AUA NEWS – September 2017 , Volume 22, Issue 9

# Erectile Dysfunction and the Shocking Truth — Is Shock Wave Therapy Effective?

## LISWT May be Considered a Safe and Effective Disease Modification Strategy for Erectile Dysfunction

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Current treatment strategies for men with erectile dysfunction (ED) may be considered “symptomatic” or “disease modification.” Evidence-based symptomatic treatment options that facilitate erectile function without modifying or reversing the underlying ED pathophysiology include oral phosphodiesterase type 5 inhibitors (PDE5is), intracavernosal injections of vasodilation agents, vacuum constriction devices, intraurethral suppositories and implantation of a penile prosthesis.

Symptomatic strategies have historically been the mainstay of ED management. While safe and effective oral agents have been revolutionary, they are not appropriate for everyone. Symptomatic medical treatments are contraindicated for some, ineffective in almost a third, with discontinuation of such therapies in more than half. Surgical symptomatic treatment for ED is irreversible.

There is an unmet need for additional ED therapies, especially ones that provide disease modification. Evidence-based disease modification ED treatment options are focused on improving underlying erectile pathophysiology and addressing the long-term restoration of physiological erectile functioning. Such strategies include sex therapy, pelvic floor physical therapy, hormone therapy, neurologic therapy (eg sacral and/ or lumbar spine surgery),[1] arterial revascularization procedures, drug eluting stents and regenerative strategies such as low intensity shock wave therapy (LISWT).

LISWT was first used in Israel and Europe as an ED treatment option in 2010. Early studies demonstrated clinically significant benefits as measured by International Index of Erectile Function-

erectile function domain (IIEF-ED) scores, achieved without serious adverse events. A meta-analysis of these early clinical data revealed that significantly increased IIEF scores were noted when the energy flux density (EFD) was less than 0.10 mJ/mm2, the number of shock waves per treatment visit was 3,000 vs 2,000 to 1,500 and the total course of treatment was less than 6 weeks vs 9 weeks.[2] However, each of the subset analyses included only a few studies performed with different shock wave machines on heterogenous patient populations.

Therefore, definitive investigations on the optimum protocol for ED are still required. Variables to be addressed include appropriate EFD in mJ/mm2, number of pulses or shocks per treatment visit, frequency of pulses (Hz), and number and frequency of treatment visits.

Kalyvianakis and Hatzichristou have been examining these critical variables in multiple prospective, randomized clinical trials.[3] For example, there was clinically significant improvement in IIEF-ED and higher minimal clinically important differences (MCID) in IIEF-ED at 6-month followup using 2 treatments vs 1 per week and 6 vs 12 treatments total during a 6-week treatment period using EFD 0.051–0.062 mJ/ mm2. They also showed that repeating treatment after 6 months, up to 18 treatments, resulted in an even further increase in MCID.

How does LISWT theoretically “disease modify” vasculogenic erectile pathophysiology? Shock waves are characterized by a short rise time from ambient pressure to high overpressure, and have been shown to produce compressive and expansive physical force stresses on penile cavernosal stem cells and endothelial cells to elicit a series of biological responses (see figure). These include endothelial progenitor stem cell recruitment and activation of signaling pathways involved in cell proliferation, as well as release of local angiogenic growth factors such as vascular endothelial cell growth factor and nitric oxide synthesis, resulting in neovascularization. [4, 5]

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There is an optimal energy flux density window for this response, so that if this energy density could be reliably delivered over the width of the penis this would ideally translate to improved penile erection response via increased arterial inflow and decreased corporal veno-occlusive dysfunction.

In the United States an open label, single arm pilot study of LISWT was conducted in 2016 in 23 patients with IIEF-ED scores 11 to 25. After a 1-month PDE5i washout, weekly sessions of LISWT (5,000 shocks per session, EFD 0.051-0.062 mJ/mm2) were delivered for 6 sessions overall. MCID were achieved in 5 of 7 patients with mild ED (71%) and 7 of 16 patients with moderate ED (44%). Of the subjects 70% noticed that LISWT improved their ability to have sexual intercourse. The adverse events observed were only mild and transient. We are currently participating in a large multi-institutional, prospective, randomized, placebo controlled, double-blind pivotal study with an open label extension.

I believe that LISWT may one day be a revolutionary disease modification ED therapy. Based on the current condensed ED Process of Care algorithm, LISWT would be considered after “Identification of ED” and “Education of the ED patient and the partner.” LISWT would be used as modification of reversible causes of ED, either avoiding first line or second line therapies, or improving their treatment efficacy. Until the Food and Drug Administration approves this therapy for general clinical use, I would only offer LISWT for ED as part of a clinical trial.

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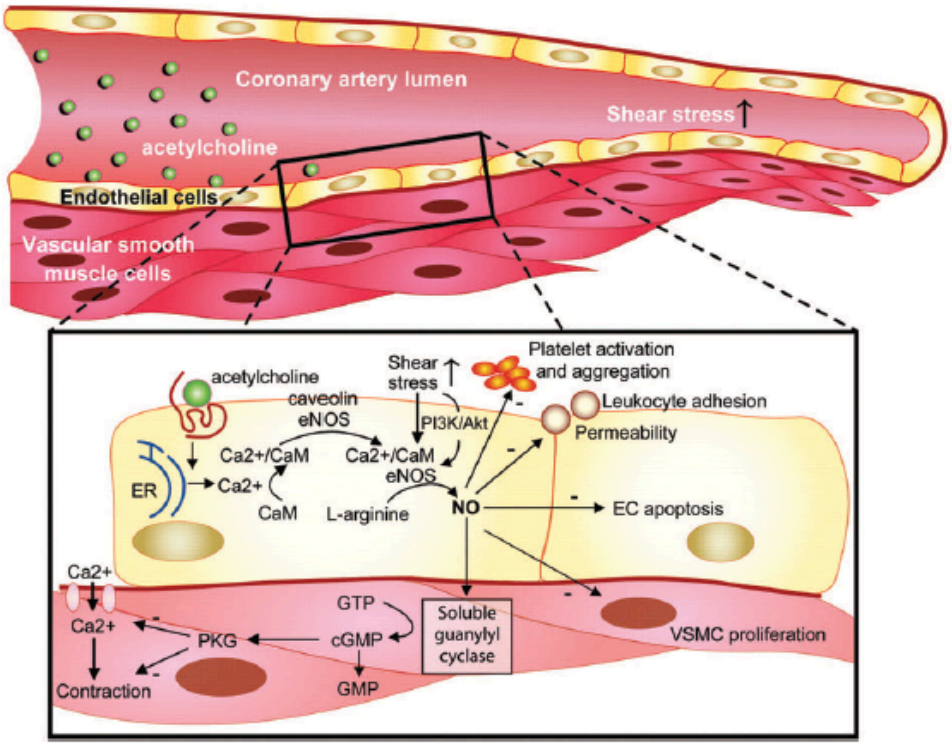


**Figure.** In response to shear stress physical forces, vascular endothelial cells release multiple factors that induce vasodilation. It is hypothesized that mechanism of improvement in penile erection from administration of low intensity penile shock wave therapy is via shock wave induced physical forces (similar to shear stress) to the penile endothelial cells.

Presented at this year's AUA meeting in Boston, Massachusetts. ♦

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