

EFFECTIVITY OF LI-ESWT FOR ERECTILE DYSFUNCTION MANAGEMENT BASED ON EHS AND IIEF-5

¹Agung Adhitya Indra, ¹Besut Daryanto, ¹Basuki Bambang.

¹Department of Urology, Faculty of Medicine/University of Brawijaya, Saiful Anwar General Hospital, Malang.

ABSTRACT

Objective: This study was conducted to determine the effectiveness of LI-ESWT as therapeutic modality in ED patients. **Material & Methods:** Erectile Hardness Scales (EHS) and International Index of Erectile Function (IIEF-5) scores was measured in 22 patients. The observation was performed before therapy started, each therapy session, and each follow-up session. Therapy sessions were carried out once a month for 8 months and follow-up was done once a month for 8 months. **Results:** There was a significant increase in IIEF-5 scores since the 5th LI-ESWT therapy session ($P < 0.05$, Wilcoxon Test). Also, there's a significant increase in EHS score in 1 month after LI-ESWT therapy sessions was completed ($P = 0.05$, Wilcoxon Test). **Conclusion:** There is a significant improvement in the EHS and IIEF-5 score before and after treatment using LI-ESWT. LI-ESWT seems to be a promising future therapy for ED.

Keywords: EHS, erectile dysfunction, IIEF-5, LI-ESWT.

ABSTRAK

Tujuan: Penelitian ini dilakukan untuk mengetahui efektivitas LI-ESWT sebagai modalitas terapi pada pasien DE. **Bahan & Cara:** Erectile Hardness Scales (EHS) serta International Index of Erectile Function (IIEF-5) diukur pada 22 pasien. Pengamatan dilakukan sebelum terapi dimulai, setiap sesi terapi, dan setiap sesi tindak lanjut. Sesi terapi dilakukan sebulan sekali selama 8 bulan dan tindak lanjut dilakukan sebulan sekali selama 8 bulan. **Hasil:** Terjadi peningkatan skor IIEF-5 yang signifikan sejak sesi terapi LI-ESWT ke-5 ($P < 0.05$, Wilcoxon Test). Selain itu, terdapat peningkatan yang signifikan pada skor EHS dalam 1 bulan setelah sesi terapi LI-ESWT selesai ($P = 0.05$, Uji Wilcoxon). **Simpulan:** Terdapat peningkatan yang signifikan pada skor EHS dan IIEF-5 saat sebelum dan sesudah perlakuan menggunakan LI-ESWT. LI-ESWT tampaknya menjadi terapi masa depan yang menjanjikan pada kasus disfungsi ereksi.

Kata Kunci: EHS, disfungsi ereksi, IIEF-5, LI-ESWT.

Correspondence: Besut Daryanto; c/o: Department of Urology, Faculty of Medicine/Brawijaya University, Saiful Anwar General Hospital, Jl. Jaksa Agung Suprpto No.2, Klojen, Kec. Klojen, Kota Malang, Jawa Timur 65112, Indonesia. Phone: +6282233678283, Fax: +62341333030, Email: urobess.fk@ub.ac.id

INTRODUCTION

Erectile dysfunction (ED) is a consistent or recurring inability to get or maintain an erection sufficient for sexual intercourse.¹ ED is a sexual dysfunction related to psychological conditions or other diseases that preceded ED.² This disorder can reduce a person's quality of life and become a psychological burden for patients and their partners.³ The World Health Organization (WHO) estimates that in Asia there are approximately 87 million men with ED. It is estimated that by 2025, there will be 322 million people in the world with this problem.⁴ The prevalence of ED in Indonesia is uncertain.

