

# COMPARISON OF THE EFFECTIVENESS OF EXTRACORPOREAL SHOCKWAVE THERAPY (ESWT) AND TADALAFIL ON ORGANIC ERECTILE DYSFUNCTION

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## ABSTRACT

**Objective:** To find a comparison of the effectiveness of ESWT and Tadalafil on organic erectile dysfunction. **Material & Methods:** This is a Quasi Experiment study that was carried out from February 2018 to April 2018. ESWT treatment was performed in Urology Outpatient Clinic. Cialis 10 mg was used in case of Tadalafil. The sample size is 40 patients consists of 20 patients each treatment. The data was processed with a significance limit of  $p < 0.05$ . **Results:** The sample age average is 61.7 years, the level of total cholesterol is 191 mg/dL, FBG 112.5 mg/dL, 2hPPBG 134.5 mg/dL, HDL 44.9 mg/dL, LDL 137.5 mg/dL, ureum 27 mg/dL, and creatinin 0.8 mg/dL. The proportion of Diabetes Mellitus patients in this study is 50% and hypertension 57.5%, which is 15% of them belong to mild erectile dysfunction category, 37.5% mild to moderate, 5% moderate, and 42.5% severe. We found an increasement of EHS on 75% patients that were treated with ESWT and 5% on patient that were treated with Tadalafil, and it is statistically significant ( $p < 0.05$ ). **Conclusion:** We found that ESWT and Tadalafil can increase EHS of organic erectile dysfunction patients, which ESWT is more effective than Tadalafil.

**Keywords:** Erectile dysfunction, ESWT, tadalafil, erection hardness score.

## ABSTRAK

**Tujuan:** Mengetahui perbandingan efektivitas ESWT dan Tadalafil pada disfungsi ereksi organik. **Bahan & Cara:** Penelitian ini merupakan studi Quasi Experimental dari Februari 2018-April 2018. Terapi ESWT dilakukan di Poliklinik Urologi RSUP Dr. M Djamil Padang. Tadalafil yang digunakan adalah Cialis 10 mg. Besar sampel adalah masing-masing 20 pasien. Data diolah dengan batas kemaknaan  $p < 0.05$ . **Hasil:** Rerata usia sampel adalah 61.7 tahun, rerata kolesterol total 191 mg/dL, GDP 112.5 mg/dL, GD2jPP 134.5 mg/dL, HDL 44.9 mg/dL, LDL 137.5 mg/dL, ureum 27 mg/dL, dan kreatinin 0.8 mg/dL. Pasien DM sebanyak 50%, hipertensi 57.5%, dan 15% termasuk kategori disfungsi ereksi ringan, 37.5% ringan-sedang, 5% sedang, 42.5% berat. Terdapat peningkatan nilai EHS pada 75% pasien yang diterapi dengan ESWT, dan 5% pada pasien yang diterapi dengan Tadalafil dan bermakna secara statistik ( $p < 0.05$ ). **Simpulan:** ESWT dan Tadalafil sama-sama terbukti meningkatkan nilai EHS pasien disfungsi ereksi organik, tetapi ESWT lebih efektif dibandingkan dengan Tadalafil.

**Kata Kunci:** Disfungsi ereksi, ESWT, tadalafil, erection hardness score.

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## INTRODUCTION

The prevalence of erectile dysfunction (ED) around the world was more than 157 million in 1995 and will become 322 million in 2025. In Europe, men with ED will reach 43 million at that time. According to the National Consensus Conference on Impotence, erectile dysfunction is defined as the inability to achieve or maintain an erection sufficient for sexual performance.<sup>1,2</sup>

Erectile Dysfunction (ED) causes a lot of problems such as anxiety, depression and lost of self-esteem. Sexual dysfunction does not only affects on male but also on his partner, and will cause a severe psychological disorder.<sup>1,3</sup>

