Submitted: 19 June, 2024 Accepted: 23 August, 2024 Published: 30 December, 2024 DOI:10.22514/j.androl.2024.026

ORIGINAL RESEARCH

REV INT ANDROL
Revista Internacional de Andrología

The efficiency of biofeedback electric stimulation therapy combined with low-intensity pulsed ultrasound in treating erectile dysfunction: a clinical study

Luo Yang[1,2,3,†], Suliya Yushanjiang[1,2,†], Sixiao Zhang[1,2], Yue Zhao[1,2], Yi Luo[1], Guo Chen[1,2], Yi Dai[1,2,3,*], Rui Qu[1,2,3,*]

[1]Department of Urology and Pelvic Surgery and Andrology, West China School of Public Health and West China Fourth Hospital, Sichuan University, 610000 Chengdu, Sichuan, China
[2]Department of Public Health Laboratory Sciences, West China School of Public Health and West China Fourth Hospital, Sichuan University, 610000 Chengdu, Sichuan, China
[3]Institute of Medical Preventive Integration and Transformation Research, West China School of Public Health and West China Fourth Hospital, Sichuan University, 610000 Chengdu, Sichuan, China

***Correspondence**
qurui@scu.edu.cn
(Rui Qu);
daiyi@scu.edu.cn
(Yi Dai)

† These authors contributed equally.

Abstract

Background: Erectile dysfunction (ED) is a prevalent condition that significantly impacts the quality of life of both patients and their partners. Current therapeutic approaches often struggle to address the diverse needs of all patients. In addition, the efficacy of low-intensity pulsed ultrasound (LIPUS) in improving ED symptoms has been insufficiently investigated. Therefore, this study aims to evaluate the effectiveness of LIPUS and to assess whether combining LIPUS with biofeedback electric stimulation for pelvic floor therapy enhances treatment outcomes. **Methods**: We retrospectively retrieved and assessed the data of 68 patients treated at West China Fourth Hospital. Of them, 30 patients received LIPUS therapy alone, while 38 underwent combined therapy of LIPUS and biofeedback electric stimulation. Both groups completed eight treatment sessions. **Results**: After the treatment, the efficacy of the treatments was measured using the International Index of Erectile Function-5 (IIEF-5), Erectile Hardness Score (EHS), and Erection Satisfaction Score (ESS) after 4 and 8 treatments. Significant improvements were observed in the LIPUS-only group in IIEF-5, EHS and ESS scores ($p < 0.001$ for all measures). The positive response rate was 79.41% after eight treatments. Improvements in IIEF-5 scores were observed in both groups (LIPUS: 11.50 to 16.60; combined therapy: 10.61 to 16.90; $p < 0.001$), as well as in EHS scores (LIPUS: 2.27 to 3.07; combined therapy: 2.26 to 3.11; $p < 0.001$). However, no statistically significant differences were found between the LIPUS-only and combined therapy groups ($p > 0.05$). **Conclusions**: LIPUS therapy demonstrates potential for alleviating ED symptoms, and the addition of biofeedback electric stimulation for pelvic floor therapy did not result in significantly superior outcomes compared to LIPUS alone. Further research with larger sample sizes and longer treatment durations is necessary to confirm these results.

Keywords

Low-intensity pulsed ultrasound; Biofeedback electric therapy stimulation for pelvic; Erectile dysfunction

La eficiencia de la terapia de estimulación eléctrica de biofeedback combinada con ultrasonido pulsado de baja intensidad en el tratamiento de la disfunción eréctil: un estudio clínico

Resumen

Antecedentes: La disfunción eréctil (DE) es una condición prevalente que impacta significativamente en la calidad de vida de los pacientes y sus parejas. Los enfoques terapéuticos actuales a menudo tienen dificultades para abordar las diversas necesidades de todos los pacientes. Además, la eficacia del ultrasonido pulsado de baja intensidad (LIPUS) en la mejora de los síntomas de DE ha sido insuficientemente investigada. Por lo tanto, este estudio tiene como objetivo evaluar la efectividad de LIPUS y determinar si combinar LIPUS con estimulación eléctrica de biofeedback para la terapia del suelo pélvico mejora los resultados del tratamiento. **Métodos**: Recuperamos y evaluamos retrospectivamente los datos de 68 pacientes tratados en el Cuarto Hopsital del oeste de China. De ellos, 30 pacientes recibieron solo terapia con LIPUS, mientras que 38 se sometieron a una terapia combinada de LIPUS y estimulación eléctrica de biofeedback. Ambos grupos completaron ocho sesiones de tratamiento. Después del tratamiento, la eficacia de los tratamientos se midió utilizando el Índice Internacional de Función Eréctil-5 (IIEF-5), el Puntaje de Dureza Eréctil (EHS) y el Puntaje de Satisfacción de Erección (ESS) después de 4 y 8 tratamientos. **Resultados**: Se observaron mejoras significativas en el grupo solo de LIPUS en los puntajes de IIEF-5, EHS y ESS ($p < 0.001$ para todas las medidas). La tasa de respuesta positiva fue del 79.41% después de ocho tratamientos. **Conclusiones**: Se observaron mejoras en los puntajes de IIEF-5 en ambos grupos (LIPUS: 11.50 a 16.60; terapia combinada: 10.61 a 16.90; $p < 0.001$), así como en los puntajes de EHS (LIPUS: 2.27 a 3.07; terapia combinada: 2.26 a 3.11; $p < 0.001$). Sin embargo, no se encontraron diferencias estadísticamente significativas entre el grupo solo de LIPUS y el grupo de terapia combinada ($p > 0.05$). En conclusión, la terapia con LIPUS muestra potencial para aliviar los síntomas de DE, y la adición de estimulación eléctrica de biofeedback para la terapia del suelo pélvico no resultó en resultados significativamente superiores en comparación con LIPUS solo. Se necesita más investigación con tamaños de muestra más grandes y duraciones de tratamiento más largas para confirmar estos resultados.

