

## ORIGINAL ARTICLE

## Can low-intensity extracorporeal shockwave therapy improve erectile dysfunction? A prospective, randomized, double-blind, placebo-controlled study

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### Abstract

**Objective.** The aim of this study was to investigate whether low-intensity extracorporeal shockwave therapy (LI-ESWT) can be used as a treatment for men with erectile dysfunction of organic origin. **Materials and methods.** This prospective, randomized, blinded, placebo-controlled study included 112 men unable to have intercourse either with or without medication. Erectile dysfunction was assessed at screening and 5, 12 and 24 weeks after treatment. Assessment was performed by interview and using the Erection Hardness Scale (EHS) and the International Index of Erectile Function (IIEF-15) questionnaire. The men were randomly assigned either to LI-ESWT ( $n = 51$ , active group) or placebo ( $n = 54$ , placebo group). They received five treatments over 5 weeks. Both the participants and the doctors were blinded to the treatment. After 10 weeks, the placebo group received active treatment (active placebo group). **Results.** Twenty-nine men (57%, active group) were able to obtain an erection after treatment and to have sexual intercourse without the use of medication. In the placebo group, only five men (9%) showed similar results ( $p = 0.0001$ ). The EHS after 5 weeks showed that men in the active group experienced a significant improvement in their erectile dysfunction, but no significant result was found with the use of the IIEF – Erectile Function domain. **Conclusions.** This placebo-controlled study over 5 weeks shows that 57% of the men who suffered from erectile dysfunction had an effect from LI-ESWT. After 24 weeks, seven (19%, active group) and nine (23%, active placebo group) men were still able to have intercourse without medication. This study shows a possible cure in some patients, but more research, longer follow-up in the placebo group and an international multi-centre randomized study are needed.

### Keywords:

Erectile dysfunction, extracorporeal shockwave, penis

### History

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### Introduction

Erectile dysfunction is a male sexual dysfunction defined as a consistent or recurrent inability to attain or maintain an erection sufficient for sexual intercourse [1,2]. Erectile dysfunction is a common disorder of middle-aged men that profoundly affects their quality of life [3,4]. For the past 15 years, oral treatment with phosphodiesterase-5 (PDE-5) inhibitors or intracavernosal injection therapy with vasodilating agents has been the preferred treatment for erectile dysfunction [2].

Extracorporeal shockwave therapy (ESWT) has been used for many years in different fields. In 1980, the clinical use of extracorporeal shockwave lithotripsy as a treatment for stone disease in the upper urinary tract began and proved effective [5–7]. Throughout the years, ESWT has been modified for use in other specialities, such as in the treatment of gallstones, sialolithiasis and Peyronie's disease [8–10]. Animal studies have demonstrated neoangiogenesis in myocardial

tissue and skin flaps [11,12], which invites the hypothesis that erectile dysfunction of vascular origin could be treated by ESWT [11–14].

Recent studies have shown promising results of low-intensity extracorporeal shockwave therapy (LI-ESWT) on patients suffering from mild to severe erectile dysfunction [15–17]. A randomized, double-blind, controlled study of men allocated in a two-to-one ratio to LI-ESWT or sham operation showed positive short-term clinical and physiological effects of LI-ESWT on erectile function in PDE-5 inhibitor responders [17].

The aim of the present study was to evaluate LI-ESWT given to men with erectile dysfunction in a one-to-one ratio, and then to investigate and monitor the effects of treatment on erectile function.

### Materials and methods

#### Study population

During the period 2012–2013, 112 men with erectile dysfunction of organic origin who had responded to PDE-5 inhibitors were included in this prospective, randomized, blinded, placebo-controlled study and followed for 5 weeks.

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# Men's Power-Pressure Wave Erectile Regeneration-Therapy: an Early Assessment

## Abstract

**Introduction:** Low intensity extracorporeal shockwave therapy for erectile dysfunction (LISWT) has been well researched as a treatment for Erectile Dysfunction (ED) and used as a first line treatment in many parts of the world as a viable alternative to oral, on-demand, phosphodiesterase type 5 inhibitors (PDE5i). Though effective, these drugs have limitations and are associated with significant non-compliance, side effects and do not reverse the underlying pathology [1-3]. Non-invasive low intensity shockwave therapy (LISWT) has been shown to significantly improve erectile function in men previously PDE5i dependent.

**Materials and Methods:** Vaughan Medical LLC based in Fort Lauderdale, USA purchased the STORZ Medical D-ACTOR 100 to treat patients with ED with the C-15 Ceramic Grey Tip at 15 Hertz and 2.6 Bar with 500 pulses per 1.5 cm on top of the shaft and 1,000 pulses right side then 1,000 left side just below the shaft on the pelvis/corporal bundle. Each patient had 6 treatments either two treatments per week for three weeks or one treatment per week for six weeks randomized by patient preference and/or to fit in with clinic schedules [4-7].

**Results:** Men's PoWER Therapy using the STORZ Medical D-ACTOR 100 (LISWT) has shown in this early experience to be an effective treatment paradigm for erectile dysfunction. All patients completed the treatment regime and all gained an improvement in their SHIM score with an average improvement from Moderate ED to Mild-Moderate after 6 treatments. It appears from this early experience that the optimal treatment regime is six (6) treatments at two treatments per week for three weeks [8-11]. The same energy settings were used for all patients of 15 Hertz and 2.6 bars with 500 pulses per 1.5 cm on top of the shaft and 1,000 pulses right side then 1,000 left sides just below the shaft on the pelvis/corporal bundle.