Comorbidities erectile dysfunction patients are Diabetes Mellitus (DM), ischemic heart disease, and peripheral vascular disease. Indonesia is on the 4<sup>th</sup> rank in Diabetes around the world with about 8.4 million people. From the study in Sanglah Denpasar

hospital, they found from 137 diabetes patients, 79.5% of them got ED.<sup>4,5</sup> Diabetes mellitus affects 0.5% to 2% of the world population, and the prevalence of ED is 3 times higher on DM.<sup>6</sup>

The goal of ED treatment is to make the patients have a better sexual function and increase their quality of life. The first line treatment for ED is using medical treatment such as Phosphodiesterase 5 inhibitor (PDE5 Inhibitor) group. Tadalafil 10 mg has an effective therapy effect and minimal side effect.<sup>7</sup>

The effectiveness of PDE5 inhibitor and intra cavernosum injection is only 70%, but the treatments are not cure the etiology and the pathophysiology. More than half of the ED patients are well-tolerate to PDE5 inhibitor, but about 30 to 40% are not. Patients who cannot tolerate to PDE5 inhibitor like patients with nitrate consumption or non respond to PDE5 inhibitor can choose Extracorporeal Shock Wave Therapy (ESWT). A recent study have shown promising result for ED patients from mild ED to severe ED.<sup>8-10</sup>

## OBJECTIVE

This study aims to find a comparison of the effectiveness of ESWT and Tadalafil on organic erectile dysfunction.

## MATERIAL & METHODS

This is a Quasi Experiment study that performed from February 2018 to April 2018. Subjects of this study were informed and consented to complete the given questionnaire at the time of diagnosing ED. Inclusion criteria were male patients visiting Urology Outpatient Clinic at Dr. M Djamil Hospital who were diagnosed with ED. ED is defined in accordance to the National Institute of Health (NIH) consensus conference. ED is defined as the inability to achieve and maintain an erection sufficient for sexual intercourse. Exclusion criteria were patients who refused to continue their treatment, patient with psychogenic ED, patient with venous leakage ED.

The self-administered questionnaire contained The International Index of Erectile Function-5 (IIEF-5), health-related comorbidities. The IIEF-5 consists of questions 1-5 for assessing erectile function. Scoring of the IIEF-5 domain of erectile function allowed classification of each patient as having no ED (22-25), mild ED (17-21),

mild to moderate (12-16), moderate ED (8-11), and severe ED (5-7). Comorbidities for ED included hypertension and diabetes mellitus.

This study compares the effectiveness of ESWT and Tadalafil on organic erectile dysfunction. Forty subjects in this study are divided into 2 groups. The first group will get ESWT and the second group will get Tadalafil. The protocol of ESWT we used in this study is 6 treatment every 3-4 days. The therapy was administered in contact manner using direct application onto the treated area. The application we used in this study is Medispec ED 1000 machine which belongs to Dr. M Djamil Hospital. During each session, 1500 shocks with 300 shocks or pulses applied in each area (three along the penile shafts and two at the crural level). Tadalafil used in this study was Cialis 10 mg. We use EHS (Erection Hardness Score) to see the effectiveness of treatment. EHS consists of 4 grade, grade 1 is penis is larger but not hard, grade 2 is penis is hard but not hard enough for penetration, grade 3 is penis is hard enough for penetration but not completely hard, grade 4 is penis is completely hard and fully rigid. EHS is rated before the treatment and after the treatment (6 sessions of ESWT or once Tadalafil consumption).

All statistical analyses were conducted using Statistical Package for Social Science v25. We used t-test and Mann-Whitney test to analyze the sample characteristic. T-test for analyze age, cholesterol level, HDL level, and Ureum level. Mann-Whitney test used to analyze Fasting Blood Glucose level, 2 hours post prandial blood glucose level, and creatinine level. We also used the Mann-Whitney test to compare the effectiveness of ESWT and Tadalafil. Chi-square test and two-sample Kolmogorov-Smirnov test were used to analyze the distribution data of comorbidities, and IIEF-5 between both groups of the sample. We used the Wilcoxon signed rank test to analyze the effectiveness of ESWT and Tadalafil. P value<0.05 was considered to represent significant difference between tested populations.