Palabras Clave

Ultrasonido pulsado de baja intensidad; Estimulación eléctrica de biofeedback para el suelo pélvico; Disfunción eréctil

1. Introduction

Erectile dysfunction (ED) is characterized by the inability to achieve or maintain an erection sufficient for satisfactory sexual intercourse [1]. A study conducted across five Asian countries revealed that approximately 63% of men aged 50 to 80 experience ED, with an increasing prevalence among men under 40 [2, 3]. In addition, the prevalence of ED is projected to reach 322 million cases by 2025 [4]. The pathophysiology of ED encompasses organic, psychogenic or mixed etiologies, with vasculogenic factors being the most prevalent among organic causes [5].

Current research indicates that the common risk factors contributing to ED include unhealthy lifestyle choices such as smoking, excessive alcohol consumption, high-fat diets and certain medications (*e.g.*, sertraline, hydrochlorothiazide, metoprolol) [6, 7]. Individuals with diabetes are particularly susceptible to ED [8], which is also associated with increased risks of cardiovascular disease and mortality [9, 10]. While phosphodiesterase type 5 inhibitors (PDE5Is) are commonly used as first-line treatments, 25–30% of patients do not respond effectively [11]. Vacuum constriction devices (VCDs) serve as a second-line treatment but are often associated with side effects. Regenerative therapies, including stem cell and gene-based approaches, have shown promise in preclinical studies but require further investigation [12].

Low-intensity pulsed ultrasound (LIPUS) is a non-invasive treatment modality that delivers low-intensity ultrasound (<3 W/cm^2) in pulse wave mode (100–1000 Hz). LIPUS has been shown to induce functional and structural changes in tissues, promoting stem cell proliferation, differentiation and regeneration of vascular, nerve and muscle tissues [13–16]. While LIPUS is commonly used in orthopedic treatments for bone healing and pain relief [17, 18], recent evaluations suggest its potential as a novel non-invasive treatment for ED. LIPUS may enhance peripheral nerve regeneration by activating Schwann cells, which could be beneficial for ED resulting from bilateral cavernous nerve injury [19]. Hence, characterizing the effects of LIPUS in ED patients could be clinically useful.

Additionally, pelvic floor therapy has demonstrated efficacy in improving ED [20]. In this regard, biofeedback electric stimulation applied to the pelvic floor has shown effectiveness in managing pelvic dysfunctions, such as urinary incontinence [21, 22]. However, the combined effect of LIPUS and biofeedback electric stimulation for pelvic floor therapy on ED has not been thoroughly investigated. Therefore, this study aims to evaluate the efficacy of LIPUS alone and in combination with biofeedback electric stimulation for pelvic floor therapy to determine whether a synergistic effect exists and to provide new insights into the treatment of ED.

2. Materials and methods

2.1 Study design

This retrospective study collected data from patients treated with either LIPUS alone or LIPUS combined with biofeedback electric stimulation therapy (referred to as the LIPUS + PELVIC group in table and combined therapy group in text) at

the Urology & Pelvic Floor Department of West China Fourth Hospital between May 2023 and January 2024. Patient consent was obtained for the collection of basic information and scale scores after each intervention.

All participants included in this study were treated with LIPUS using a device set at a frequency of 1.7 MHz and an energy level of 3 W/cm^2. During each treatment session, LIPUS was applied to both sides of the penile crus and corpus cavernosum for 5 minutes per side, totaling 20 minutes per session. Treatment was administered over 8 consecutive sessions, 2–3 times per week.

In subgroups, participants received the LIPUS therapy only or LIPUS combined with biofeedback electric stimulation therapy. In the combined therapy group, patients received both LIPUS and biofeedback electric stimulation for pelvic floor therapy. The biofeedback electric stimulation was administered using the MyoTrac therapy device (MLD B2Plus), which evaluated the patient's pelvic floor condition. Based on this evaluation, a treatment program was developed that included 30 minutes of neuromuscular electrical stimulation and a home-rehabilitation training program. Both groups underwent treatment over 8 consecutive sessions, 2–3 times per week.

