Research Square

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Comparative study on treatment satisfaction of low-intensity extracorporeal shock wave therapy versus on-demand sildenafil for erectile dysfunction in young men and their partners

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Research Article

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Abstract

Background: Recently, it is reported that erectile dysfunction (ED) is very prevalent among young males that has a great impact on patients' and their partners' sexual satisfaction. PDE5is and other more invasive options merely provide symptom relief rather than a permanent improvement of the condition, while the lasting improvement of low-intensity extracorporeal shockwave therapy (Li-ESWT) on ED has been confirmed. We aimed to compare treatment satisfaction rates in young men and their partners who received treatment for with sildenafil and Li-ESWT.

Methods: Patients complaining of ED during a consultation at our andrology and urology outpatient clinic between April 2019 and April 2020 were considered candidates for study. Participants choose to enter one of 2 active treatment groups according to their treatment intention after a 4-week washout period of past ED treatment, either 9-week Li-ESWT or 100mg on-demand sildenafil. The erectile function was evaluated by the erectile function domain of the International Index of Erectile Function questionnaires (IIEF-EF), while the treatment satisfaction in patients and their partners was evaluated by the Erectile Dysfunction Inventory of Treatment Satisfaction questionnaires (EDITS) of patient version and partner version respectively.

Results: 72 participants completed the study (42 in the Li-ESWT group and 30 in the sildenafil group). Patients in both groups are young men. 4-week after the last session, the score of IIEF-EF for Li-ESWT and sildenafil was 16.3± 5.5 and 18.3± 6.5 ($P>0.05$) respectively. The total EDITS index of patient version and partner version are similar in the two groups. Among EDITS questions measuring overall satisfaction and efficacy lasting time, the score was higher in the Li-ESWT group.

Conclusions: We found that Li-ESWT may have better satisfaction than on-demand sildenafil for young ED patients. However, Further studies are needed to determine the factors influencing satisfaction.

Trial registration: This is a non-randomized clinical trial, registered at Chinese Clinical Trial Registry (ChiCTR, http://www.chictr.org.cn/edit.aspx?pid=36572&htm=4), number ChiCTR1900021685, date 05/03/2019.

Background

Erectile dysfunction (ED) is a common condition affecting more than 50% of men aged 40–70 years [1]. However, recently, it is reported that ED is very prevalent among young males [2]. Moreover, ED is a shared sexual problem that has a great impact on patients' and their partners' sexual satisfaction [3].

Although phosphodiesterase type 5 inhibitors (PDE5is) are a huge step forward in the management of ED, they are far from flawless. Prominent shortcomings of PDE5is are their non-universal success rate, absence of spontaneity, and life-long drug commitment [4]. PDE5is and other more invasive options merely provide symptom relief rather than a permanent improvement of the condition [5, 6].

Over the last decade, penile low-intensity extracorporeal shockwave therapy (LI-ESWT) has emerged as a promising option for the treatment of ED. The major potential advantage of low-intensity extracorporeal shockwave therapy (Li-ESWT) is the promising restoration of the ability to have spontaneous erections [7, 8]. Improvement in erectile function by Li-ESWT to the corporal bodies has been validated in human clinical trials [9, 10, 11]. To our knowledge, no comparative study of sildenafil versus Li-ESWT has been conducted concerning the satisfaction aspect. Herein, we performed a comparative analysis of two treatments by validated instruments to assess patients' and partners' treatment satisfaction for ED.

Methods

1. Inclusion and Exclusion Criteria

This study is a prospective, non-randomized, controlled clinical trial, registered at Chinese Clinical Trial Registry (ChiCTR, http://www.chictr.org.cn/edit.aspx?pid=36572&htm=4), number ChiCTR1900021685, date 05/03/2019. From April 2019 to April 2020, patients complaining of ED during a consultation at our andrology outpatient clinic were considered candidates. Inclusion criteria were men who had the complaint of ED for at least 6 months, at least 18 years old, and in stable relationships. During the first visit, subjects were screened according to the eligibility criteria and filled out the Internation Index of Erectile Function (IIEF) questionnaire.

Patients were excluded on the grounds of an International Index of Erectile Function–Erectile Function domain (IIEF-EF) score ≥26, anatomic penile deformation or penile prosthesis, unstable medical (including clinically significant hepatobiliary or renal disease, and unstable cardiovascular disease) or psychiatric condition, treatment with anticoagulants, a previous history of a neurological pathology, radical pelvic surgery, irradiations, as well as hypogonadism.