## RESULTS

Table 1 shows the distribution of characteristics of the 40 subjects and table 2 shows the distribution of characteristic of both groups.

Subjects Characteristic could be seen on table 1 and on table 2 we could see the characteristic on both groups. In this study, subjects characteristics were analyzed with the Shapiro-Wilk test. Fasting blood glucose, 2 hours post prandial blood glucose,

LDL, and creatinine have abnormal distribution data ( $p$  value $<0.05$ ). We got a significant difference in data distribution on age and LDL level. Confounding factors could be seen in table 3 and been analyzed with chi-square test and the results were there were no association between the confounding factors with result of the treatment ( $p>0.05$ ). Table 4 and 5 show the result of ESWT and Tadalafil, which made an

increasement of EHS. Table 6 and 7 show the effectiveness of ESWT and Tadalafil as treatment for organic erectile dysfunction, they were analyzed with the Wilcoxon signed rank test.

In table 8, we can see a comparison of the effectiveness of ESWT and Tadalafil. It was analyzed with the Mann-Whitney test, and we got that ESWT was more effective than Tadalafil.

**Table 1.** Subjects characteristic.

| Characteristic | Mean              | Median            |
|----------------|-------------------|-------------------|
| Age            | 61.7 $\pm$ 11.86  | 64 (32 – 78)      |
| FBG            | 112.5 $\pm$ 28.09 | 104 (81 – 178)    |
| 2-hPPBG        | 134.5 $\pm$ 45.77 | 119.5 (73 – 293)  |
| Total Chol     | 191 $\pm$ 41.86   | 184.5 (119 – 287) |
| HDL            | 44.9 $\pm$ 8.30   | 42 (32 – 66)      |
| LDL            | 137.5 $\pm$ 39.95 | 133 (84 – 218)    |
| Ureum          | 27 $\pm$ 8.56     | 25 (13 – 47)      |
| Creatinin      | 0.8 $\pm$ 0.32    | 0.8 (0.6 - 2.1)   |

**Table 2.** Subjects Characteristic on ESWT and Tadalafil.

| Characteristic | Mean               |                   | Median          |                | P       |
|----------------|--------------------|-------------------|-----------------|----------------|---------|
|                | ESWT               | Tadalafil         | ESWT            | Tadalafil      |         |
| Age            | 57.8 $\pm$ 13.5    | 65.65 $\pm$ 8.58  | 56.5 (32 -78)   | 66 (40–78)     | 0.036** |
| FBG            | 122.25 $\pm$ 32.2  | 102.7 $\pm$ 19.3  | 118 ( 83–178)   | 99.5 (79–173)  | 0.083*  |
| 2-hPPBG        | 144.25 $\pm$ 45.1  | 124.85 $\pm$ 45.4 | 141 (73–241 )   | 112.5 (90–293) | 0.068*  |
| Total Chol     | 195.75 $\pm$ 43.6  | 186.3 $\pm$ 40.61 | 184.5 (135–287) | 185 (119–274)  | 0.482** |
| HDL            | 44.1 $\pm$ 6.19    | 45.7 $\pm$ 10.08  | 42 (36–59)      | 43.5 (32–66)   | 0.549** |
| LDL            | 150.79 $\pm$ 44.05 | 120 $\pm$ 29.44   | 152 (38–218 )   | 113 (84–181)   | 0.003*  |
| Ureum          | 25.85 $\pm$ 7.19   | 28.15 $\pm$ 9.79  | 25 (15–39 )     | 26 (13–47)     | 0.403** |
| Creatinin      | 0.85 $\pm$ 0.28    | 1.15 $\pm$ 0.35   | 0.95 (0.6–1.8 ) | 1.1 (0.8–2.1)  | 0.090*  |