2.2 Participants

The inclusion criteria for the LIPUS group were as follows: patients received LIPUS therapy alone, were aged 20–60 years, had an International Index of Erectile Function-5 (IIEF-5) score $<$21 (indicating severe ED: $<$7, moderate ED: 8–11, mild ED: 12–21), tested negative on Audiovisual Sexual Stimulation (AVSS), and had nocturnal penile tumescence and rigidity (NPTR) measured by Rigiscan. Participants had a stable female sexual partner for more than 3 months and provided written informed consent after a detailed study explanation. Exclusion criteria included the use of PDE5Is or any other ED medications in the past 2 weeks, neurological or hormonal abnormalities, a history of hypogonadism, pelvic surgery, substance abuse, kidney disease, liver failure or coronary artery disease.

The inclusion criteria for the combined therapy group were the same as those for the LIPUS-only group, with the additional criterion being participation in the biofeedback electric stimulation for pelvic therapy.

Our preliminary analyses indicated that there were no statistically significant differences between the two groups regarding age, severity of ED or baseline scores of outcome measures.

2.3 Outcome measures

The outcome measures collected in this study were obtained in the form of questionnaires administered to patients after each intervention session, with consent obtained and organized during the study. The primary efficacy indices included the IIEF-5, Erectile Hardness Score (EHS), and Erection Satisfaction Score (ESS), which covers morning erections, sexual stimulation, and masturbation erections. Scores were compared before treatment, after four sessions and after eight sessions. A positive response in the IIEF-5 was defined as an increase of $\geq$2 points for mild ED (baseline IIEF-5 score $>$11) or $\geq$5 points for moderate and severe ED (baseline IIEF-5 score $\leq$11). In the combined therapy group, pelvic floor function was assessed by pelvic floor muscles electrical activity testing using instrumentation before and after treatment (normal, $>$80).

2.4 Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics version 27 (Armonk, NY, USA). Baseline data and pelvic floor scores were described using mean $\pm$ standard deviation (95% confidence interval). For normally distributed data, comparisons were made using the *t*-test; for non-normally distributed data, the Mann-Whitney U test was used. Outcome data were described using mean $\pm$ standard deviation (95% confidence interval). For normally distributed and homogenous data, repeated measures analysis of variance was employed; for non-normally distributed or non-homogenous data, the Friedman test was used. Enumeration data were presented as percentages (%) and analyzed using the chi-square test. Statistical significance was set at a two-sided significance level of $p < 0.05$.

3. Results

3.1 General characteristics of the subjects

The study included 30 patients in the LIPUS group and 38 patients in the combined group. These patients met the specified inclusion and exclusion criteria. The overall mean age of patients was 37.46 years, with 27.94% having severe ED, 25% having moderate ED, and 47.06% having mild ED (Table 1). The mean ages for the LIPUS and the combined groups were 37.77 and 37.21 years, respectively ($p = 0.802$). There were no significant differences in body mass index (BMI), smoking and drinking habits between the two groups ($p = 0.644$, $p = 0.861$ and $p = 0.255$, respectively). Pretreatment scores for the IIEF-5, EHS, morning erection, sexual stimulation and masturbation erection were similar between the two groups ($p = 0.459$, $p = 0.988$, $p = 0.173$, $p = 0.813$, $p = 0.560$, respectively).

3.2 Comparison between pretreatment and posttreatment outcomes in the overall cohort

All 68 patients who received LIPUS showed improvements in IIEF-5, EHS and ESS after 4 and 8 treatments. Specifically, the IIEF-5 score increased from 11.00 to 16.77 and the EHS score from 2.27 to 3.09 after 8 treatments (Table 2), both changes being statistically significant ($p < 0.001$). Additionally, morning erection scores improved from 2.02 to 2.91, sexual stimulation scores from 1.92 to 2.76, and masturbation erection scores from 2.44 to 3.10, with all changes significant ($p < 0.001$). After 4 treatments, the positive response rate for IIEF-5 was 27.94%, increasing to 79.41% after 8 treatments.

TABLE 1. Baseline characteristics of the investigated cohort.