However, it is estimated that 16% of men aged 20-75 years old experience erectile dysfunction.⁵

The first line therapy of ED is lifestyle modification.³ Lifestyle modifications include quitting smoking, eliminating obesity, increasing physical activity, avoiding alcohol consumption, avoiding psychological stress, and controlling medical comorbidities (hypertension, diabetes, and hyperlipidemia).⁶ Current therapies available for management beyond lifestyle modification include Testosterone Replacement Therapy (TRT), PDE5 inhibitors (PDE5i), intracavernous injection therapy, vacuum constriction devices (VCD), intraurethral prostaglandin suppositories, and

surgical placement of penile prosthesis.³ It has been reported that Low Intensity - Extracorporeal Shockwave Therapy (LI-ESWT) improved erectile function by 67%. Furthermore, 28% of samples achieved normal erections.⁷ A patient's erectile ability can be assessed by the Erection Hardness Score (EHS) and his erectile function can be assessed by the International Index of Erectile Function (IIEF-5). A meta-analysis study with 7 Randomized Clinical Trials (RCTs) with a total of 522 participants reported that the use of LI-ESWT significantly improved EHS and IIEF-5 scores.⁸ This report shows that LI-ESWT is a promising candidate for use as a therapeutic modality for ED problems. Research is needed on the use of this therapeutic modalities.

OBJECTIVE

This study was conducted to determine the effectiveness of the use of LI-ESWT therapeutic modalities in cases of ED by evaluating the EHS and IIEF-5 score as parameters.

MATERIAL & METHODS

This was a Single Group Pre and Post Test Observation. In this study, we followed a group of research subjects from before being given therapy, to after being given therapy. Before therapy, we carried out IIEF-5 and EHS score measurement. After the treatment started, the same parameters were remeasured during the LI-ESWT therapy session and once monthly for 8 months after the series of LI-ESWT therapy sessions were completed. The study has obtained approval from Saiful Anwar General Hospital's Research Ethics Committee No: 400/206/K.3/302/2020.

The participants of this study were patients who had been diagnosed with erectile dysfunction at Saiful Anwar General Hospital, Malang from January to March 2019. The sample collection method used was total sampling. So that all patients who met the diagnosis of erectile dysfunction at the visit to our hospital will be followed (observed) during this research duration. Informed consents were collected from all participants before this study begins. Participants will be excluded if they cannot complete 8 sessions of therapy with LI-ESWT or cannot be followed 8 months after a series of therapy sessions with LI-ESWT were completed.

In this study, the ESWT unit used was PiezoWave2 Multi Use 60 from Elvation® (Deutsch) with a Linear focused FBL 10x5G2 therapy source probe. The Probe was pointed to the cavernous body and is driven along the penis (corpus cavernosa) and perineum (penile crura).

The EHS score was measured by asking the participants about the description of the erectile condition they experienced most frequently during the current month (the last 4 weeks) with reference to: Score 0 if the penis was not enlarged; 1 if the penis is enlarged but not hard; 2 if the penis is hardened but not hard enough to penetrate; 3 if the penis is hard enough for penetration but not maximal hardness; 4 if the penis is maximally hard and stiff. The IIEF-5 score is measured by a questionnaire as published by Hackett in 2017¹². The ED condition was categorized based on the scores by following rules: 1-7: severe erectile dysfunction, 8-11: moderate erectile dysfunction, 12-16: mild-moderate erectile dysfunction, 17-21: mild erectile dysfunction.

Data in the form of EHS and IIEF-5 scores were analyzed for the normality of the data distribution based on the Standardized Residual value of the data. Then if the distribution is normal, the analysis is continued with the Paired T-Test and Post Hoc Analysis of Tukey HSD. However, if the data is not normally distributed, then a non-parametric test is performed using the Friedman test and the Wilcoxon test. The analysis aimed to determine the significant of difference in EHS and IIEF-5 scores between before intervention with LI-ESWT therapy and after intervention. The data is said to be significant if the P-value is less than 0.05 (Confident Interval=95%).

RESULTS

In this study, there were 22 patients who met the inclusion criteria. There were no participants who dropped out (met the exclusion criteria). The characteristics of the research sample are shown in Table 1.

The mean IIEF-5 score of all participants is presented in Figure 1. Based on the Normality Test on the Standardized Residual value of IIEF-5 Scores, it was found that $P < 0.05$ in all groups (Saphiro-Wilk), so the data were not normally distributed. Then we performed Friedman and Wilcoxon Test. The Friedman test for IIEF-5 data yields $P < 0.001$. This suggests that Erectile Dysfunction therapy with

Table 1. Characteristics of The Participants.