\*Mann-Whitney test , \*\*t-test

**Table 3.** Confounding factors.

| Factors           | ESWT |    | Tadalafil |    | Total |      | P       |
|-------------------|------|----|-----------|----|-------|------|---------|
|                   | F    | %  | F         | %  | F     | %    |         |
| Diabetes Mellitus |      |    |           |    |       |      | 0.058*  |
| Yes               | 13   | 65 | 7         | 35 | 20    | 50   |         |
| No                | 7    | 35 | 13        | 65 | 20    | 50   |         |
| Hypertension      |      |    |           |    |       |      | 0.749*  |
| Yes               | 11   | 55 | 12        | 60 | 23    | 57.5 |         |
| No                | 9    | 45 | 8         | 40 | 17    | 42.5 |         |
| IIEF-5            |      |    |           |    |       |      | 0.978** |
| Mild              | 3    | 15 | 3         | 15 | 6     | 15   |         |
| Mild-moderate     | 9    | 45 | 6         | 30 | 15    | 37.5 |         |
| Moderate          | 0    | 0  | 2         | 10 | 2     | 5    |         |
| Severe            | 8    | 40 | 9         | 45 | 17    | 42.5 |         |

\*Chi-square test, \*\*Two-sample Kolmogorov-Smirnov test

**Table 4.** EHS change on the ESWT group.

| EHS                 | Increase | No | Decrease |
|---------------------|----------|----|----------|
| Proportion (person) | 15       | 5  | 0        |
| Percentage (%)      | 75       | 25 | 0        |

**Table 5.** EHS change on the Tadalafil group.

| EHS                 | Increase | No | Decrease |
|---------------------|----------|----|----------|
| Proportion (person) | 5        | 15 | 0        |
| Percentage (%)      | 25       | 75 | 0        |

**Table 6.** ESWT effectiveness on Organic ED.

| EHS       | Mean         | Median  | P        |
|-----------|--------------|---------|----------|
| Pre-ESWT  | 1.45 ± 0.51  | 1 (1-2) | < 0.001* |
| Post-ESWT | 2.75 ± 0.851 | 3 (1-4) |          |

\*Wilcoxon signed rank test

**Table 7.** Tadalafil effectiveness on Organic ED

| EHS             | Mean        | Median  | P      |
|-----------------|-------------|---------|--------|
| Pre- Tadalafil  | 1.8 ± 0.768 | 2 (1-3) | 0.038* |
| Post- Tadalafil | 2.2 ± 1.005 | 2 (1-4) |        |

\*Wilcoxon signed rank test

**Table 8.** Comparison of the effectiveness of ESWT and Tadalafil on Organic ED.

| Treatment | Δ EHS      |           | P      |
|-----------|------------|-----------|--------|
|           | Mean       | Med       |        |
| ESWT      | 1.3 ± 0.92 | 1.5 (0-3) | 0.002* |
| Tadalafil | 0.4 ± 0.75 | 0.1 (0-2) |        |

\*Mann-Whitney test

## DISCUSSION

The mean age of ED patients in this study was 61.7 ± 11.86 years ranged from 32-78 years. It closed to Lei et al. study, they got a conclusion that ED seldom affects young men, and the incidence will increase as the age increase and the highest incidence is above 60 years.<sup>8</sup>

In Kimura et al. study, they found ED prevalence about 1%-10% on patient under 40 years and will become 50% on 40-70 years. They also found that age is correlated with EHS, age above 70 years have 16 times probability to have a lower EHS than 20-29 years patient.<sup>11</sup>

Based on laboratory finding, the mean level of total cholesterol was 191 mg/dL, HDL was 44.9

mg/dL and LDL was 137.5 mg/dL. In the study of Skeldon et al. and Kimura et al., they got there is not a significant correlation between ED and dyslipidemia.<sup>11,12</sup>

Based on the kidney function test, we got the mean level of ureum and creatinine was 27 mg/dL and 0.8 mg/dL. Patient with chronic kidney disease will get a decrease of testosterone level due to disturbance of the Hipofise-Gonadal pathway, and the erection function will become better after kidney transplantation. The other things that make ED on patients with chronic kidney disease are polyneuropathy uremia, depression, anxiety, loss of self-esteem, and finally will decrease the libido.<sup>13</sup> But in this study, we found a normal level on kidney function because the etiology of ED in this study was



not kidney disorder but another factor like DM and hypertension.