Variables	TOTAL (n = 68)	LIPUS group (n_1 = 30)	LIPUS + PELVIC group (n_2 = 38)	*p* value
Age (yr)	37.46 ± 8.96 (36.00)	37.77 ± 9.44 (33.50)	37.21 ± 8.69 (36.00)	0.802
BMI (kg/m^2)	24.01 ± 4.28 (23.88)	23.74 ± 2.44 (23.88)	24.22 ± 5.33 (23.12)	0.644
Smoking	28 (41.18%)	12 (40.00%)	16 (42.11%)	0.861
Drinking	37 (53.41%)	14 (44.47%)	23 (60.53%)	0.255
IIEF-5	11.00 ± 4.91 (11.00)	11.50 ± 5.09 (12.50)	10.61 ± 4.78 (10.50)	0.459
Severe ED	19 (27.94%)	8 (26.67%)	11 (28.95%)	0.601
Moderate ED	17 (25.00%)	6 (20.00%)	11 (28.95%)	
Mild ED	32 (47.06%)	16 (53.33%)	16 (42.10%)	
EHS	2.27 ± 0.91 (2.50)	2.27 ± 1.08 (3.00)	2.26 ± 0.76 (2.00)	0.988
Morning erection[a]	2.02 ± 0.98 (2.00)	1.83 ± 1.07 (2.00)	2.16 ± 0.90 (2.00)	0.173
Sexual stimulation[b]	1.92 ± 0.93 (2.00)	1.96 ± 1.07 (2.00)	1.88 ± 0.81 (2.00)	0.813
Masturbation erection[c]	2.44 ± 1.01 (2.00)	2.53 ± 1.12 (3.00)	2.38 ± 0.94 (2.00)	0.560
Diabetes	5 (7.35%)	3 (10.00%)	2 (5.26%)	0.457
Hypertension	4 (5.88%)	3 (10.00%)	1 (2.63%)	0.200

Data are presented as mean ± standard deviation (median) or n (%). LIPUS: low-intensity pulsed ultrasound. LIPUS + PELVIC: LIPUS combined with biofeedback electrical stimulation for pelvic floor therapy. IIEF-5: International Index of Erectile Function-5 (scores: severe ED <7; moderate ED 8–11; mild ED 12–21). EHS: Erectile Hardness Score (scores: 0–4). BMI: body mass index; ED: erectile dysfunction. [a], n_1 = 29, n_2 = 37; [b], n_1 = 28, n_2 = 34; [c], n_1 = 19, n_2 = 29.

TABLE 2. Comparison of outcomes after treatments in the overall study cohorts.

Outcome index	Treatment times			*p* value			
				Whole group	Within-group comparison		
	T-0	T-4	T-8		0–4	0–8	4–8
IIEF-5	11.00 ± 4.91 (9.81, 12.18)	14.10 ± 4.75 (12.95, 15.25)	16.77 ± 4.36 (15.71, 17.82)	<0.001*	<0.001*	<0.001*	<0.001*
EHS	2.27 ± 0.91 (2.04, 2.48)	2.88 ± 0.63 (2.73, 3.04)	3.08 ± 0.57 (2.95, 3.23)	<0.001*	<0.001*	<0.001*	0.113
Morning erection	2.02 ± 0.98 (1.77, 2.26)	2.42 ± 1.11 (2.15, 2.70)	2.91 ± 1.12 (2.63, 3.18)	<0.001*	<0.001*	<0.001*	0.055
Sexual stimulation	1.92 ± 0.93 (1.68, 2.16)	2.50 ± 0.99 (2.25, 2.75)	2.76 ± 0.95 (2.52, 3.00)	<0.001*	0.002*	<0.001*	0.001*
Masturbation erection	2.44 ± 1.01 (2.14, 2.73)	2.81 ± 1.04 (2.51, 3.12)	3.10 ± 1.10 (2.79, 3.42)	<0.001*	0.003*	<0.001*	0.064

*Data are presented as mean ± standard deviation (95% Confidence Interval for Mean). *p < 0.05. IIEF-5: International Index of Erectile Function-5 (scores: severe ED <7; moderate ED 8–11; mild ED 12–21). EHS: Erectile Hardness Score (scores: 0–4). T-0, T-4 and T-8: before the first treatment, after 4 treatments and after 8 treatments. Comparisons are indicated as follows: 0–4 (comparison before treatment and after 4 treatments); 0–8 (comparison before treatment and after 8 treatments); 4–8 (comparison after 4 treatments and after 8 treatments).*

3.3 Comparison between pretreatment and posttreatment outcomes in subgroups

In both the LIPUS and combined groups, IIEF-5 scores improved significantly (Table 3) with treatment ($p < 0.001$ for both). There were no significant differences between the two groups in IIEF-5 scores ($p > 0.05$). After 4 treatments, positive response rates were 40% for the LIPUS group and 44.7% for the combined group ($p > 0.05$). After 8 treatments, positive response rates were 76.7% for the LIPUS group and 81.6% for the combined group. EHS scores also increased after 4 and 8 treatments in both groups ($p < 0.05$), with no significant differences between the groups.

Morning erection and sexual stimulation scores improved significantly after 4 and 8 treatments (Table 4) in both groups ($p < 0.05$). Masturbation erection scores increased in the combined group ($p < 0.001$) but did not show significant changes in the LIPUS group ($p = 0.083$).

Comparisons of pelvic floor scores before and after treatment with biofeedback electric stimulation therapy showed that the pelvic floor score increased significantly from a baseline of 66.21 (±10.28) to 73.89 (±10.27) following the com-

TABLE 3. Comparison of IIEF-5 and EHS scores after treatments in the study subgroups.