**Conclusion:** The early experience of LISWT has shown an improvement in the sexual function of patients and a treatment regime of two treatments per week for three weeks appears optimal but further research is required [12-15].

**Keywords:** Men's PoWER Therapy; Low intensity extracorporeal shockwave therapy; Erectile Dysfunction

## Review Article

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**Abbreviations:** LISWT: Low Intensity Extracorporeal Shockwave Therapy for Erectile Dysfunction; ED: Erectile Dysfunction; PDE5i: Phosphodiesterase Type 5 Inhibitors; PDE5: Phosphodiesterase Type 5

## Introduction

Used in medicine since the 1980s, shockwave therapy involves the aiming of shockwaves-energy waves that travel faster than the speed of sound-toward treatment areas from outside the body. The approach is sometimes used to break up kidney stones and treat conditions like joint pain, bursitis, and tendinitis. More recently, scientists have examined its use in the treatment of ED, with encouraging results. Low-intensity extracorporeal shock wave therapy (LIESWT) to the penis has recently emerged as a new and promising modality in the treatment of erectile

dysfunction (ED). Shock waves are acoustic waves that generate a pressure impulse and that carry energy when propagating through a medium [16,17]. The degree of focus can be modulated noninvasively, resulting in variable concentration of energy at a desired location. When shock waves are applied to an organ, the focused waves interact with the targeted deep tissues and act as transient micromechanical forces that initiate several biological changes [18].


This initial study focused on the first initial experience of the LISWT procedure known under the name Men's PoWER Therapy with 22 patients with ED who did not have success with phosphodiesterase type 5 (PDE5) inhibitors or required spontaneous erections. Many patients found the medications are not suitable and some they don't respond to them. Some participants also had vascular risk factors that could contribute

## Shockwave treatment of erectile dysfunction

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### Abstract

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Low-intensity extracorporeal shock wave therapy (LI-ESWT) is a novel modality that has recently been developed for treating erectile dysfunction (ED). Unlike other current treatment options for ED, all of which are palliative in nature, LI-ESWT is unique in that it aims to restore the erectile mechanism in order to enable natural or spontaneous erections. Results from basic science experiments have provided evidence that LI-ESWT induces cellular microtrauma, which in turn stimulates the release of angiogenic factors and the subsequent neovascularization of the treated tissue. Extracorporeal shock wave therapy (ESWT) has been clinically investigated and applied in several medical fields with various degrees of success. High-intensity shock wave therapy is used for lithotripsy because of its focused mechanical destructive nature, and medium-intensity shock waves have been shown to have anti-inflammatory properties and are used for treating a wide array of orthopedic conditions, such as non-union fractures, tendonitis, and bursitis. In contrast, LI-ESWT has angiogenetic properties and is therefore used in the management of chronic wounds, peripheral neuropathy, and in cardiac neovascularization. As a result of these characteristics we initiated a series of experiments evaluating the effect of LI-ESWT on the cavernosal tissue of patients with vasculogenic ED. The results of our studies, which also included a double-blind randomized control trial, confirm that LI-ESWT generates a significant clinical improvement of erectile function and a significant improvement in penile hemodynamics without any adverse effects. Although further extensive research is needed, LI-ESWT may create a new standard of care for men with vasculogenic ED.

**Keywords:** erectile dysfunction, male impotence, shockwaves, therapy

### Introduction

[Go to:](#)

The current nonsurgical treatment modalities in the management of erectile dysfunction (ED) mainly consist of oral phosphodiesterase type 5 inhibitors (PDE5is) and/or intracavernosal injections of vasodilating agents. These treatments are very effective and are reasonably safe with rare unwanted or adverse effects. However, they all share the same major drawback: they do not alter the underlying pathophysiology of the erectile mechanism. These treatments are usually taken on demand, prior to the sexual act, and their effect is essentially time limited. Although daily administration of a PDE5i instead of on-demand treatment does address some of these problems, it still does not modify the pathophysiology of the erectile process. Moreover, the evidence that its effect on the erectile tissue is long-lasting is very limited. Presently, only a small number of men with ED can be offered treatment that would restore their spontaneous erectile function. This group includes those who would benefit from various lifestyle or

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## Sexual Medicine

# Can Low-Intensity Extracorporeal Shockwave Therapy Improve Erectile Function? A 6-Month Follow-up Pilot Study in Patients with Organic Erectile Dysfunction

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### Abstract

**Background:** Low-intensity extracorporeal shockwave therapy (LI-ESWT) is currently under investigation regarding its ability to promote neovascularization in different organs.

**Objective:** To evaluate the effect of LI-ESWT on men with erectile dysfunction (ED) who have previously responded to oral phosphodiesterase type 5 inhibitors (PDE5-I).  
**Design, setting, and participants:** We screened 20 men with vasculogenic ED who had International Index of Erectile Function ED (IIEF-ED) domain scores between 5–19 (average: 13.5) and abnormal nocturnal penile tumescence (NPT) parameters. Shockwave therapy comprised two treatment sessions per week for 3 wk, which were repeated after a 3-wk no-treatment interval.

**Intervention:** LI-ESWT was applied to the penile shaft and crura at five different sites.  
**Measurements:** Assessment of erectile function was performed at screening and at 1 mo after the end of the two treatment sessions using validated sexual function questionnaires, NPT parameters, and penile and systemic endothelial function testing. The IIEF-ED questionnaire was answered at the 3- and 6-mo follow-up examinations.

