of Peyronie's disease treatment using ESWT in 17 study groups*

References	Mean Mos Followup (range)	Evaluation Mode	No. Plaque Size Reduction/Total No. (%)	No. Penile Curvature Reduction/No. Total (%)	No. Decrease Pain During Erection/ Total No. (%)	No. Sexual Function Improvement/Total No. (%)
Abdel-Salam et al[1]	(3–9)	Photo, ultrasound, interview, examination	14/24 (58)	14/24 (58)	17/24 (72)	14/24 (58)
Awogu et al[15]	3	IIEF, angulation measurement	Unknown	23/31 (74) 34 (unknown)	17/17 (100)	18/31 (58)
Baumann et al[2]	24 (4–69)	Telephone, interview, examination	Unknown	37/74 (50)	42/47 (89)	41/74 (55)
Bellorofonte et al[3]	12	Ultrasound, artificial erection, RigiScan*	Unknown	3/9 (33)	Unknown	5/9 (55)
Butz[4]	12	Photo/drawing, ultrasound, interview	Unknown	36%	66%	50%
Colombo and Nicola[5]	Less than 1	Photo, questionnaire, ultrasound, examination	34/82 (41)	24/78 (31)	31/44 (70)	Unknown
Gianneo et al[16]	Unknown	Photo, examination, questionnaire	96/153 (62)	35/151 (23)	48/50 (96)	46/74 (62)
Hamm et al[6]	Unknown	Artificial erection, photo, IIEF, questionnaire, ultrasound, examination	Unknown	18/28 (64)	13/16 (81)	20/28 (71)
Hauck et al[7]	9 (3–13)	Artificial erection, photo, ultrasound, interview, examination	2/20 (10)	10/20 (50)	5/9 (56)	3/20 (15)
Husain et al[8]	8 (5–11)	Artificial erection, questionnaire, ultrasound, examination	Unknown	15/32 (47)	12/20 (60)	Unknown
Kiyota et al[9]	Less than 1	Unknown	1/4 (25)	0/4 (0)	4/4 (100)	Unknown
Lebret et al[10]	13 (3–unknown)	IIEF, photo, questionnaire, examination	23/54 (43)	29/51 (54)	31/34 (91)	6/24 (25)
Manikandan et al[11]	6 (2–18)	Artificial erection, photo, interview, examination	Unknown	22/38 (58)	21/25 (84)	5/42 (12)
Michel et al[12]	18	Artificial erection, pain scale, interview, examination	0	5/24 (21)	16/17 (94)	9/35 (26)
Mirone et al[13]	Unknown	Ultrasound, interview, examination	260/380 (68)	Unknown	312/340 (92)	303/380 (80)
Oeynhausen et al[14]	4	Photo, interview, ultrasound, examination	20/30 (67)	17/29 (58)	13/16 (81)	17/30 (56)
Sautter et al[17]	Unknown	Interview, self-examination	Unknown	Unknown	9/9 (100)	6/14 (42)

* Uro-Health Systems, Inc., Laguna Niguel, California.

Comparison of 4 control groups with each other (see Appendix). Gelbard et al's description of the natural history relies on retrospective self reports and self-examination, and, therefore, is subject to additional bias.[18] The data of Kadioglu et al are based on clinical examinations.[19] Their outcomes are unfavorable, eg penile deformities remained unchanged or worsened in 97% of all cases, in comparison with 79% (Mann-Whitney test $p < 0.0005$) in the Hauck et al series.[7] The improvement of sexual function in the Gelbard et al data[18] is less frequent than in the other 2 control groups, Mirone et al[13] (Mann-Whitney test $Z = -5{,}167$, $p < 0.0005$) or Hauck et al[7] (Mann-Whitney test $Z = -1{,}963$, $p < 0.050$, $F = 11.180$, $p < 0.0005$). In the 2 outcome measures available for the latter 2 studies (painful erections and sexual function)[7,20] no differences were evident between the 2 control groups, 1 receiving no therapy[7] and the other receiving verapamil injections.[20]

Comparison of treatment groups with each other. Table 4 provides the results of the 4 outcome variables. Success rates vary widely for all outcomes including a decrease in plaque size from 0% to 68%, decrease in penile curvature from 21% to 74%, decrease in penile pain from 56% to 100% and improvement of sexual function from 12% to 80%.

Comparison of treatment groups with controls by study. The results are summarized in table 5. There are almost no differences in the decrease in plaque size among separate

TABLE 4. *Comparison of treatment groups from 15 studies*

Outcome Measure	% Maximum Success Rate	% Av Success Rate	% Min Success Rate	Statistics
Plaque size reduction	68	63	0	$F = 5.101$, $p < 0.0005$, $R^2 = 0.049$
Penile curvature reduction	74	52	21	$F = 5.215$, $p < 0.0005$, $R^2 = 0.117$
Decreases pain during erection	100	85	56	$F = 5.078$, $p < 0.0005$, $R^2 = 0.114$
Sexual function improvement	80	7	12	$F = 14.101$, $p < 0.0005$, $R^2 = 0.082$

Studies by Bellorofonte[3] and Kiyota[9] et al excluded from analysis due to limited database.