Outcome index	IIEF-5		EHS		*p* value		
	LIPUS group	LIPUS + PELVIC group	LIPUS group	LIPUS + PELVIC group	Whole group	Between-group comparison	
						T-4	T-8
T-0	11.50 ± 5.09 (9.60, 13.40)	10.61 ± 4.78 (9.03, 12.18)	2.27 ± 1.08 (1.86, 2.67)	2.26 ± 0.76 (2.01, 2.51)	-	-	-
T-4							
Mean ± SD (95% CI)	14.50 ± 4.95 (12.65, 16.35)	13.79 ± 4.63 (12.27, 15.31)	2.80 ± 0.71 (2.53, 3.07)	2.95 ± 0.57 (2.76, 3.13)	<0.001*	0.544	0.784
Change from baseline	3.00 (1.49, 4.51)	3.18 (2.17, 4.20)	0.53 (0.18, 0.88)	0.68 (0.44, 0.93)			
T-8							
Mean ± SD (95% CI)	16.60 ± 4.92 (14.76, 18.43)	16.90 ± 3.92 (15.61, 18.18)	3.07 ± 0.74 (2.79, 3.34)	3.11 ± 0.39 (2.98, 3.23)	<0.001*	0.346	0.782
Change from baseline	5.10 (3.64, 6.56)	6.29 (4.97, 7.61)	0.80 (0.45, 1.15)	0.84 (0.59, 1.09)			

*Data are presented as mean ± standard deviation (SD) (95% CI: 95% Confidence Interval for Mean). *p < 0.05. LIPUS: low-intensity pulsed ultrasound; LIPUS + PELVIC: LIPUS combined with biofeedback erectile stimulation for pelvic; IIEF-5: International Index of Erectile Function-5 (score: severe ED, <7; median ED, 8–11; mild ED, 12–21). EHS: Erectile Hardness Score (score: 0–4). T-0, T-4 and T-8: before 1st treatment, after 4 treatments and 8 treatments.*

bined therapy ($p < 0.001$).

4. Discussion

Micro-energy treatments, including LIPUS and low-intensity extracorporeal shock wave therapy (LI-ESWT), are widely used in regenerative medicine. LIPUS has been primarily applied to bone healing and muscle injury, with its advantages well-documented [17]. Recently, its potential benefits for ED have begun to emerge. In a study using a Type 1 diabetic rat model, LIPUS was shown to enhance intracavernous pressure and smooth muscle content, as well as activate the TGF-B1 (Transforming Growth Factor Beta 1)/Smad/CTGF (Connective Tissue Growth Factor) signaling pathway, thereby improving ED in the rats [23]. Additionally, LIPUS has demonstrated efficacy in treating conditions such as chronic prostatitis/chronic pain syndrome (CP/CPPS) [24] and ED. Current ED treatments include PDE5Is, vacuum therapy, intracavernous injections, and surgery. LIPUS offers a promising non-invasive alternative with minimal side effects. In this study, LIPUS treatment led to significant improvements in the IIEF-5, EHS and ESS for 68 patients after 4 and 8 treatments. Notably, the IIEF-5 scores showed a 79.1% positive response rate after 8 treatments, which is slightly higher than previously reported findings [25], indicating that LIPUS is a promising option for improving ED.

Based on the observed efficacy of LIPUS and the reported benefits of pelvic floor therapy for ED, we divided patients into two subgroups to evaluate whether adding biofeedback electric stimulation for pelvic floor therapy enhances the effects of LIPUS alone. To our knowledge, our present study represents the first one to investigate the combination of LIPUS with biofeedback electric stimulation for ED. After 4 and 8 treatments, IIEF-5 scores improved in both subgroups. However, there were no statistically significant differences in IIEF-5 scores between the two groups at either the 4-treatment or 8-treatment points. Despite this, the response rate after 8 treatments was slightly higher in the combined therapy group (81.6%) compared to the LIPUS group only (76.7%). Additionally, morning erection scores and sexual stimulation scores increased in both groups. The masturbation erection score improved only in the combined group. While the addition of biofeedback electric stimulation did not significantly enhance the effectiveness of LIPUS alone, this result may be attributed to the need for a larger sample size and longer follow-up duration to better assess the treatment's efficacy.

Although combined biofeedback electric stimulation therapy did not significantly enhance the effects of LIPUS, it does not entirely discount its potential advantages. Pelvic floor muscle training has been shown to be effective in treating conditions such as pelvic pain, urinary incontinence and even in female sexual function recovery [26, 27]. Biofeedback electric stimulation therapy has demonstrated significant benefits in managing urinary incontinence and pelvic pain, which may indirectly improve ED by enhancing pelvic floor muscle function. This supports its potential as an adjunctive treatment. The advantage of biofeedback electric stimulation lies in its ability to be individualized, allowing treatment to be tailored to each patient's specific needs. Real-time feedback and adjustment enable more precise targeting of the pelvic floor muscles, which may improve overall treatment outcomes. In our study, pelvic floor scores significantly improved from 66.21 to 73.89, indicating the potential benefits of the therapy. Although combined therapy with biofeedback electric stimulation did not

TABLE 4. Comparison of ESS score after treatments in the study subgroups.