Patients' Characteristics	(n=22)
Age (year) (mean \pm SD)	55 \pm 8.06
40-44	1 (4.5%)
45-49	8 (36.4%)
50-54	2 (9.1%)
55-59	4 (18.2%)
60-65	4 (18.2%)
>60	3 (13.6%)
Smoking (n)	
Yes	17 (77.3%)
No	5 (22.7%)
Type 2 Diabetes Mellitus	
Yes	3 (13.6%)
No	19 (86.4%)
Hypertension	
Yes	4 (18.2%)
No	18 (80.0%)
Dyslipidemia	
Yes	5 (22.7%)
No	17 (77.3%)
Erectile Dysfunction	
Duration (year)	
1	7 (31.8%)
2	5 (22.7%)
3	4 (18.2%)
4	2 (9.1%)
5	4 (18.2%)

LI-ESWT can significantly increase the IIEF-5 score, or that there is a significant difference between the IIEF-5 score measured before and after therapy administration. To find out in more detail the timing of a significant change, the Wilcoxon Test was performed. It appears that there has been a significant increase in IIEF-5 scores since the 5th LI-ESWT therapy ($P < 0.05$).

The EHS scores of all participants are illustrated in Figure 2. Clinically, the majority of patients (77.2%) had achieved an EHS score as high as 3-4 in the first month after the LI-ESWT therapy series was completed. In other words, there were 5 patients who had not experienced improved EHS scores. Then in the second month, there were 3 patients (13.6%) who until the end of follow-up did not experience any clinically significant increase in their EHS scores (EHS score < 3). Based on the Normality Test on the Standardized Residual value, it was found that $P < 0.05$ in all groups (Saphiro-Wilk), so the data were not normally distributed. Then a different test was performed using the Non-Parametric method, namely the Friedman and Wilcoxon Test. The Friedman test for EHS scores yields $P < 0.001$. This suggests that Erectile Dysfunction therapy with LI-ESWT can significantly improve the EHS score, or that there is a significant difference between the EHS scores measured before and after therapy. To find out in more detail the timing of a significant change the Wilcoxon Test was performed. It appears that there has been a significant increase in EHS score in 1 month after LI-ESWT therapy sessions was completed ($P = 0.05$).

Table 2. Summary of Wilcoxon Test Results.

Treatment Session	Before Treatment (P)	Post Treatment (Month)	Before Treatment (P)
1st	1.000	1st	0.002*
2nd	0.564	2nd	$< 0.001^*$
3rd	0.317	3rd	$< 0.001^*$
4th	0.083	4th	$< 0.001^*$
5th	0.023*	5th	$< 0.001^*$
6th	0.010*	6th	$< 0.001^*$
7th	0.009*	7th	$< 0.001^*$
8th	0.016*	8th	$< 0.001^*$

All IIEF-5 Scores recorded during treatment sessions and post treatment sessions were compared to IIEF-5 scores before treatment was given. *significantly difference (Wilcoxon test).

Table 3. Summary of Wilcoxon Test Results

Treatment Session	Before Treatment (P)	Post Treatment (Month)	Before Treatment (P)
1st	0.157	1st	0.008*
2nd	0.157	2nd	0.001*
3rd	0.157	3rd	0.001*
4th	0.157	4th	0.001*
5th	0.157	5th	< 0.001*
6th	0.564	6th	< 0.001*
7th	0.317	7th	< 0.001*
8th	0.317	8th	< 0.001*

All EHS Scores recorded during treatment sessions and post treatment sessions were compared to EHS scores before treatment was given. *significantly difference (Wilcoxon test).