**Results and limitations:** We treated 20 middle-aged men (average age: 56.1 yr) with vasculogenic ED (mean duration: 34.7 mo). Eighteen had cardiovascular risk factors. At 1 mo follow-up, significant increases in IIEF-ED domain scores were recorded in all men ( $20.9 \pm 5.8$  vs  $13.5 \pm 4.1$ ,  $p < 0.001$ ); these remained unchanged at 6 mo. Moreover, significant increases in the duration of erection and penile rigidity, and significant improvement in penile endothelial function were demonstrated. Ten men did not require any PDE5-I therapy after 6-mo follow-up. No pain was reported from the treatment and no adverse events were noted during follow-up.

**Conclusions:** This is the first study that assessed the efficacy of LI-ESWT for ED. This approach was tolerable and effective, suggesting a physiologic impact on corporeal hemodynamics. Its main advantages are the potential to improve erectile function and to contribute to penile rehabilitation without pharmacotherapy. The short-term results are promising, yet demand further evaluation with larger sham-control cohorts and longer follow-up.

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# Low-Intensity Extracorporeal Shock Wave Therapy—A Novel Effective Treatment for Erectile Dysfunction in Severe ED Patients Who Respond Poorly to PDE5 Inhibitor Therapy

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## ABSTRACT

**Introduction.** Low-intensity shock wave therapy (LI-ESWT) has been reported as an effective treatment in men with mild and moderate erectile dysfunction (ED).

**Aim.** The aim of this study is to determine the efficacy of LI-ESWT in severe ED patients who were poor responders to phosphodiesterase type 5 inhibitor (PDE5i) therapy.

**Methods.** This was an open-label single-arm prospective study on ED patients with an erection hardness score (EHS)  $\leq 2$  at baseline. The protocol comprised two treatment sessions per week for 3 weeks, which were repeated after a 3-week no-treatment interval. Patients were followed at 1 month (FU1), and only then an active PDE5i medication was provided for an additional month until final follow-up visit (FU2).

At each treatment session, LI-ESWT was applied on the penile shaft and crus at five different anatomical sites (300 shocks, 0.09 mJ/mm<sup>2</sup> intensity at 120 shocks/min).

Each subject underwent a full baseline assessment of erectile function using validated questionnaires and objective penile hemodynamic testing before and after LI-ESWT.

**Main Outcome Measures.** Outcome measures used are changes in the International Index of Erectile Function-erectile function domain (IIEF-ED) scores, the EHS measurement, and the three parameters of penile hemodynamics and endothelial function.

**Results.** Twenty-nine men (mean age of 61.3) completed the study. Their mean IIEF-ED scores increased from  $8.8 \pm 1$  (baseline) to  $12.3 \pm 1$  at FU1 ( $P = 0.035$ ). At FU2 (on active PDE5i treatment), their IIEF-ED further increased to  $18.8 \pm 1$  ( $P < 0.0001$ ), and 72.4% ( $P < 0.0001$ ) reached an EHS of  $\geq 3$  (allowing full sexual intercourse).

A significant improvement ( $P = 0.0001$ ) in penile hemodynamics was detected after treatment and this improvement significantly correlated with increases in the IIEF-ED ( $P < 0.05$ ). No noteworthy adverse events were reported.

**Conclusions.** Penile LI-ESWT is a new modality that has the potential to treat a subgroup of severe ED patients. These preliminary data need to be reconfirmed by multicenter sham control studies in a larger group of ED patients. Gruenwald I, Appel B, and Vardi Y. Low-intensity extracorporeal shock wave therapy—A novel effective treatment for erectile dysfunction in severe ED patients who respond poorly to PDE5 inhibitor therapy. *J Sex Med* \*\*;\*\*:\*\*\_\*\*.

**Key Words.** Low Intensity Extracorporeal Shock Wave Therapy; Erectile Dysfunction; Penis

## Introduction

Erectile dysfunction (ED) is one of the most common disorders of middle-aged men that profoundly affect their quality of life [1]. Although tremendous advances for treating this disorder have been made in the past decade, most currently

available treatment modalities still rely on an “on demand” regime, of which up to 35% are unsuccessful [2–4]. From our experience, ED patients who were treated with a phosphodiesterase type 5 inhibitor (PDE5i) tend to search for an alternative treatment modality that would ameliorate their ED. Hence, there is a need for an effective new

## Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis

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## ABSTRACT

**Introduction:** Low-intensity extracorporeal shock wave therapy (Li-ESWT) has been proposed as an effective non-invasive treatment option for erectile dysfunction (ED).

**Aim:** To use systematic review and meta-analysis to assess the efficacy of Li-ESWT by comparing change in erectile function as assessed by the erectile function domain of the International Index of Erectile Function (IIEF-EF) in men undergoing Li-ESWT vs sham therapy for the treatment of ED.

**Methods:** Systematic search was conducted of MEDLINE, EMBASE, and [ClinicalTrials.gov](http://ClinicalTrials.gov) for randomized controlled trials that were published in peer-reviewed journals or presented in abstract form of Li-ESWT used for the treatment of ED from January 2010 through March 2016. Randomized controlled trials were eligible for inclusion if they were published in the peer-reviewed literature and assessed erectile function outcomes using the IIEF-EF score. Estimates were pooled using random-effects meta-analysis.