Outcome index	Variables	Treatment times			*p* value		
		T-0	T-4	T-8	Whole group	Between-group comparison	
						T-4	T-8
Morning erection							
LIPUS group	mean ± SD (95% CI)	1.83 ± 1.07 (1.42, 2.24)	2.31 ± 1.07 (1.90, 2.72)	2.72 ± 1.31 (2.23, 3.22)	0.001*	0.465	0.238
	Change from baseline	-	0.48 (0.07, 0.90)	0.90 (0.57, 1.22)			
LIPUS + PELVIC group	mean ± SD (95% CI)	2.16 ± 0.90 (1.86, 2.46)	2.51 ± 1.15 (2.13, 2.90)	3.05 ± 0.94 (2.74, 3.37)	<0.001*		
	Change from baseline	-	0.35 (0.09, 0.61)	0.89 (0.59, 1.19)			
Sexual stimulation							
LIPUS group	mean ± SD (95% CI)	1.96 ± 1.07 (1.55, 2.38)	2.61 ± 1.17 (2.16, 3.06)	2.78 ± 1.07 (2.37, 3.20)	<0.001*	0.443	0.838
	Change from baseline	-	0.64 (0.29, 1.00)	0.82 (0.56, 1.19)			
LIPUS + PELVIC group	mean ± SD (95% CI)	1.88 ± 0.81 (1.60, 2.16)	2.41 ± 0.82 (2.13, 2.70)	2.74 ± 0.86 (2.43, 3.04)	<0.001*		
	Change from baseline	-	0.53 (0.27, 0.79)	0.85 (0.59, 1.11)			
Masturbation erection							
LIPUS group	mean ± SD (95% CI)	2.53 ± 1.12 (1.98, 3.07)	2.68 ± 1.16 (2.13, 3.24)	2.95 ± 1.08 (2.43, 3.47)	0.083	0.497	0.428
	Change from baseline	-	0.53 (0.27, 0.79)	0.85 (0.59, 1.11)			
LIPUS + PELVIC group	mean ± SD (95% CI)	2.38 ± 0.94 (2.02, 2.74)	2.90 ± 0.98 (2.53, 3.27)	3.21 ± 1.11 (2.78, 3.63)	<0.001*		
	Change from baseline	-	0.52 (0.26, 0.78)	0.83 (0.47, 1.18)			

*Data are presented as mean ± standard deviation (SD) (95% CI: 95% Confidence Interval for Mean). *p < 0.05. LIPUS: low-intensity pulsed ultrasound; LIPUS + PELVIC: LIPUS combined with biofeedback electrical stimulation for pelvic floor therapy; ESS: Erection Satisfaction Score (scores: 0–5), including morning erection, sexual stimulation, and masturbation reaction. T-0, T-4 and T-8 refer to measurements taken before the first treatment, after 4 treatments, and after 8 treatments, respectively.*

lead to significant short-term improvements in ED treatment outcomes, it holds promise for enhancing overall patient function and quality of life. By improving the control and strength of pelvic floor muscles, biofeedback electric stimulation may contribute to better sexual function and overall health.

The multifactorial nature of ED requires addressing the diverse treatment needs of different patient types. Present research indicates that LIPUS has shown promise in improving neurogenic ED in rat models and in mitigating endothelial cell damage under hyperglycemic conditions [28, 29]. Additionally, biofeedback electrical stimulation has proven effective in pelvic muscle training and enhancing patients' quality of life. Thus, combining biofeedback electrical stimulation with LIPUS may offer particular benefits for patients with pelvic floor dysfunction, organic or mixed forms of ED. Future research should focus on determining which patient populations might benefit most from this combined approach. Identifying these groups will aid in optimizing treatment protocols, improving therapeutic outcomes, and developing personalized treatment strategies for various types of ED.

Chen *et al*. [30] defined the effectiveness of interventions for ED as a change in the International Index of Erectile Function-5 (IIEF-5) score from a baseline of ≥2 for mild ED or ≥5 for moderate ED. Our study did not strictly adhere to this minimal clinically important difference (MCID) [31] and did not exclude patients with severe ED. Consequently, this may have led to an overestimation of the positive response rate, which represents a limitation of our study.

Additional limitations include the relatively small sample size of 68 patients. While the collection of outcome measures immediately post-intervention aims to minimize recall bias, larger sample sizes and longer follow-up periods are necessary

to enhance the validity of the results. Furthermore, the positive response rate may be inflated due to the absence of adjustments for the severity of ED. Future research should involve randomized controlled trials with extended follow-up to address these limitations and better assess the effectiveness of the treatment.