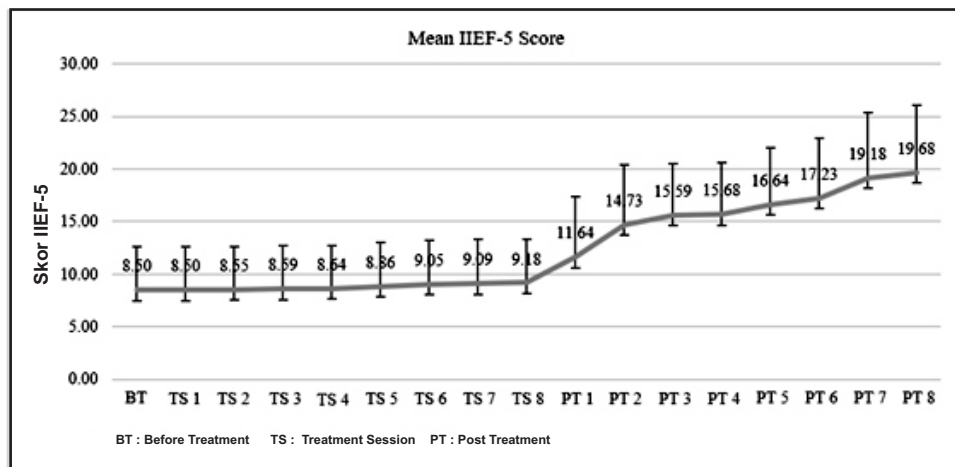


Figure 1. Mean IIEF-5 Score As the duration of follow-up goes. It appears that there is a trend of increasing IIEF-5 scores in patients after treatment with LI-ESWT.

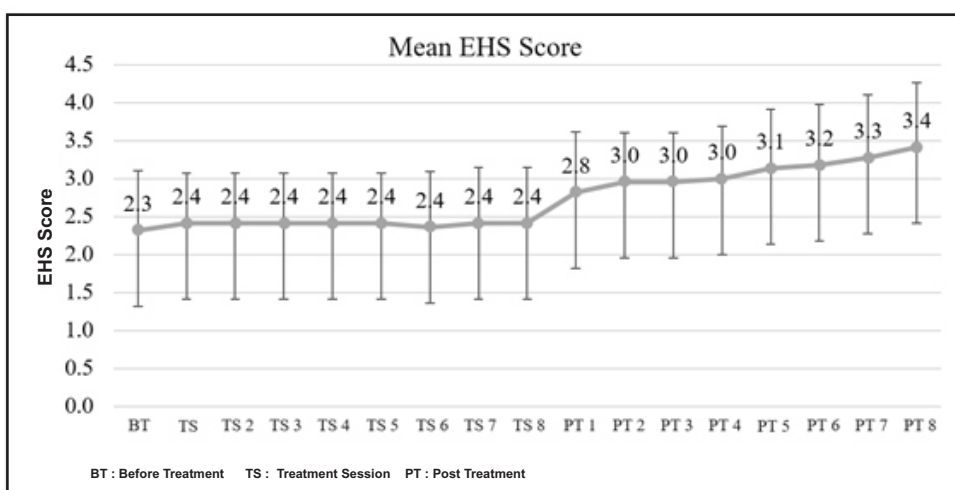


Figure 2. Average EHS Score As the duration of follow-up increased. it appears that there is a trend of increasing EHS scores in patients following LI-ESWT therapy.

DISCUSSION

In this study, 22 participants were gathered as research subjects. All participants in this study were over 40 years old. The majority were aged 45-49 years (36.4%). In the age range of 40-44 years there was 1 patient (4.5%). in the 50-54 years age range there were 9.1% of participants. and 4 participants (18.2%) in the 55-59. the same numbers were found in 60-55 years old age group. Furthermore, there were 3 participants (13.6%) who were over 60 years old. This study is in line with other studies which found that the incidence of erectile dysfunction often begins at the age of 40 and is indeed closely related to increasing age.⁹⁻¹⁰ Increasing age in men can cause vascular disorders. Vasoconstriction and vasodilation disorders as well as the presence of atherosclerosis often cause erectile disorders in men over 40 years old.⁹

In this study, it was also found that the majority of participants were smokers (77%). In several studies, smoking has been positively associated with an increased risk of ED. Longitudinal epidemiological studies have reported the relative risk of developing ED to be 1.5-2 times greater in smokers than in nonsmokers. In the Boston Area Community Health survey (a cross-sectional study of 2,301 men), it was reported that there was a dose-response relationship between smoking and ED. The significance of the association between smoking and ED was achieved at 20-year cumulative exposure after adjusting for risk factors for age, cardiovascular disease, and diabetes.⁶