From 40 subjects, we got 50% patients with DM. As we know that 60% DM patients have a vascular disorder and peripheral vascular disease in DM will decrease the penile blood flow. ED is found on 60% patient with DM.<sup>6,14</sup>

Patients with ED, especially on the middle-age have to underwent DM screening because ED patients have 4.58 times higher risk to have DM if we compare to non ED patients.<sup>12</sup>

In this study, we also found 57.5% patients with hypertension. In the study of Skeldon et al. and Kimura et al., they found that hypertension patients have a higher risk to have ED, 1.2 times until 2.35 times higher, but on statistical analysis, the correlation is not significant.<sup>12</sup>

Based on the grading of ED, we use IIEF-5 scoring, and in this study, we found 15 % patients with mild ED, 37.5% mild-moderate ED, 5% moderate ED, and 42.5% with severe ED. It is different from Vardi et al. and Reisman et al. study, which they found the most patient were in mild to moderate grade. But the result of this study is similar to Saraswati et al. study, they found the most patient were in severe grade (34.4%).<sup>5,15,16</sup>

Based on ESWT treatment, we found an EHS increasement 75% patients and it is statistically significant. The same result from the study of Olsen et al. found an increasement of sexual function in 57% patients.<sup>10</sup> The study of Reisman et al. also found an increasement of sexual function in 82.5% ED patient that was treated with ESWT.<sup>15</sup> In the study of Gruenwald et al., they found 75% patient have a better erectile function, and they also got a significant increasement of endothelial function and penile blood flow.<sup>17</sup>

In Qiu et al. study, they did a study in DM rat, and the treated with ESWT, after two weeks, they found increasement of erectile function by measured intracavernosum pressure. They did a histology test and found an increasement of nNOS-positive in neural, endothelial, and smooth cell. ESWT can treat ED by stimulating regeneration of nNOS-positive in neural, endothelial, and smooth cell.<sup>9</sup>

In the subjects that treated with Tadalafil, we found EHS increasement on 25% patients, and it was statistically significant with  $p=0.038$ . In the study of Chen et al., they did a study on 47.626 patients with ED that treated with PDE5 inhibitor and they found a better erectile function on the patients.<sup>7</sup> PDE5 inhibitor is the first line therapy for ED, but in this

study, from 20 subjects, only 5 subjects that respond to the treatment. This is because so many factors that influence the effectiveness of PDE5 inhibitor which in this case was Tadalafil, such as sexual stimulation, and the waiting-time.<sup>7</sup>

From statistical analysis about comparison of the effectiveness of ESWT and Tadalafil, that we got from the delta of EHS before and after treatment. We got the p-value was 0.002. In this study, we could not eliminate the other factors that can relate to ED besides Diabetes mellitus and hypertension like low testosterone level that can decrease sexual desire that will cause ineffectiveness of Tadalafil because Nitric Oxide that been released is decrease and affected on inadequate of erection. In this study, the author also could not control the waiting-time of Tadalafil because it is one of the factors that make inadequacy of PDE5 inhibitor except dose, and sexual stimulation.<sup>18</sup>

## CONCLUSION

ESWT and Tadalafil can increase EHS of organic erectile dysfunction patients, which ESWT is more effective than Tadalafil.