Patients of various pathogenesis were enrolled, comprising psychogenic, organic, and mixed ED. Positive signs, such as diabetes, cardiovascular comorbidities, and negative nocturnal and morning erections, defined the organic pathogenesis. Participants who had significant psychological abnormalities with the presence of nocturnal or morning erections were diagnosed as psychogenic. Rigiscan was used to record nocturnal penile tumescence and rigidity (NPTR) parameters. Men of both psychogenic and organic manifestations were diagnosed as mixed ED.

2. Study protocol

After a 4-week washout period of past treatment, participants entered one of 2 active treatment groups, either 9-week Li-ESWT (treatment group) or 100mg on-demand sildenafil therapy (control group) according to the intention of treatment. Erectile function was assessed by IIEF-EF score, that are sensitive to ED treatment. IIEF-EF score of ≤25 was defined as ED [12].

For the Li-ESWT protocol, the treatment scheme comprised 2 sessions per week for 3 weeks and repeated after a 3-week interval. Omnispec ED1000 (Medispec Ltd., Yehud, Israel) was used to produce low-

intensity shock waves [13]. Li-ESWT was applied in each treatment session for 3 min at 5 different penile anatomical sites (3 locations on the penile shaft and 2 on the penile crura). Each Li-ESWT comprised 300 shocks per treatment point at an energy density of 0.09 mJ/mm^2 and a frequency of 120/min. For the sildenafil protocol, the participants self-administered sildenafil at a dose of 100mg 1 hour before each event of intercourse.

The follow-up visit was scheduled 4 weeks after the final session when participants completed the IIEF-EF and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaires. All patients stopped using Li-ESWT or sildenafil during follow-up. The study and treatment flow chart is presented in Fig.1. Erectile function improvement was evaluated by IIEF-EF. 4-score improvement of IIEF-EF defined a positive result of minimal clinically important difference (MCID) [14]. The primary outcome was the patients' and partners' satisfaction as measured by EDITS [15].

3. Statistical Analysis

The baseline characteristics were compared using Student's t-test or Mann-Whitney U test for quantitative variables, and the chi-square test for categorical variables. Descriptive statistics for the duration of disease in both groups were shown as median along with the 25th (P25) and 75th percentile (P75) because of skewed distribution, and the Mann-Whitney U test was used to compare the differences in median levels for the duration of disease between both groups. The means of overall IIEF-EF and the overall EDITS scores between the two treatment groups were compared using Student's t-test, and further using the analysis of covariance for adjustment for appropriate potential confounding variables. Statistical significance was defined as $P < 0.05$. All data were analyzed using SPSS for Windows software (ver. 20.0; SPSS Inc., Chicago, IL, USA).

Results

Initially, a total of 126 patients were screened and met the inclusion criteria. 31 patients were excluded in terms of the exclusion criteria, and 95 participants were recruited for the study. Follow-up was carried out from September 2019 to August 2020. Nine participants dropped out in the Li-ESWT group, and fourteen participants dropped out in the sildenafil group. Overall, 72 patients and their partners were analyzed. The patients flow chart is presented in Fig. 2. The patients in the two groups have similar demographic profiles except age (31.2 ± 5.2 in the sildenafil group vs 33.9 ± 6.2 in the Li-ESWT group, $p < 0.05$) (Table 1).