Other risk factors for ED recorded in this study were history of type 2 diabetes mellitus, hypertension, and dyslipidemia. However, these risk factors were owned by patients in this study with a percentage of 13.6%, 18.2%, and 22.7% respectively for type 2 diabetes mellitus, hypertension, and dyslipidemia. These factors are known to increase the risk of developing ED, so it is common to find a history of these risk factors in ED patients.⁶

This study found that there was a statistically significant increase in the EHS score since the 1st month after the completion of LI-ESWT therapy when compared to before treatment with LI-ESWT. The EHS score which was clinically significant (≥ 3) was obtained on average since the 2nd month after LI-ESWT therapy series was completed. In accordance with the significant increase in the EHS score. In this study, it was found that there was also a significant increase in the IIEF-

5 score since the 5th week of starting therapy when compared to the IIEF-5 score before LI-ESWT therapy was begun. A clinically significant increase in IIEF-5 scores based on the mean was achieved at the 2nd month after treatment with LI-ESWT (mean IIEF-5 scores was improved from moderate to mild-moderate category). Then an even better category was achieved at 6 months after the completion of all sessions (8 sessions) of therapy with LI-ESWT (means IIEF-5 scores achieved mild ED). At the end of the follow-up for 8 months after the last session of therapy with LI-ESWT, it was found that 9 patients (40.9%) no longer had ED (IIEF-5 score > 21). and 10 other patients reached the mild ED category (45.5 %). Meanwhile, 3 patients (13.6%) still experienced severe ED.

The finding of improvement in EHS and IIEF-5 scores supports previous reports that indeed therapy with LI-ESWT can improve conditions of erectile dysfunction as measured by the IIEF-5 score. A meta-analysis study with 14 Randomized Clinical Trials and 833 patients reported that therapy with LI-ESWT improved the patient's erectile function and significantly increased IIEF-5 along with an increase in their EHS score as well.¹¹ The possible mechanisms underlying this improvement are angiogenesis, vasodilation modulation, and nerve regeneration. Angiogenesis can occur as a result of direct mechanical stress on the penile tissue, including vascular tissue, and through an increase in pro-angiogenesis factors due to the rapid size change of gases in the blood as an implication of the shockwave and the large amplitude generated by the LI-ESWT. Mechanical stress, and rapid changes in the size of the gas bubbles in the vascular area will cause minor endothelial damage and increased shear stress. This will induce the production of Vascular Endothelial Growth Factor (VEGF) and an increase in pro-angiogenesis mRNA expression.¹²

In this study, there were 3 patients who did not experience improvement. Among them, there were 2 patients of whom have multiple risk factors: smoking, dyslipidemia, and hypertension. Both of these patients were not obese when examined. It has previously been reported that LI-ESWT is effective for patients with diabetes as well as patients with a history of hypertension.¹³ In severe arteriogenic erectile dysfunction, LI-ESWT has also been reported to be ineffective.¹⁴ Furthermore, there was 1 more patient in this study who did not improve with LI-ESWT. This particular patient had a history of radical cystectomy. The radical cystectomy

procedure is indeed at risk of causing erectile dysfunction up to 89%.¹⁵ In this surgical procedure, damage to the cavernous nerve often occurs so that nerve stimulation for an erection will decrease.¹⁶ It is likely that in such patients, the LI-ESWT is not sufficient to induce the necessary nerve regeneration.

This study has several limitations. In this study, there is a very limited number of samples and only conducted in a single center. So maybe in a wider population, different results will be found. In addition, this study used a single group only design, so that there was no comparison group of patients who experienced ED but did not undergo therapy with LI-ESWT as a comparison. This study also did not analyze the factors that might affect the patient's erectile ability; including age, lifestyle modification, control of comorbidities (diabetes, hypertension, and dyslipidemia), psychological conditions, and risk factors for vasculopathy and other neuropathies. This study also did not analyze the relationship between the history of PDE5 inhibitor use and the success of therapy using LI-ESWT.

CONCLUSION

We concluded that all ED patients in our hospital was over 40 years old. The majority are aged 45-49 years. The majority of patients are smokers. Other risk factors for ED recorded in this study were a history of type 2 diabetes mellitus, hypertension, and dyslipidemia. Finally, there is a significant improvement in the EHS and IIEF-5 score before and after treatment using LI-ESWT. LI-ESWT seems to be a promising future therapy for ED.

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