**Main Outcome Measures:** Change in IIEF-EF score after treatment with Li-ESWT in patients treated with active treatment vs sham Li-ESWT probes.

**Results:** Data were extracted from seven trials involving 602 participants. The average age was 60.7 years and the average follow-up was 19.8 weeks. There was a statistically significant improvement in pooled change in IIEF-EF score from baseline to follow-up in men undergoing Li-ESWT vs those undergoing sham therapy (6.40 points; 95% CI = 1.78–11.02;  $I^2 = 98.7\%$ ;  $P < .0001$  vs 1.65 points; 95% CI = 0.92–2.39;  $I^2 = 64.6\%$ ;  $P < .0001$ ; between-group difference,  $P = .047$ ). Significant between-group differences were found for total treatment shocks received by patients ( $P < .0001$ ).

**Conclusion:** In this meta-analysis of seven randomized controlled trials, treatment of ED with Li-ESWT resulted in a significant increase in IIEF-EF scores.

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**Key Words:** Erectile Dysfunction; Shock Waves; Randomized Controlled Trial; Meta-Analysis

## INTRODUCTION

Erectile dysfunction (ED) is when a man is unable to achieve or maintain an erection for satisfactory sexual performance. ED is estimated to affect one in every five men and, given the aging male population and increasing prevalence of comorbid conditions, it is likely to become even more prevalent.<sup>1</sup> Phosphodiesterase type 5 inhibitors (PDE5is) are often

effective in treating patients with ED and are associated with few side effects; however, a significant proportion of men do not respond to therapy.<sup>2</sup> In men who do not respond to PDE5is or cannot tolerate them because of side effects, options such as medicated urethral suppositories for erection, intracorporeal injections, and penile prostheses are available.<sup>3</sup> Although these treatment options can be effective, long-term usage rates are hindered by side effects and potential complications.<sup>4</sup> Furthermore, these treatments attempt to improve erectile function without treating the underlying pathophysiology of ED.<sup>5</sup>

Low-intensity extracorporeal shockwave therapy (Li-ESWT) has been proposed as a treatment option for ED with minimal side effects. Vardi et al<sup>6</sup> first reported on the use of Li-ESWT for ED; their rationale was extrapolated from cardiac literature reporting improvements in neovascularization. Recent studies of a diabetic rat model have recently supported the notion that Li-ESWT indeed might induce structural changes that regenerate penile tissue.<sup>7</sup>

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# Low intensity extracorporeal shockwave therapy for erectile dysfunction: a study in an Indian population

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SRINI VS, REDDY RK, SHULTZ T, DENES B. Low intensity extracorporeal shockwave therapy for erectile dysfunction: a study in an Indian population. *Can J Urol* 2015;22(1):7614-7622.

*Introduction:* Erectile dysfunction (ED) has been shown to be associated with a number of physical conditions and affects not only physical but also psychosocial health. Currently oral, on-demand phosphodiesterase type 5 inhibitors (PDE5i) are preferred first line treatment. Though effective, these drugs have limitations and are associated with significant non-compliance, side effects and do not reverse the underlying pathology. **Non-invasive low intensity shockwave therapy (LISWT) has been shown to significantly improve erectile function in men previously PDE5i dependent.** We describe our experience and results with this therapy in an Indian population of men with ED. This study assessed the efficacy of low intensity extracorporeal shockwave therapy (LI-ESWT) on Indian men with organic ED who had previously responded to PDE5i.

*Materials and methods:* All the patients underwent a 1 month PDE5i washout period. Men were randomized to receive either 12 sessions of LI-ESWT (n = 95) or placebo/sham therapy (n = 40). Before the first treatment, erectile function and penile hemodynamics were assessed to substantiate a vascular etiology for the ED. Outcomes were assessed using Erection Hardness Score (EHS), International Index of Erectile Function-Erectile Function

Domain (IIEF-EF domain) and Clinical Global Impression of Change (CGIC) scores at 1, 3, 6, 9 and 12 months post-treatment.

*Results:* We found a significant increase in the EHS and IIEF-EF Domain scores from visit 1 to follow up 5 (12 months) in the treated group compared to the placebo group. By 1 month after treatment there were highly significant differences between the LI-ESWT and placebo groups ( $p < 0.0001$ ). Out of 60 men in the LI-ESWT group who completed the study, 47 (78%) men at FU1 and 43 (71%) at FU5 who were initially unable to achieve spontaneous erections hard enough for penetration (EHS  $\leq 2$ ) were able to do so (EHS  $\geq 3$ ) compared to none in the placebo group. The treatment was well tolerated and none of the men experienced treatment related discomfort or reported any adverse effects from the treatment.

**Conclusions:** In this double-blind, placebo-controlled study, LI-ESWT demonstrated a positive long term clinical effect with improvement in erectile function of Indian men with vasculogenic ED who were prior responders to PDE5i therapy. The efficacy and tolerability of this treatment, coupled with its long term benefits and rehabilitative characteristics, make it an attractive new therapeutic option for men with vasculogenic erectile dysfunction.

**Key Words:** erectile dysfunction, low intensity, penis, hemodynamics, shockwaves

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Editorial by XXX on pp. x–y of this issue

## Low-intensity Extracorporeal Shock Wave Treatment Improves Erectile Function: A Systematic Review and Meta-analysis

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### Abstract

**Context:** As a novel therapeutic method for erectile dysfunction (ED), low-intensity extracorporeal shock wave treatment (LI-ESWT) has been applied recently in the clinical setting. We feel that a summary of the current literature and a systematic review to evaluate the therapeutic efficacy of LI-ESWT for ED would be helpful for physicians who are interested in using this modality to treat patients with ED.

