Comment on "Low-intensity Extracorporeal Shock Wave Therapy for Erectile Dysfunction: A Systematic Review and Meta-analysis"

Dear Editor:

We recently read with great interest the article published in *Urology* by Man Libo et al,[1] which described a systematic review and meta-analysis of low-intensity extracorporeal shock wave therapy (LI-ESWT) for erectile dysfunction (ED). Their meta-analysis included 9 randomized controlled trials (RCTs) to investigate the LI-ESWT for patients with ED, the therapeutic efficacy of LI-ESWT for patients with ED, and the relationship of therapeutic efficacy and different setup parameters and protocols. However, it may have the deviation in the direction of the effect of LI-ESWT due to the clinical heterogeneity of included studies.

First, the effect of LI-ESWT should be classified because of the mechanisms underlying the 3 types of ED are different. LI-ESWT is believed to be effective primarily by regenerating microvasculature and improving penile hemodynamics.[2] This could explain why it has been studied mainly in men with vasculogenic ED but not in men with neurogenic ED. In the study by Man Libo et al,[1] both Peyronie's disease (PD) and Chronic Pelvic Pain Syndrome (CPPS)-associated ED were also included. In this situation, in addition to local vascular function impairment, the erectile function will decrease with pain symptoms in CPPS-associated ED patients. And PD-associated ED patients are also related to penile deformity, painful erection, etc.[3] Therefore, the effect on PD/CPPS-associated ED patients is limited owing to their nonvasculogenic origin.

Moreover, with the International Index of Erectile Function (IIEF) of ED, we have the possibility to evaluate the clinically minimal change in the IIEF, which is much more related to a real success rate.[4] The minimal clinically important difference (MCID) is defined as the smallest difference in the IIEF of the erectile function domain that patients perceive as beneficial. For example, the MCID was estimated using IIEF question 7 (Q7): "Over the past 4 weeks, when you attempted sexual intercourse how often was it satisfactory for you?" The following responses are possible: 0, "Did not attempt intercourse"; 1, "Almost never or never"; 2, "A few times (much less than half the time)"; 3, "Sometimes (about half the time)"; 4, "Most times (much more than half the time)"; and 5, "Almost always or always." Minimal improvement in the anchor from baseline to week 12 is defined as a change from little or no satisfactory intercourse at baseline (either 1, "almost never," or 2, "a few times") to satisfactory intercourse sometimes (3, "sometimes"). The significant improvement in MCID is much more related to the improvement of LI-ESWT effect on ED, rather than simple improvement of IIEF.

According to the considerations outlined above, the studies included in the meta-analysis had substantial clinical heterogeneity; the outcome might have underestimated the role of LI-ESWT in organic ED. Instead, it would be more accurate to group depending on distinct pathogenesis when evaluating the therapeutic efficacy of LI-ESWT.

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Reply to Letter to the Editor Comment on "Low-intensity Extracorporeal Shock Wave Therapy for Erectile Dysfunction: A Systematic Review and Meta-analysis"

There are relatively few studies on using low-intensity extracorporeal shock wave therapy (LI-ESWT) for

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erectile dysfunction (ED), and the available studies have small sample sizes and heterogeneous populations. The heterogeneity among the studies could not be avoided completely, since many factors may contribute to ED, such as older age, hypertension, and diabetes. We did realize that there was heterogeneity in our meta-analysis.[1] Currently, a practical way to decrease the heterogeneity is to use subgroup analysis to reduce confounders. As such, we divided the studies into two subgroups according to different ED etiologies: ED (ED only) and ED associated with both PD and chronic pelvic pain syndrome to reduce the influence of heterogeneity.[1]

In our meta-analysis, we intentionally included all etiologies of ED to determine whether LI-ESWT affects all ED, not just vasculogenic ED. Qiu et al and Li et al showed in animal studies that LI-ESWT increases vascularity, increases the number of progenitor cells in the tissue, and promotes nerve regeneration.[2,3] In the correspondence, Zhao simplified the mechanism of LI-ESWT as being exclusively vasculogenic, which we have established as inaccurate.

Zhao comments that the significant improvement in the minimal clinically important difference (MCID) is much more related to the improvement of LI-ESWT effect on ED, rather than simple improvement of the International Index of Erectile Function (IIEF). However, anchor-based MCIDs were estimated using data from 17 randomized, double-blind, placebo-controlled, parallel-group clinical trials of the phosphodiesterase type 5 inhibitor (PDE5-I) tadalafil for 3345 patients treated for 12 weeks.[4] Moreover, MCIDs varied significantly according to baseline ED severity (mild: 2; moderate: 5; severe: 7), and results need to be replicated in studies using other PDE5-Is or in nonpharmacologic intervention studies. Another potential limitation for MCID is the selection of the clinical anchor for the analyses (ie, IIEF Q7). Anchor-based approaches to defining MCIDs should ideally use patient ratings of change administered at different periods of time or on exit from a clinical trial. Actually, the IIEF we applied was recommended by the International Consultation on Sexual Medicine in 2004 and 2010 as the gold standard self-report questionnaire for measuring erectile function (EF) in clinical trials and observational studies, and has already been accepted and recommended by regulatory agencies worldwide for approval of erectile dysfunction (ED) therapies. A recent PubMed search indicated more than1400 citations of the IIEF since its development in 1996. Multiple validation studies and systematic reviews of the IIEF have been published supporting its use in both clinical and research settings.[5] Consequently, we applied IIEF for our meta-analysis.

Based on the above, despite of those limitations mentioned above, the major aim of this meta-analysis was to evaluate the currently available clinical trials of LI-ESWT for ED to determine whether or not LI-ESWT improves penile function, to stimulate more research, and to encourage scientists and clinicians to design high-quality clinical trials that will help identify the real benefits of LI-ESWT and the ideal patient population for treatment.

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"Re: Direct Vision Internal Urethrotomy for Short Anterior Urethral Strictures and Beyond: Success Rates, Predictors of Treatment Failure, and Recurrence Management"

Dear Editor,

I have read the articles of Kluth et al named "*Direct Vision Internal Urethrotomy for Short Anterior Urethral Strictures and Beyond: Success Rates, Predictors of Treatment Failure and Recurrence Management*" with interest.[1] In the discussion part of the article, publications of Zehri et al were referenced.[2] It is stated in the article that the success rate after internal urethrotomy is given as 37% in writing of Zehri et al titled "*Predictors of recurrence of urethral stricture disease following optical Urethrotomy*." However, in abstract section of original article of Zehri et al, it is said: "For a mean follow up of 8.9+/-11 months, the overall recurrence rate was

I have no commercial relationship that could create any conflict of interest.
I have reviewed the final version of the letter and approve it for publication.