Table 1
Baseline characteristics of participants in two treatment groups

Characteristics	LI-ESWL (n = 42)	Sidenafil (n = 30)	P
Age(y)	33.9 ± 6.2	31.2 ± 5.2	< 0.05
BMI (kg/m2)	24.4 ± 3.5	25.2 ± 3.1	> 0.05
Duration of disease (P25-P75) (m)	24.0 (12.0–36.0)	12.0 (11.5–24.0)	> 0.05
Educational status			
University	26(61.9)	20(66.7)	> 0.05
High or middle school	15(35.7)	10(33.3)	> 0.05
Primary school	1(2.4)	0(0.0)	> 0.05
Comorbidities			
Hypertension	6(14.3)	8(26.7)	> 0.05
Diabetes	2(4.8)	4(13.3)	> 0.05
Hyperlipidemia	6(14.3)	6(20.0)	> 0.05
ED etiology			
Organic	15(35.7)	11(36.7)	> 0.05
Psychogenic	14(33.3)	8(26.6)	> 0.05
Mixed	13(31.0)	11(36.7)	> 0.05
IIEF-EF before treatment	8.6 ± 3.6	7.1 ± 2.7	> 0.05
IIEF-EF, after treatment	16.3 ± 5.5	18.3 ± 6.5	> 0.05
Values other than the duration of disease are expressed as mean ± standard deviation or number (%).			
The duration of disease is measured using the median and interquartile range.			
BMI: body mass index.			
ED: erectile dysfunction.			
Li-ESWT: low-intensity extracorporeal shock wave therapy.			
IIEF-EF: International Index of Erectile Function–Erectile Function domain.			

4-week after the final session, the mean (SD) score in IIEF-EF for Li-ESWT and sildenafil was 16.3 ± 5.5 and 18.3 ± 6.5 (P > 0.05), respectively. According to MCID criteria, the ratio of patients who reported positive results was 80.0% in the sildenafil group and 59.5% in the Li-ESWT group respectively (κ2 = 0.09, P > 0.05).

The total EDITS score and index score of patient version and partner version are both similar in two groups (Table 2). More detailed analysis of each question in EDITS indicated that a significantly higher number of patients and partners in the Li-ESWT group responded 3 or 4 (very satisfied or somewhat satisfied) to question 1 of patient and partner version assessing overall satisfaction with treatment than those in the sildenafil group. Furthermore, patients and partners gave the same response to question 6 of the EDITS patient version and question 4 of the partner version respectively, which both addresses the satisfaction with the duration of intercourse (Table 3).

Table 2
The total EDITS score and index score at the first-month follow-up after treatment by adjustment†

Health parameters	**LI-ESWL(n = 42)**	**Sildenafil(n = 30)**	**t**	**P**
Patient version				
Total EDITS score	25.5 ± 6.4	24.1 ± 8.2	0.58	> 0.05
Total EDITS index score	57.9 ± 14.4	54.7 ± 18.6	0.58	> 0.05
Partner version				
Total EDITS score	11.1 ± 3.1	10.3 ± 4.2	0.99	> 0.05
Total EDITS index score	55.2 ± 15.3	51.7 ± 21.1	0.99	> 0.05
Values are presented as mean ± standard deviation.				
Li-ESWT: Low-intensity extracorporeal shock wave therapy.				
EDITS: Erectile Dysfunction Inventory of Treatment Satisfaction				
† means were adjusted for age by GLM model.				

Table 3
Comparison of patients and female partners' degree of treatment satisfaction assessed by EDITS by adjustment†

EDITS item	Li-ESWT		Sildenafil		Chi-Square	P
	n†	%††	n†	%††		
Patient version						
1	37	88.1	19	63.3	4.54	< 0.05
2	32	76.2	19	63.3	0.77	> 0.05
3	39	92.9	25	83.3	0.90	> 0.05
4	32	76.2	20	66.7	0.42	> 0.05
5	35	83.3	29	96.7	0.00	> 0.05
6	37	88.1	19	63.3	4.94	< 0.05
7	41	97.6	28	93.3	1.15	> 0.05
8	30	71.4	18	60.0	0.01	> 0.05
9	38	90.5	30	100.0	0.00	> 0.05
10	36	85.7	25	83.3	1.09	> 0.05
11	40	95.2	30	100.0	0.00	> 0.05
Partner version						
1	31	73.8	14	46.7	5.14	< 0.05
2	32	76.2	17	56.7	1.81	> 0.05
3	37	88.1	29	96.7	1.18	> 0.05
4	33	78.6	18	60.0	4.18	< 0.05
5	41	97.6	27	90.0	0.00	> 0.05

† means were adjusted for age by GLM model.

†† Number of patients or partners who responded 3 or 4 (somewhat or very satisfied) to items of EDITS.

††† % of patients or partners who responded 3 or 4 (somewhat or very satisfied) to items of EDITS.

Li-ESWT: Low-intensity extracorporeal shock wave therapy.

EDITS: Erectile Dysfunction Inventory of Treatment Satisfaction.