**Objective:** A systematic review of the evidence regarding LI-ESWT for patients with ED was undertaken with a meta-analysis to identify the efficacy of the treatment modality.  
**Evidence acquisition:** A comprehensive search of the PubMed and Embase databases to November 2015 was performed. Studies reporting on patients with ED treated with LI-ESWT were included. The International Index of Erectile Function (IIEF) and the Erection Hardness Score (EHS) were the most commonly used tools to evaluate the therapeutic efficacy of LI-ESWT.

**Evidence synthesis:** There were 14 studies including 833 patients from 2005 to 2015. Seven studies were randomized controlled trials (RCTs); however, in these studies, the setup parameters of LI-ESWT and the protocols of treatment were variable. The meta-analysis revealed that LI-ESWT could significantly improve IIEF (mean difference: 2.00; 95% confidence interval [CI], 0.99–3.00;  $p < 0.0001$ ) and EHS (risk difference: 0.16; 95% CI, 0.04–0.29;  $p = 0.01$ ). Therapeutic efficacy could last at least 3 mo. The patients with mild-moderate ED had better therapeutic efficacy after treatment than patients with more severe ED or comorbidities. Energy flux density, number of shock waves per treatment, and duration of LI-ESWT treatment were closely related to clinical outcome, especially regarding IIEF improvement.

**Conclusions:** The number of studies of LI-ESWT for ED have increased dramatically in recent years. Most of these studies presented encouraging results, regardless of variation in LI-ESWT setup parameters or treatment protocols. These studies suggest that LI-ESWT could significantly improve the IIEF and EHS of ED patients. The publication of robust evidence from additional RCTs and longer-term follow-up would provide more confidence regarding use of LI-ESWT for ED patients.

**Patient summary:** We reviewed 14 studies of men who received low-intensity extracorporeal shock wave treatment (LI-ESWT) for erectile dysfunction (ED). There was evidence that these men experienced improvements in their ED following LI-ESWT.

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## ORIGINAL ARTICLE

## Initial experience with linear focused shockwave treatment for erectile dysfunction: a 6-month follow-up pilot study

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Low-intensity shockwaves (LISW) are known to produce revascularization and have been in evaluation and in use to treat erectile dysfunction (ED). The present single-arm pilot study is aimed to assess the safety and efficacy of a dedicated shockwave device (Renova) on vasculogenic ED patients. Fifty-eight patients with mild to severe ED were treated by LISW and their erectile function was evaluated by the International Index of Erectile Function–Erectile Function Domain (IIEF–EF), Sexual Encounter Profile and Global Assessment Questions questionnaires, at baseline and at 1, 3 and 6 months post treatment. The average IIEF–EF increased significantly from 14.78 at baseline to 21.93 at 3 months post treatment and stabilized at 22.26 at 6 months post treatment. Out of 58 patients, 47 (81%) had a successful treatment. No adverse events were reported during the treatment and the follow-up duration. In conclusion, it suggests that the performance of LISW could add a new advanced treatment for ED.

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## INTRODUCTION

Vasculogenic erectile dysfunction (ED) is defined as inability to get or keep an erection firm enough for satisfying sexual intercourse and is maybe originated by diseases, such as diabetes mellitus (DM) and atherosclerotic vascular occlusive disease. Current methods for treating vasculogenic ED aim at reducing symptoms instead of reversing the source of the dysfunction, which in the majority of the patients is due to arterial or inflow disorders.<sup>1</sup> It has been demonstrated that shockwaves can enhance intrinsic angiogenesis and are used to treat ischemic heart disease.<sup>2</sup> Low-intensity shockwaves (LISW) have been evaluated for treating ED in both pilot and randomized sham-controlled studies. The encouraging results that were seen in these studies were the first to show the effect of LISW on ED symptoms,<sup>3–4</sup> but have never been evaluated elsewhere. Recently published study conducted on rats with DM-associated ED showed that low-energy shockwave therapy (LESWT) significantly restored erectile function to levels almost similar to normal levels of controls. The therapeutic efficacy of LESWT is possibly mediated by increased recruitment of mesenchymal stem cells (MSCs) that promote the regeneration of DM-damaged erectile tissues.<sup>5</sup>

The present study was aimed to assess the safety and efficacy of a new dedicated shockwave device, 'Renova', which was designed to achieve substantially superior organ coverage, compared with the existing devices and hence produces positive results with a shorter protocol in a multicenter study.

## SUBJECTS AND METHODS

## Study protocol

This study was a multicenter open-label prospective pilot study, conducted at four sites. It was conducted in accordance with the principles of the Declaration of Helsinki of World Medical Association. Patients gave their written informed consent before participation in the study. This study consisted of a screening phase, treatment phase and a 6-month follow-up

phase. At screening phase, patients had an extensive medical and sexological history evaluation, as well as a physical examination. Inclusion criteria were heterosexual men in stable heterosexual relationship for at least 3 months, aged 20–80 years, with vascular ED (according to physician judgment) for at least 6 months, International Index of Erectile Function–Erectile Function Domain (IIEF–EF)<sup>6</sup> score of 6–25 points. Recruited patients were both responders and nonresponders to phosphodiesterase type 5 inhibitors (PDE5-i). The exclusion criteria were hormonal, neurological or psychological pathology, past radical prostatectomy, any unstable medical or psychiatric condition, spinal cord injury, penile anatomical abnormalities, clinically significant chronic hematological disease, usage of antiandrogens, recovering from cancer in the past 5 years or radiotherapy in pelvic region.