5. Conclusions

In conclusion, LIPUS therapy demonstrated significant improvements in patients with ED, reinforcing its efficacy as a treatment modality. Our present study is the first to explore the combination of LIPUS with biofeedback electrical stimulation for pelvic floor therapy, and the results showed no significant differences between the treatment subgroups. However, it confirms that biofeedback electrical stimulation may contribute to pelvic floor improvement. Further research is needed to evaluate whether the combined therapy enhances the efficacy of LIPUS. Future studies should involve larger sample sizes and extended follow-up periods to better determine the potential benefits of this combined approach.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding authors.

AUTHOR CONTRIBUTIONS

LY, RQ and YD—designed the research study and supervised. YL and GC—performed the treatment. SXZ—provided help and advice on research performance technic. SY—collected the data; wrote the manuscript. SY and YZ—analyzed the data. SY and LY—draft the paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All experimental protocols were approved by the Medical Ethics Committee of West China Fourth Hospital of Sichuan University (Ethics approval number: HXSY-EC-2023028) and were conducted following the Declaration of Helsinki. The patients provided written informed consent to participate in this study.

ACKNOWLEDGMENT

We thank Ran Lu from the West China School of Public Health, Sichuan University, for his support in writing, and Shengyin He from the Department of Urology and Pelvic Floor, West China Fourth Hospital, Sichuan University, for his advice on treatment techniques.

FUNDING

This research was funded by the Natural Science Foundation of Sichuan Province, grant number 2023NSFSC0341.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Salonia A, Bettocchi C, Boeri L, Capogrosso P, Carvalho J, Cilesiz NC, *et al*. European association of urology guidelines on sexual and reproductive health-2021 update: male sexual dysfunction. European Urology. 2021; 80: 333–357.

[2] Li MK, Garcia LA, Rosen R. Lower urinary tract symptoms and male sexual dysfunction in Asia: a survey of ageing men from five Asian countries. BJU International. 2005; 96: 1339–1354.

[3] Ludwig W, Phillips M. Organic causes of erectile dysfunction in men under 40. Urologia Internationalis. 2014; 92: 1–6.

[4] Ayta IA, McKinlay JB, Krane RJ. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. BJU International.1999; 84: 50–56.

[5] Pantazis A, Franco I, Gitlin J. Erectile dysfunction in adolescents and young adults. Current Urology Reports. 2024; 25: 225–232.

[6] Xiong Y, Zhang F, Zhang Y, Wang W, Ran Y, Wu C, *et al*. Insights into modifiable risk factors of erectile dysfunction, a wide-angled Mendelian Randomization study. Journal of Advanced Research. 2024; 58: 149–161.

[7] Sivaratnam L, Selimin DS, Abd Ghani SR, Nawi HM, Nawi AM. Behavior-related erectile dysfunction: a systematic review and meta-analysis. The Journal of Sexual Medicine. 2021; 18: 121–143.

[8] Defeudis G, Mazzilli R, Tenuta M, Rossini G, Zamponi V, Olana S, *et al*. Erectile dysfunction and diabetes: a melting pot of circumstances and treatments. Diabetes/Metabolism Research and Reviews. 2022; 38: e3494.

[9] Terentes-Printzios D, Ioakeimidis N, Rokkas K, Vlachopoulos C. Interactions between erectile dysfunction, cardiovascular disease and cardiovascular drugs. Nature Reviews Cardiology. 2022; 19: 59–74.

[10] Selvin E, Wang D, Tang O, Fang M, Christenson RH, McEvoy JW. Elevated cardiac biomarkers, erectile dysfunction, and mortality in U.S. men: NHANES 2001 to 2004. JACC: Advances. 2023; 2: 100380.

[11] Moncada I, Martinez-Salamanca JI, Allona A, Hernandez C. Current role of penile implants for erectile dysfunction. Current Opinion in Urology. 2004; 14: 375–380.

[12] Argiolas A, Argiolas FM, Argiolas G, Melis MR. Erectile dysfunction: treatments, advances and new therapeutic strategies. Brain Sciences. 2023;13: 802.

[13] Qin H, Luo Z, Sun Y, He Z, Qi B, Chen Y, *et al*. Low-intensity pulsed ultrasound promotes skeletal muscle regeneration via modulating the inflammatory immune microenvironment. International Journal of Biological Sciences. 2023; 19: 1123–1145.

[14] Liu X, Zou D, Hu Y, He Y, Lu J. Research progress of low-intensity pulsed ultrasound in the repair of peripheral nerve injury. Tissue Engineering Part B: Reviews. 2023; 29: 414–428.

[15] Chen R, Du W, Zhang X, Xu R, Jiang W, Zhang C,*et al*. Protective effects of low-intensity pulsed ultrasound (LIPUS) against cerebral ischemic stroke in mice by promoting brain vascular remodeling via the inhibition of ROCK1/p-MLC2 signaling pathway. Cerebral Cortex. 2023; 33: 10984–10996.