No participant discontinuation due to adverse events was observed. The only treatment-emergent adverse event in the sildenafil group were flushing and headache (1/30, 3.3%). Other than local penile pain (1/42, 2.4%), no adverse effects were encountered in the Li-ESWT group.

Discussion

The international consensus panel defined ED treatment effectiveness as “a combination of two factors, treatment responsiveness and treatment satisfaction”. In addition, treatment satisfaction was based on a combined assessment of the patient and partner satisfaction [16]. We applied standardized subjective outcome measurements —IIEF-EF to evaluate the erectile function and EDITS to evaluate treatment satisfaction. Furthermore, treatment satisfaction of partners was also evaluated. To our knowledge, this is the first study to compare treatment effectiveness in patients with ED treated with sildenafil and Li-ESWT from three dimensions: erectile function, patients’ and partners’ treatment satisfaction.

In this trial, Li-ESWT showed a similar treatment outcome to sildenafil for general ED patients. More than 50% of patients in the two groups were observed a high response to treatment (5-point increase). The improvements of IIEF-EF score indicated both therapies were effective for improving erectile function, which is consistent with our earlier result [11]. However, in comparison with the results performed previously, the improvement of erectile function of Li-ESWT for ED in this study is relatively low. For example, significant increases in IIEF-EF scores were recorded in all men in a precursor study by application of Li-ESWT for ED in 20 middle-aged men [13]. Another study revealed that 72.4% of participants reached an Erection Hardness Score of ≥ 3 after treatment of Li-ESWT [17]. The reason for less obvious improvement in the trial may be related to the younger cohort population, as many young couples are prone to have more serious emotional disorders [18].

We only analyzed male adults aged about 30 years. The main reason is that elderly Chinese men still feel embarrassed talking about erectile function [19]. Although a slight difference in patients’ age between the two groups was identified, participants in both groups are young men, thus the age difference would not affect the final results.

Satisfaction is one of the most important factors to determine patients' treatment compliance [6], which is particularly evident in young ED patients [20]. Moreover, patients’ partners with more satisfied sexual intercourse might play a positive role in sustaining compliance of patients [3, 21]. In this study, the results showed that patients and partners in the Li-ESWT group had similar total EDITS and EDITS Index scores as those in the sildenafil group. Nevertheless, more patients and partners in the Li-ESWT group were very satisfied and somewhat satisfied with the duration of intercourse compared with those in the sildenafil group. The improvement effect sustained 1 month after Li-ESWT treatment without any additional active intervention, implying that LI-ESWT exerted a genuine physiologic effect on cavernosal tissue. The result is in accordance with other clinical trials [22, 23]. The underlying basis of the lasting effect might attribute to its neovascularization mechanisms [8, 24]. Another unexpected finding was the higher rate of

satisfaction with overall satisfaction from patients and partners in the Li-ESWT group, indicating the potential advantage of Li-ESWT.

This study had several limitations. First, a small cohort was included in this study, which is a universal drawback among LI-ESWT clinical trials [22, 25, 26]. Second, penile hemodynamics were not measured to confirm the improvement of cavernous blood inflow or penile rigidity. NPTR recording in our study was only applied to measure the baseline of male erectile capacity and diagnose vasculogenic ED, which should have offered an objective assessment of erection potency change after treatment. In addition, penile doppler ultrasound could be considered to measure arterial inflow and venous outflow [27]. Third, the follow-up duration of 1 month may be short, considering that angiogenesis induced by Li-ESWT require a longer time [27]. Fourth, subgroup comparison was not applied to identify different etiologic groups. Considering the underlying neovascularization mechanisms of Li-ESWT, vasculogenic ED is expected to be the best candidate for this treatment. Nevertheless, in terms of mechanisms like nerve regeneration, other patients may be the optimal choice [28, 29]. Last, the study was non-randomized and single centered, these results need multicentered and randomized studies to further support.

Conclusions

Our results suggested Li-ESWT had better satisfaction than on-demand sildenafil for young ED patients and their partners, while the efficacy of the two treatment methods was similar. However, further studies are needed to determine the factors influencing satisfaction.