At baseline and follow-up visits IIEF–EF and Sexual Encounter Profile (SEP)—questions 2 and 3 questionnaires were used.<sup>7–8</sup> Global Assessment Questions<sup>9</sup> (GAQ) were used at follow-ups as well. The IIEF–EF questionnaire is widely accepted as the best method to verify ED progress. It includes six questions regarding erectile function and its score range is 1–30 points. Safety was assessed at each treatment and follow-up visits, by answering questions regarding side effects and pain as part of the case report form (CRF). Patients were instructed to inform the investigators if any side effects occur.

Almost all of the patients were using PDE5-i during baseline evaluation. No PDE5-i were used 3 weeks prior to treatment, during shockwave treatment, and until the first follow-up, 1 month post treatments. Answering the questionnaires at the 3 and 6 months post-treatment follow-ups was made, whereas the patients were using PDE5-i, as was done in previously done studies.<sup>3</sup> At all follow-up sessions, patients were instructed to return to the exact PDE5-i consumption as at baseline, as shown in Figure 1. Patients committed to avoid using any ED treatment other than PDE5-i oral medication throughout the study duration.

The treatment consisted of 4 weekly treatment sessions. During each session 3600 shocks of 0.09 mJ mm<sup>2</sup> were applied. Shocks were applied at the penis shaft at right corpus cavernosum and left corpus cavernosum, and at the crura at right crus and left crus, 900 shocks at each area. The treatment areas were the same for each session, so that at the end of the full treatment (four sessions) each area has received 3600 shocks of 0.09 mJ mm<sup>2</sup>.

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# Penile Low Intensity Shock Wave Treatment is Able to Shift PDE5i Nonresponders to Responders: A Double-Blind, Sham Controlled Study

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### Abbreviation and Acronyms

CGIC = Clinical Global Impression of Change

ED = erectile dysfunction

EF = erectile function

FMD = flow mediated dilatation

LIST = low intensity shock wave treatment

MCID = minimal clinically important difference

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**Purpose:** We performed sham controlled evaluation of penile low intensity shock wave treatment effect in patients unable to achieve sexual intercourse using PDE5i (phosphodiesterase type 5 inhibitor).

**Materials and Methods:** This prospective, randomized, double-blind, sham controlled study was done in patients with vasculogenic erectile dysfunction who stopped using PDE5i due to no efficacy. All patients had an erection hardness score of 2 or less with PDE5i. A total of 58 patients were randomized, including 37 treated with low intensity shock waves (12 sessions of 1,500 pulses of 0.09 mJ/mm<sup>2</sup> at 120 shock waves per minute) and 18 treated with a sham probe. In the sham group 16 patients underwent low intensity shock wave treatment 1 month after sham treatment. All patients were evaluated at baseline and 1 month after the end of treatment using validated erectile dysfunction questionnaires and the flow mediated dilatation technique for penile endothelial function. Erectile function was evaluated while patients were receiving PDE5i.

**Results:** In the low intensity shock wave treatment group and the sham group 54.1% and 0% of patients, respectively, achieved erection hard enough for vaginal penetration, that is an EHS (Erection Hardness Score) of 3 ( $p < 0.0001$ ). According to changes in the IIEF-EF (International Index of Erectile Function-Erectile Function) score treatment was effective in 40.5% of men who received low intensity shock wave treatment but in none in the sham group ( $p = 0.001$ ). Of patients treated with shock waves after sham treatment 56.3% achieved erection hard enough for penetration ( $p < 0.005$ ).

**Conclusions:** Low intensity shock wave treatment is effective even in patients with severe erectile dysfunction who are PDE5i nonresponders. After treatment about half of them were able to achieve erection hard enough for penetration with PDE5i. Longer followup is needed to establish the place of low intensity shock wave treatment in these challenging cases.

**Key Words:** testis, erectile dysfunction, high energy shock waves, phosphodiesterase 5 inhibitors, questionnaires

EXTRACORPOREAL LIST of the penis is a novel therapeutic modality for vasculogenic ED.<sup>1</sup> Extracorporeal shock wave therapy has been clinically examined and applied for various

indications.<sup>2</sup> The exact mechanism of LIST is not yet clear, although basic and clinical research have been performed to understand its effect. The acoustic energy of LIST generates

# Evaluation of clinical efficacy, safety and patient satisfaction rate after low-intensity extracorporeal shockwave therapy for the treatment of male erectile dysfunction: an Australian first open-label single-arm prospective clinical trial

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## Objective

To evaluate the efficacy, safety and patient satisfaction rate with low-intensity extracorporeal shockwave therapy (LiESWT) in Australian men with erectile dysfunction (ED), as LiESWT induces neovascularisation and potentially enhances penile perfusion and improves erectile function.

## Patients and Methods

Open-label single-arm prospective study of patients with ED with five-item version of the International Index of Erectile Function (IIEF-5) scores of >12 at baseline were enrolled after informed consent. Patient demographics, change in IIEF-5 and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) scores, and overall satisfaction score (on a 5-point scale) were recorded. Treatment consists of 3000 shockwaves (1000 shockwaves to the distal penis, base of penis and corporal bodies at the perineum) twice weekly for 6 weeks.