TABLE 5. *Comparison of treatment groups with controls by study*

References	No. Pts*	p Value (Mann-Whitney test)						
		Plaque Size Reduction	Penile Curvature Reduction		Decreased Pain erections		Sexual Function Improvement	
			Without Controls	With Controls[19]	Without Controls[19]	Including Controls[18]	Without controls[18]	Including controls[18]
Abdel-Salam et al[1]	24	—	Not significant	<0.0005†	Not significant	Not significant	—	—
Awogu et al[15]	31	—	<0.013†	<0.0005†	<0.0005†	<0.0005†	<0.013†	<0.005†
Baumann et al[2]	74	Not significant	—	<0.0005†	<0.0005†	<0.0005†	Not significant	<0.001†
Butz[4]	72	—	<0.002†	<0.0005†	<0.0005†	<0.0005†	Not significant	<0.016†
Colombo and Nicola[5]	82	Not significant	—	<0.0005†	<0.010†	<0.001†	—	—
Gianneo et al[16]	153	<0.0005†	<0.016†	<0.0005†	<0.0005†	<0.0005†	Not significant	<0.0005†
Hamm et al[6]	28	—	<0.0005†	<0.0005†	<0.020†	<0.003†	—	—
Hauck et al[7]	20	Not significant	Not significant	<0.0005†	Not significant	Not significant	Not significant	Not significant
Husain et al[8]	34	—	Not significant	<0.0005†	Not significant	Not significant	—	—
Lebret et al[10]	54	—	Not significant†	<0.0005†	<0.0005†	<0.0005†	Not significant	Not significant
Manikandan et al[11]	42	—	<0.0005†	<0.0005†	<0.0005†	<0.0005†	—	—
Michel et al[12]	35	Not significant	—	<0.001†	<0.001†	<0.001†	Not significant	Not significant
Mirone et al[13]	472	<0.075†	—	—	<0.0005†	<0.0005†	<0.0005†	<0.0005†
Oeynhausen et al[14]	30	<0.007†	Not significant	<0.0005†	<0.010†	<0.010†	Not significant	<0.008†
Sautter et al[17]	15	—	—	—	<0.0005†	<0.0005†	—	—

Dash indicates an effect in the opposite direction with controls faring better than treated subjects.
* Available at followup.
† Effect in the predicted direction as treated patients had better results than controls.

study treatment groups. Hauck et al reported no decrease in plaque size compared with controls[7] while Mirone et al[13] reported a slight decrease. These results remained unchanged after grouping controls from both studies together. If there had been the same outcome in controls compared to the controls of Hauck et al[7] and Mirone et al[13] 2 studies[2,14] would report strongly significant therapy results.

In the majority of cases no decrease in penile curvature was observed in comparison with the controls of Hauck et al[7] and Mirone et al.[13] It should be noted that the significance levels of effects in 4 of 5 studies[6,8,12,15,16] reporting success would not survive a proper alpha correction that, in view of the deficient data, should not be performed here. If the data set of Kadioglu et al[19] is included in the controls a massive effect of ESWT became apparent. It can be concluded from most studies that ESWT may decrease pain during erection faster than pain decreases in the natural course. This finding is the result of comparing treated cases with 3 of the control groups.[7,18,19] Only 1 paper reported a substantial and significant improvement of sexual function after ESWT.[13]

Comparing treatment groups from all studies with control groups. If all treated subjects combined are compared with the controls either from the 2 controlled clinical studies or augmented with 1 or both natural history studies, the results (table 6) would indicate a strong therapeutic effect of ESWT in the decrease in erectile pain and improvement of impaired sexual function. However, positive effects on the 2 objective outcome measures, curvature and plaque size, are less impressive.

DISCUSSION

A variety of contributing factors will likely influence the outcome of ESWT in Peyronie's disease. The case history ranged widely within different studies with individual histories between 3[4,5,7] and 240 months.[1] Data on plaque calcification as a possible marker of disease chronicity are often missing. Only 4 studies included stable cases.[1,2,12,15] However, penile pain is frequently regarded as indicative of an active, inflammatory stage of disease. Doubts arise whether these patients were really in a stable phase because in all these series erectile pain was described and improved by ESWT.[1,2,12,15] ESWT outcome may be greatly influenced if patients without previous treatment[10] are compared to pretreated patients.[2,7,9,11,14,15,20] Arguably the variety of technical device characteristics and treatment protocols may also explain a considerable portion of variance in results.