Abbreviations

ED
erectile dysfunction Scale
PDE5is
phosphodiesterase type 5 inhibitors
Li-ESWT
low-intensity extracorporeal shock wave therapy
IIEF-EF
International Index of Erectile Function–Erectile Function domain (IIEF-EF)
EDITS
Erectile Dysfunction Inventory of Treatment Satisfaction
BMI
body mass index.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The present study protocol was reviewed and approved by the Ethics Committee of the Peking Union Medical College Hospital (Reg. No. S-K696). Informed consent was submitted by all subjects when they were enrolled.

Consent for publication

The consent for publication had been obtained from all participants.

Availability of data and materials

We would like to share data collected for my study to others who are willing to do meta-analysis or pooled analysis 1 year after publication. And the data can be obtained by contacting corresponding author. Any data and materials that can be shared will be released via a Material Transfer Agreement.

Competing interests

The authors declare that they have no competing interests.

Funding

There was no funding for this project.

Authors' contributions

The trial protocol was designed and written by the authors (Dong Wang, Shijun Wang and Su Yan).

Su Yan coordinated the trial initiation and study procedures. Yingjie Li analyzed the clinical data. Dong Wang, Shijun Wang and Su Yan interpreted clinical data. Yingjie Li performed statistical analyses. Yongqiang Li, Yinsheng Zhang and Chunhui Liu informed patients and were responsible for patient care. Yongqiang Li, Yinsheng Zhang and Chunhui Liu performed Li-ESWT. The manuscript was written by Dong Wang, Shijun Wang and Su Yan, together with all co-authors, who vouch for the accuracy of the data reported and adherence to the protocol. All authors edited and approved the manuscript.

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Not applicable.

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Figures

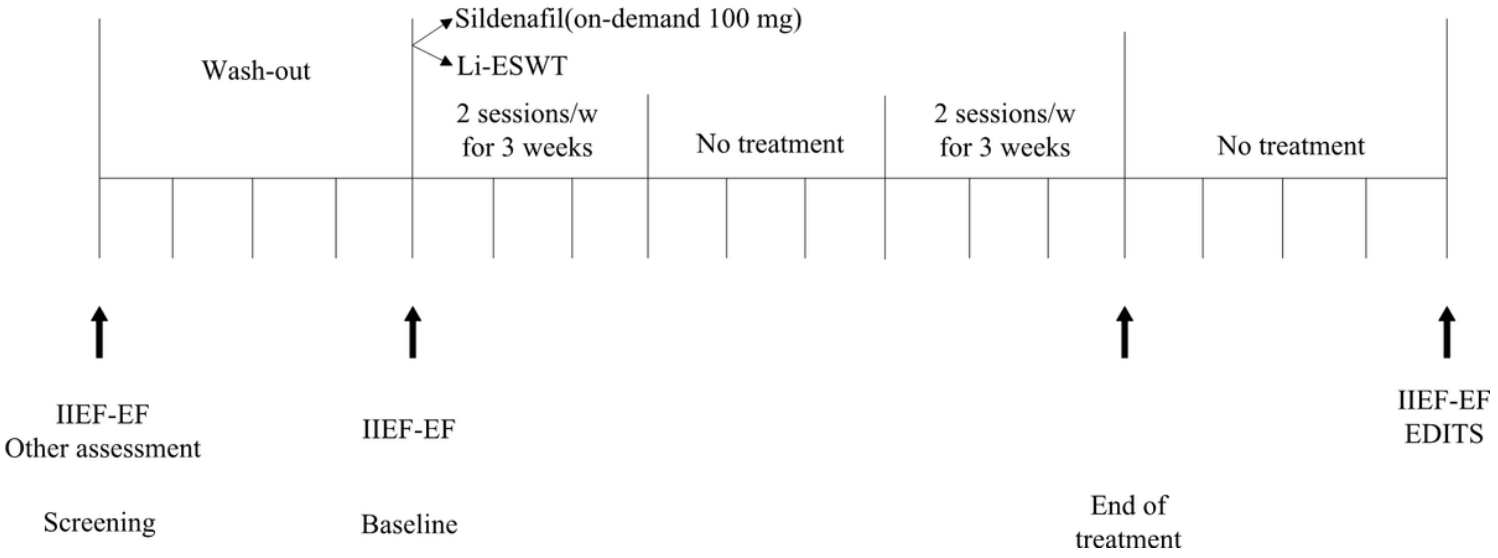

Figure 1

Study and treatment flow chart.

IIEF-EF: International Index of Erectile Function–Erectile Function domain.