## Results

All patients had tried and failed oral phosphodiesterase type 5 inhibitors and most of the patients had had ED for >18 months [mean (range) 21.8 (6–60) months]. No side-effects to LiESWT were reported. Most patients reported an improvement in IIEF-5 score by 5 points (60%) and EDITS Index score by >50% (70%). Most patients were satisfied (scoring 4 out of 5; 67%) and would recommend the therapy to their friends (80%).

## Conclusion

LiESWT appears to improve erectile function, is safe and potential plays an important role in penile rehabilitation in men whom failed medical therapy.

## Keywords

low-intensity extracorporeal shockwave therapy, erectile dysfunction, clinical outcomes, patient satisfaction, erectile function

## Introduction

Erectile dysfunction (ED) is a common psychosexual condition affecting men across all ages and the current management strategies consist of a step-wise approach with modification of risk factors, optimisation of existing medical comorbidities followed by medical therapy, such as oral phosphodiesterase type 5 (PDE5) inhibitors and intracavernosal injection of vasoactive agents, with penile prosthesis implant reserved in the advanced stage [1]. While the efficacy of medical therapy is relatively high and the drugs are generally safe with minimal adverse effects, they treat the symptom of ED only and do not alter the underlying pathophysiology of the disease process.

The concept of penile rehabilitation is based on the premise that such therapy will eventually restore the erectile mechanism and allow men to regain spontaneous erection. Recent reports have indicated that low-intensity extracorporeal shockwave therapy (LiESWT) to the corpora cavernosa could play a role in penile rehabilitation [2,3]. Animal studies showed that LiESWT significantly improves penile haemodynamics and restores pathological changes in the penis of diabetic ED rat models [4,5]. Furthermore, LiESWT induces cellular microtrauma, and promotes angiogenesis by enhancing the expression of vascular endothelial growth factor [6,7] and recruitment of endothelial progenitor cells [8].



# Safety and efficacy of low intensity shockwave (LISW) treatment in patients with erectile dysfunction

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## ABSTRACT

The primary goal in the management strategy of a patient with ED would be to determine its etiology and cure it when possible, and not just to treat the symptoms alone. One of the new therapeutic strategies is the use of low intensity extracorporeal shockwave (LISW) therapy. The mechanism of shockwave therapy is not completely clear. It is suggested that LISW induces neovascularization and improvement of cavernosal arterial flow which can lead to an improvement of erectile function by releasing NO, VEGF and PCNA.

**Materials and Methods:** 31 patients between February and June 2013 with mild to severe ED and non-Phosphodiesterase 5 inhibitors responders were enrolled. Patients underwent four weekly treatment sessions. During each session 3600 shocks at 0.09mJ/mm<sup>2</sup> were given, 900 shocks at each anatomical area (right and left corpus cavernosum, right and left crus). Improvement of the erectile function was evaluated using the International Index of Erectile Function (IIEF-EF), the Sexual Encounter Profile (SEP) diaries (SEP-Questions 2 and 3) and Global Assessment Questions (GAQ-Q1 and GAQ-Q2).

**Results:** At 3-month follow-up IIEF-EF scores improved from 16.54±6.35 at baseline to 21.03±6.38. Patients answering 'yes' to the SEP-Q2 elevated from 61% to 89% and from 32% to 62% in the SEP-Q3. A statistically significant improvement was reported to the Global Assessment Questions (GAQ-Q1 and GAQ-Q2).

**Conclusion:** In conclusion, we can affirm that LISW is a confirmed therapeutic approach to erectile dysfunction that definitely needs more long-term trials to be clarified and further verified.

## ARTICLE INFO

### Key words:

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## INTRODUCTION

Erectile dysfunction (ED) is the main complaint in male sexual medicine and is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Although ED is a benign disorder, it may affect physical and psychosocial health and may have a significant impact on the quality of life (QoL) of patients and their partners (1).

ED seems to affect 52% of 40-70-year-old men (2). Advances in basic and clinical research on ED during the past 15 years have led to the development of a variety of new treatment options, including pharmacological agents for intracavernous, intraurethral, and oral use and the use of vacuum erection devices (1).

Oral therapies have changed the diagnostic and therapeutic approach to ED becoming a major tool in treating ED. In fact, phosphodiesterase-5

**Original Article: Clinical Investigation****Extracorporeal shockwave therapy in the treatment of erectile dysfunction: A prospective, randomized, double-blinded, placebo controlled study**

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**Abbreviations & Acronyms**

ED = erectile dysfunction  
EHS = Erection Hardness Score  
IIEF-ED = International Index of Erectile Function-ED  
Li-ESWT = low-intensity extracorporeal shockwave therapy  
PDE5I = phosphodiesterase type 5 inhibitors  
SHIM = Sexual Health Inventory for Men

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**Objectives:** To investigate the role of low-intensity extracorporeal shockwave therapy in the treatment of erectile dysfunction.

**Methods:** This was a double-blinded, single-center, prospective, randomized, placebo-controlled trial. After a 2-week phosphodiesterase type 5 inhibitor washout period, patients were assessed with Sexual Health Inventory for Men, International Index of Erectile Function-ED domain scores and Erection Hardness Score. Randomization into either the low-intensity extracorporeal shockwave therapy group or the sham group took place. After the 9-week treatment period, patients were followed up 4 weeks later. Follow-up assessment was in the form of International Index of Erectile Function-ED domain score and Erection Hardness Score.