Mean followup ranged from less than 1 month[5,9] to 24 months,[2] with most studies having only a short followup (table 3). Subsequently the long-term effect, important in the long natural history of Peyronie's disease,[18] may be unclear in most series. Outcomes were measured by telephone interviews,[2] self-examination[17] and self-photography or intracavernous injection tests.[12] Remarkably the only study that used artificial erection before and after intervention did not report any significant improvement in curvature.[12] Only a few studies gave clear information when a decrease in curvature was considered as success, eg less than 30% of the degree of the finding before treatment.[7] Here the percentage of patients who reported a decrease in curvature was almost always lower than in studies in which any degree of decrease was regarded as a success.

Thus it is not amazing that the results differ in all outcome dimensions in the 17 different series. Decrease in plaque size was reported in 0% to 68% of cases, decrease in curvature reported as no significant findings to 74% of cases and decrease in penile pain in 56% to 100%. Sexual function, typically not clearly defined, improved in 12% to 80%. These different results could be explained by the different groups of patients, modes of evaluation, techniques and study designs before we consider the effects of this technique.

However, the core handicap of this exploratory meta-analysis is the lack of real controls (table 4). Many patients

TABLE 6. *Comparison of treatment groups from all studies combined with control groups*

Reference Controls Vs All ESWT Treated Subjects	p Value (Mann-Whitney test)*			
	Plaque Size Reduction	Penile Curvature Reduction	Decrease Pain During Erection	Sexual Function Improvement
Gelbard,[18] Hauck,[7] Kadioglu,[19] Mirone[13] et al	<0.035	<0.0005	<0.0005	<0.0005
Hauck,[7] Kadioglu,[19] Mirone[13] et al	<0.035	<0.0005	<0.0005	<0.0005
Gelbard,[18] Hauck,[7] Mirone[13] et al	<0.035	<0.0005	<0.0005	<0.0005
Hauck,[7] Mirone[13] et al	<0.035	<0.130	<0.0005	<0.0005

* Effect in the predicted direction as treated patients had better results than controls.

pretreated without success may not be willing to participate in a control arm. Consequently, most studies just report on ESWT as a clinical trial to improve patient symptoms. Taking control groups from different studies[7,13,18,19] is not optimal for comparison but has been the only chance to estimate any effect size of treatment at all. Remarkably the control outcome of 1 group[7] is nearly the same as that of 1 control group receiving intralesional injections of verapamil.[13] According to these data intralesional verapamil therapy is not effective in Peyronie's disease although its positive effect was described repeatedly in prospective series without controls.

The wide range of success rates in treatment groups from all studies (table 4) indicates that the groups of subjects in the various studies cannot be regarded as a series of random samples taken consecutively from a single population of patients. All cell variances are the same in the population, a finding that is strongly supported by test statistics. The relatively low R^2 values indicate that the factor "studies" explains only a small fraction of variation among outcomes.

Once all patients are set vs all controls in single comparisons, a massive effect of ESWT appears (table 5), most likely due to incompatible measurement protocols in the various studies. Many cases with a decrease in penile curvature would have been categorized as "unchanged" by Kadioglu et al[19] or, conversely, many "unchanged" cases from these controls would have been categorized as at least modest successes in several treatment studies. All studies support that pain resolves faster with ESWT than during the natural history of the disease. Only Mirone et al report a substantial improvement in sexual function after ESWT.[13] This solitary finding calls for replication. Once all patients are set vs all controls together (table 6) the strong therapeutic effect of ESWT on erectile pain and sexual function remains. However, positive effects on the 2 objective outcome measures, decrease in plaque size and curvature, look less impressive.

CONCLUSIONS

At this time ESWT for Peyronie's disease is not an evidence based therapy. To evaluate the real effect of ESWT in Peyronie's disease a controlled (preferably pairwise matched), single blind, multicenter study, with careful, detailed documentation of disease symptoms before intervention and of outcomes is required, including measurement of plaque size by caliper, ruler and by ultrasound, as well as documentation of sonographically obtained properties, especially calcifications. In addition, measurement of penile curvature and possible changes must be documented by a reliable protocol. This process would probably require careful calibration of examiners. Photo documentation from 3 different angles (frontal, lateral and from above) is required. An intracavernous injection test before and after therapy would be optimal. Improvement or any change in sexual function should be evaluated by validated instruments such as the IIEF or the IIEF-5. It would also be necessary to reexamine subjects and controls after a sufficiently long interval identical for all study groups. Patients should be evaluated separately in groups depending on degree of curvature before treatment, eg 0 to 30, less than 30 to 60 and less than 60 to 90 to allow a better definition of possible responders.

APPENDIX: OUTCOME MEASURES FOR WHICH INDIVIDUAL LONGITUDINAL INFORMATION HAS BEEN PUBLISHED

References	Decrease in Plaque Size	Decrease in Penile Curvature	Decrease in Pain During Erection	Improvement of Sexual Function
Mirone et al[13]	Information published	—	Information published	Information published
Hauck et al[7]	Information published	Information published	Information published	Information published
Gelbard et al[18]	—	Information published	Information published	Information published
Kadioglu et al[19]	—	Information published	—	—

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