Li-ESWT: low-intensity extracorporeal shock wave therapy.

EDITS: Erectile Dysfunction Inventory of Treatment Satisfaction questionnaire

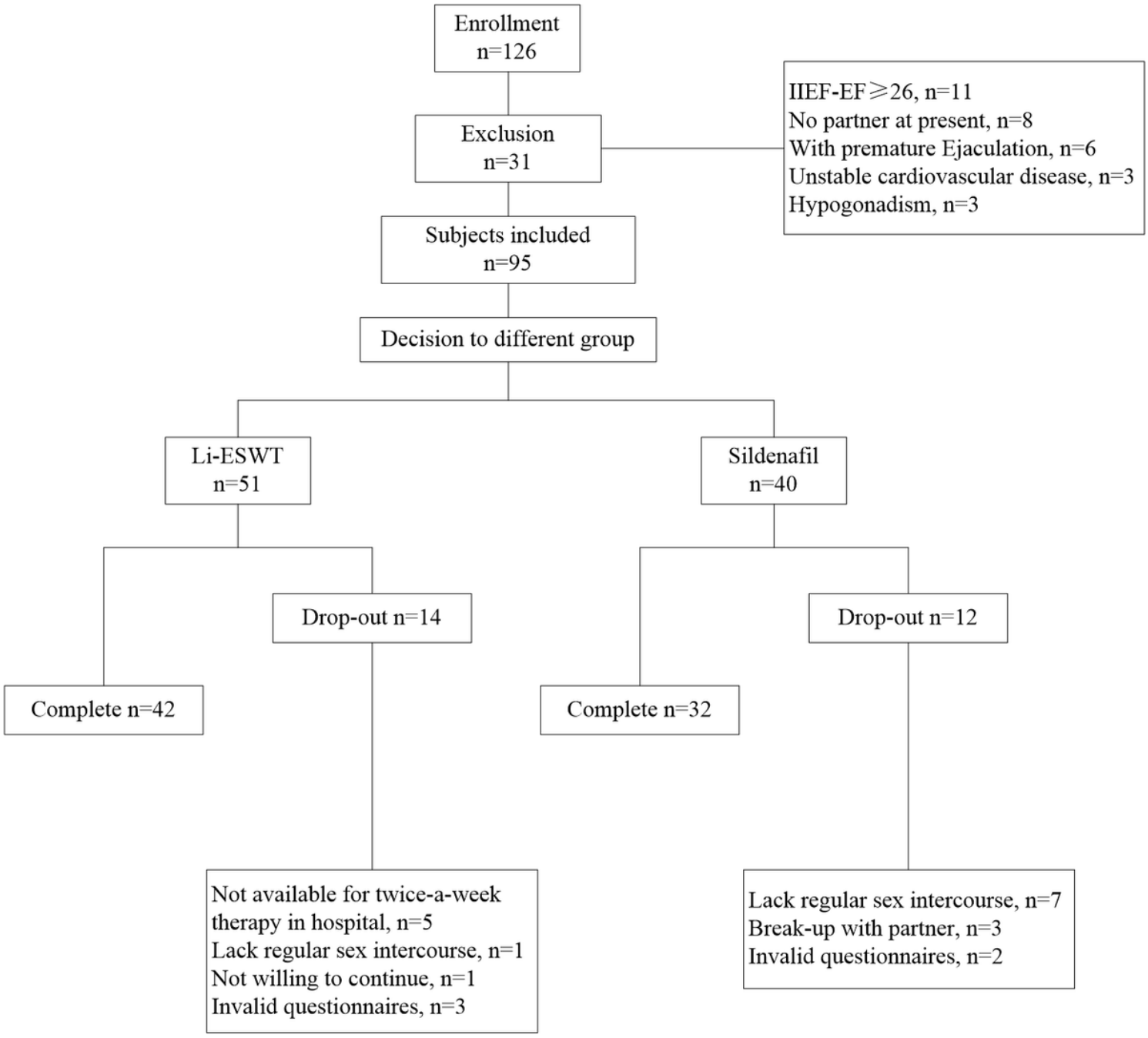

Figure 2

Patients flow chart.

Li-ESWT: low-intensity extracorporeal shock wave therapy.

IIEF-EF: International Index of Erectile Function–Erectile Function domain.