[16] Lin Z, Gao L, Hou N, Zhi X, Zhang Y, Che Z, *et al*. Application of low-intensity pulsed ultrasound on tissue resident stem cells: potential for ophthalmic diseases. Frontiers in Endocrinology. 2023; 14: 1153793.

[17] Palanisamy P, Alam M, Li S, Chow SKH, Zheng YP. Low-intensity pulsed ultrasound stimulation for bone fractures healing: a review. Journal of Ultrasound in Medicine. 2022; 41: 547–563.

[18] Leighton R, Phillips M, Bhandari M, Zura R. Low intensity pulsed ultrasound (LIPUS) use for the management of instrumented, infected, and fragility non-unions: a systematic review and meta-analysis of healing proportions. BMC Musculoskeletal Disorders. 2021; 22: 532.

[19] Li Z, Ye K, Yin Y, Zhou J, Li D, Gan Y, *et al*. Low-intensity pulsed ultrasound ameliorates erectile dysfunction induced by bilateral cavernous nerve injury through enhancing Schwann cell-mediated cavernous nerve regeneration. Andrology. 2023; 11: 1188–1202.

[20] Myers C, Smith M. Pelvic floor muscle training improves erectile dys-

function and premature ejaculation: a systematic review. Physiotherapy. 2019; 105: 235–243.

[21] Alouini S, Memic S, Couillandre A. Pelvic floor muscle training for urinary incontinence with or without biofeedback or electrostimulation in women: a systematic review. International Journal of Environmental Research and Public Health. 2022; 19: 2789.

[22] Kannan P, Winser SJ, Fung B, Cheing G. Effectiveness of pelvic floor muscle training alone and in combination with biofeedback, electrical stimulation, or both compared to control for urinary incontinence in men following prostatectomy: systematic review and meta-analysis. Physical Therapy & Rehabilitation Journal. 2018; 98: 932–945.

[23] Lei H, Xin H, Guan R, Xu Y, Li H, Tian W, *et al*. Low-intensity pulsed ultrasound improves erectile function in streptozotocin-induced type i diabetic rats. Urology. 2015; 86: 1241.e11–e18.

[24] Lin G, Reed-Maldonado AB, Lin M, Xin Z, Lue TF. Effects and mechanisms of low-intensity pulsed ultrasound for chronic prostatitis and chronic pelvic pain syndrome. International Journal of Molecular Sciences. 2016; 17: 1057.

[25] Cui W, Li H, Guan R, Li M, Yang B, Xu Z, *et al*. Efficacy and safety of novel low-intensity pulsed ultrasound (LIPUS) in treating mild to moderate erectile dysfunction: a multicenter, randomized, double-blind, sham-controlled clinical study. Translational Andrology and Urology. 2019; 8: 307–319.

[26] Ferreira CH, Dwyer PL, Davidson M, De Souza A, Ugarte JA, Frawley HC. Does pelvic floor muscle training improve female sexual function? A systematic review. International Urogynecology Journal. 2015; 26: 1735–1750.

[27] Parra NS, Jaramillo AP, Zambrano J, Segovia D, Castells J, Revilla JC. The effectiveness of pelvic floor muscle exercise in urinary incontinence: a systematic literature review and meta-analysis. Cureus. 2023; 15: e45011.

[28] Liu Y, Pan XY, Zhang XX, Sun JL, Mao YH, Yang Y, *et al*. Role of mechanotransduction mediated by YAP/TAZ in the treatment of neurogenic erectile dysfunction with low-intensity pulsed ultrasound. Andrology. 2023; 11: 1514–1527.

[29] Chen Y, Xiao M, Zhao L, Huang Y, Lin Y, Xie T, *et al*. Low-intensity pulsed ultrasound counteracts advanced glycation end products-induced corpus cavernosal endothelial cell dysfunction via activating mitophagy. International Journal of Molecular Sciences. 2022; 23: 14887.

[30] Chen H, Li Z, Li X, Yang Y, Dai Y, Xie Z, *et al*. The efficacy and safety of thrice *vs* twice per week low-intensity pulsed ultrasound therapy for erectile dysfunction: a randomized clinical trial. The Journal of Sexual Medicine. 2022; 19: 1536–1545.

[31] Rosen RC, Allen KR, Ni X, Araujo AB. Minimal clinically important differences in the erectile function domain of the International Index of Erectile Function scale. European Urology. 2011; 60: 1010–1016.

How to cite this article: Luo Yang, Suliya Yushanjiang, Sixiao Zhang, Yue Zhao, Yi Luo, Guo Chen, *et al*. The efficiency of biofeedback electric stimulation therapy combined with low-intensity pulsed ultrasound in treating erectile dysfunction: a clinical study. Revista Internacional de Andrología. 2024; 22(4): 17-24. doi: 10.22514/j.androl.2024.026.