## REFERENCES

1. Sumampouw AM, Tendean L, Wantouw B. Penanganan disfungsi ereksi secara dini. Dalam Jurnal Kedokteran Komunitas dan Tropik. 2015; 3(3): 196-1999.
2. Smith-Harrison, Patel A, Smith RP. The devil is in the details: an analysis of the subtleties between phosphodiesterase inhibitors for erectile dysfunction. In Transl Androl Urol. 2015; 5(2): 181-186.
3. Kirby R. An Atlas of Erectile Dysfunction 2<sup>nd</sup> edition. The Parthenon Publishing Group. London; 2004.
4. Sugiharso MA, Saraswati MR. Hubungan disfungsi ereksi pada penderita Diabetes Melitus tipe 2 terhadap kualitas hidup di Poliklinik Penyakit Dalam RSUP Sanglah Provinsi Bali. Dalam E-Jurnal Medika. 2016; 5(5): 1-8.
5. Saraswati MR, Sanjaya D, Suastika K. Prediktor disfungsi ereksi pada penderita Diabetes tipe 2 di Poliklinik Penyakit Dalam RS Sanglah Denpasar. Dalam J Peny Dalam. 2008; 9(2): 129-133.
6. Lue T. Physiology of penile erection and pathophysiology of erectile dysfunction. In Campbell-Walsh Urology 10<sup>th</sup> edition. Philadelphia: Saunders Elsevier; 2012. p. 688-720.
7. Chen L, Stauble S, Schneider M, Kessels A, Ivic S, Bachmann L, Kessler T. Phosphodiesterase 5 inhibitors for the treatment of erectile dysfunction: A trade-off network meta-analysis. In European

- Association of Urology. 2015; 68: 674-680.
8. Lei H, Liu J, Li H, Wang L, Xu Y, Tian W, Lin G, et al. Low-intensity shock wave therapy and its application to erectile dysfunction. In *World J Mens Health*. 2013; 31(3): 208-214.
9. Qiu X, Lin G, Xin Z, Ferretti L, Zhang H, Lue TF, Lin CS. Effects of low-energy shockwave therapy on the erectile function and tissue of a diabetic rat model. In *J Sex Med*. 2013; 10: 738-746.
10. Olsen A, Persiani M, Boie S, Hanna M, Lund L. Can low-intensity extracorporeal shockwave therapy improve erectile dysfunction? A prospective, randomized, double-blind, placebo-controlled study. In *Scandinavian Journal of Urology*. 2014: 1-5.
11. Kimura M, Shimura S, Tai T, Kobayashi H, Baba S, Kano M, Nagao K. A web-based survey of erection hardness score and its relationship to aging, sexual behaviour, confidence, and risk factors in Japan. In *Sex Med*. 2013; 1: 76-86.
12. Skeldon S, Detsky A, Godenberg S, Law M. erectile dysfunction and undiagnosed diabetes, hypertension, and hypercholesterolemia. In *Annals of Family Medicine*. 2015; 13(4): 331-334.
13. Papadopoulou E, Varouktsi A, Lazaridis A, Boutari C, Doumas M. Erectile dysfunction in chronic kidney disease: From pathophysiology to management. In *WJN*. 2014; 4: 379-387.
14. Wylie K, MacInnes I. Erectile Dysfunction. In *handbook of sexual dysfunction*. Taylor and Francis Group, New York. 2005: 156-185.
15. Reisman Y, Hind A, Varanekas A, Motil I. Efficacy and safety of linear focused shockwaves for erectile dysfunction (RENOVA)-a second generation technology. In *Clinical Review of Low Intensity Shockwave Therapy*. 2013.
16. Vardi Y, Appel B, Kilchevsky A, Gruenwald I. Does low intensity shock wave therapy have a physiological effect on erectile function? Short term results of a randomized, double-blind, sham controlled study. In *The Journal of Urology*. 2012; 187: 1769-1775.
17. Gruenwald I, Kitrey N, Appel B, Vardi Y. Low-intensity extracorporeal shock waves therapy in vascular disease and erectile dysfunction: Theory and Outcomes. In *Sex Med Rev*. 2013; 1: 83-90.
18. Park K, Hwang E, Kim S. Prevalence and medical management of erectile dysfunction in Asia. In *Asian Journal of Andrology*. 2011; 13: 543-549.