**Results:** A total of 70 patients were recruited into the study, 58 patients completed the study. A total of 28 patients were randomized into the sham therapy arm, and 30 patients were randomized into the low-intensity extracorporeal shockwave therapy arm. There was no significant difference between these two groups in baseline International Index of Erectile Function-ED domain score and Erection Hardness Score. The mean International Index of Erectile Function-ED domain score of the low-intensity extracorporeal shockwave therapy arm and sham arm in week 13 were  $17.8 \pm 4.8$  and  $15.8 \pm 6.1$ , respectively ( $P = 0.156$ ). The mean Erection Hardness Scores in week 13 were  $2.7 \pm 0.5$  and  $2.4 \pm 0.9$ , respectively ( $P = 0.163$ ). When patients were stratified into different baseline Sexual Health Inventory for Men subgroups, the pre-intervention and post-intervention difference in low-intensity extracorporeal shockwave therapy was found to be significant in the subgroup with severe erectile dysfunction (low-intensity extracorporeal shockwave therapy International Index of Erectile Function-ED domain improvement:  $10.1 \pm 4.1$  vs sham therapy International Index of Erectile Function-ED domain improvement:  $3.2 \pm 3.3$ ;  $P = 0.003$ ).

**Conclusion:** The present trial shows the tolerability and clinical efficacy of low-intensity extracorporeal shockwave therapy in a subgroup of patients with erectile dysfunction.

**Key words:** andrology, erectile dysfunction, randomized controlled trial, shockwave therapy.

**Introduction**

The current mainstream non-surgical treatment for ED is the use of oral PDE5I and intracavernosal injections of vasodilating agents.<sup>1</sup> These were proved to be effective and safe treatments;<sup>2</sup> however, they all share the inability to modify the underlying pathophysiology of the erectile mechanism. Alternative treatment modalities have undergone development to address these issues. For example, various lipid-lowering agents (statins and niacin) have been used to counteract the atherosclerotic process.<sup>3,4</sup>

Li-ESWT was proved to be useful in various other medical conditions; for example, neovascularization in myocardial ischemia.<sup>5</sup> Recently, Vardi *et al.* have investigated the impact of Li-ESWT in the treatment of ED, and found a positive short-term clinical effect on men who responded to PDE5I.<sup>6</sup> However, at the moment, evidence on this area is still scarce in the literature.

We carried out a prospective, randomized, placebo-controlled trial to study the role of Li-ESWT in the treatment of ED.



# Penile Low-Intensity Shock Wave Therapy: A Promising Novel Modality for Erectile Dysfunction

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Penile extracorporeal low-intensity shock wave therapy (LIST) to the penis has recently emerged as a novel and promising modality in the treatment of erectile dysfunction (ED). LIST has angiogenic properties and stimulates neovascularization. If applied to the corpora cavernosa, LIST can improve penile blood flow and endothelial function. In a series of clinical trials, including randomized double-blind sham-controlled studies, LIST has been shown to have a substantial effect on penile hemodynamics and erectile function in patients with vasculogenic ED. LIST is effective in patients who are responsive to phosphodiesterase 5 inhibitors (PDE5i) and can also convert PDE5i non-responders to responders. The response to LIST wanes gradually over time, and after 2 years, about half of the patients maintain their function. Extensive research is needed to understand the effect of LIST on erectile tissue, to modify the treatment protocol to maximize its outcomes, and to identify the patients who will benefit the most from this treatment.

**Keywords:** Erectile dysfunction; Penile; Shockwave treatment; Therapy

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## INTRODUCTION

Great advances in the understanding and treatment of erectile dysfunction (ED) have been made in the past two decades. Most patients suffering from ED respond to the available options for treatment, including oral phosphodiesterase type 5 inhibitors (PDE5i) and intracavernosal injections of vasodilating agents. However, these medications are unable to alter the underlying pathophysiology of the erectile mechanism. They are usually taken on demand, prior to the sexual act, and do not improve spontaneous erections [1]. Therefore, a need exists for an effective new treatment concept that would have a durable effect on spontaneous erectile function. Recently, a promising modality was introduced: the application of low-intensity extracorporeal shock wave therapy (LIST) on the penis [2].

Shock waves are acoustic waves that generate a pressure impulse and that carry energy when propagating through a medium. The degree of focus can be modulated non-invasively, resulting in variable concentration of energy at a desired location [3]. When shock waves are applied to an

organ, the focused waves interact with the targeted deep tissues and act as transient micromechanical forces that initiate several biological changes [4]. Extracorporeal shock wave therapy has been clinically examined and applied in various medical fields. High-intensity shock wave therapy is used for lithotripsy because of its focused mechanical destructive nature. Medium-intensity shock waves have been shown to have anti-inflammatory properties and are used for treating a wide range of orthopedic conditions, such as nonunion fractures, tendonitis, and bursitis. Low-intensity shock waves probably have angiogenic properties and are used in the management of chronic wounds, peripheral neuropathy, and in cardiac ischemic tissue [1,2,5,6].

When LIST is applied to an organ, the relatively weak yet focused shock waves interact with the targeted deep tissues where they cause mechanical stress and micro-trauma, also known as shear stress [3]. This shear force then triggers a chain of events that cause the release of angiogenic factors inducing neovascularization of the affected tissues and enhancing the blood flow. Extrapolation