



Sildenafil Improves Erectile Function in Men with Chronic Heart Failure

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ABSTRACT

Background: Patients with Chronic Heart Failure (CHF) have been shown to have enhanced risk of Erectile Dysfunction (ED) due to low cardiac output, endothelial dysfunction, medications, co-morbid conditions, and psychogenic factors.

Objectives: The present study aimed to evaluate the effects of sildenafil on erectile function of patients with stable CHF using the abridged 5-item version of the International Index of Erectile Function (IIEF-5).

Patients and Methods: Using convenience sampling, 222 sexually-active adult males with NYHA class I-III stable CHF were included in this cross-sectional study. All the patients filled out the IIEF-5 questionnaire, in which they were required to score the five domains of male sexual function, including erectile function, orgasm function, sexual desire, intercourse satisfaction, and overall satisfaction. All the analyses were performed using the SPSS statistical software (v. 19) and $P < 0.05$ was considered as statistically significant.

Results: In our sample, the patients' mean age was 47.14 ± 11.86 years, their mean left ventricular ejection fraction was 20% (15% - 25%), and the prevalence of ED was 70.3%. In addition, severe, moderate, mild to moderate, and mild ED were seen in 57%, 17%, 7%, and 19% of the patients with ED, respectively. ED was significantly more prevalent in the patients with ischemic heart failure compared to those with idiopathic dilated cardiomyopathy (84.68% vs. 55.85%, $P < 0.001$). Moreover, the prevalence of ED was significantly lower in the patients taking sildenafil compared to the other group (42.85% vs. 82.89%, $P < 0.001$).

Conclusions: Sildenafil appears to provide satisfactory results toward improving sexual function in patients with CHF.

► Implication for health policy/practice/research/medical education:

Erectile Dysfunction (ED) is a common problem among middle-aged and older men. Low cardiac output, endothelial dysfunction, medications, and co-morbid conditions further enhance the risk of ED in patients with chronic heart failure. The considerable prevalence of ED in this population as well as its effects on quality of life warrants special awareness of physicians to extend their knowledge and clinical experience to improve patients' satisfaction, interpersonal relationships, self-esteem, and quality of life.

1. Background

Erectile Dysfunction (ED), defined as persistent inability to achieve and/or maintain sufficient erection for satisfactory sexual performance (1), is a common problem among middle-aged and older men. Low cardiac output, endothelial dysfunction, medications, co-morbid conditions

such as hypertension, atherosclerosis, coronary artery disease, diabetes mellitus, autonomous neuropathy, vascular disease of the penile arteries and veins, and psychogenic factors have been presumed as the predisposing factors which enhance the risk of ED in patients with Chronic Heart Failure (CHF) (2-6). The considerable prevalence of ED among CHF patients as well as its effects on quality of life warrants special awareness of physicians to extend their knowledge and clinical experience to improve patients' satisfaction, interpersonal relationships, self-esteem, and

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quality of life (7).

Sildenafil is a phosphodiesterase 5 inhibitor shown to be effective against ED of diverse etiologies (8-10). Several clinical trials on the use of sildenafil in healthy men with ED have shown that the cardiovascular side effects, including headache, facial flushing, and nasal congestion which result from vasodilation induced by the medication, are inconspicuous. Moreover, in a recent study by Amin et al. (11), sildenafil was shown to be clinically safe and well-tolerable in CHF patients without considerable effects on hemodynamics. However, the effect of sildenafil on improving erectile function in CHF patients has not been adequately explored in the previous literature. On the other hand, multifactorial etiology of ED in this population may necessitate use of other effective treatments.

2. Objectives

The present cross-sectional study aims to evaluate the efficacy of sildenafil in improving erectile function among patients with stable CHF using the abridged 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for assessment of erectile function (1).

3. Patients and Methods

3.1. Study Sample

The study sample included 222 male CHF patients (Left Ventricular Ejection Fraction (LVEF) of less than 40%) evaluated at the Heart Failure and Transplantation Clinic of Rajaei Cardiovascular, Medical, and Research Center from March 2011 to December 2012. The participants were selected through convenience sampling. Men above 18 years old were eligible if they were married or were currently in a stable relationship with a single partner. The patients with New York Heart Association (NYHA) functional class IV were excluded from the study. It should be noted that the frequency of sexual activity was not among the inclusion or exclusion criteria of the study.

3.2. Study Design

This cross-sectional survey was conducted on male patients with stable CHF who were currently sexually active. The effect of sildenafil on ED was assessed using the simplified IIEF-5. As a diagnostic instrument for ED, IIEF-5 is a validated questionnaire which consists of five questions to assess five domains of male sexual function: erectile function, orgasm function, sexual desire, intercourse satisfaction, and overall satisfaction (12). Each question is scored on a five-point ordinal scale ranging from 1 to 5, where lower values represent lower sexual dysfunction.

Besides, the total score of IIEF-5 is computed by summing up the responses to the 5 items. Thus, the total score of IIEF-5 ranges from 5 to 25. According to this scale, ED is classified into four categories based on the total scores: mild (scores 17 - 21), mild to moderate (scores 12 - 16), moderate (scores 8 - 11), and severe (scores 5 - 7). The patients with IIEF-5 scores of 22 to 25 were considered to have no ED. The patients filled out the questionnaire in an individual room with a total guarantee of confidentiality. They had learned how to use the questionnaire and to answer as many questions as possible to the best of their knowledge. The study protocol was approved by the institutional review board. Also, all the subjects provided written informed consents before participation.

3.3. Statistical Analysis

All the analyses were conducted by Statistical Package for Social Sciences (SPSS) software, version 19 (SPSS Inc., Chicago, IL, USA). A descriptive analysis of the demographic and clinical data of the patients was carried out. Categorical variables were presented as numbers and percentages and quantitative data as median \pm interquartile range. Categorical data were compared by chi-square test, while quantitative variables were compared using Student's t-test, Manne-Whitney test, one-way ANOVA, and Kruskale Wallis tests as appropriated. Besides, the relationships were assessed using Pearson or Spearman tests depending on their distribution. All P-values were two-tailed and $P < 0.05$ was considered as statistically significant.

4. Results

In our sample of 222 individuals, the prevalence of ED was 70.3%. In addition, 57%, 17%, 7%, and 19% of these patients had severe, moderate, mild to moderate and mild ED, respectively. The patients' age ranged from 21 to 65 years [median (interquartile range): 49 (40 - 57) years]. The patients' demographics have been presented in Table 1. The results showed a significant correlation between the patients' age and their IIEF class (Spearman's rho = 0.440, $P < 0.001$). The patients' age distribution was also significantly different among the five stages of ED in both the patients taking sildenafil [S(+)] and those not taking the medication [S(-)] ($P < 0.001$) (Figure 1).

According to the results, seventy patients (31.5%) were taking sildenafil at the time of interview. Among these patients, 36 (51.4%) had idiopathic Dilated Cardiomyopathy (DCM) and 34 (48.6%) had ischemic Heart Failure (HF). The frequency of ED was significantly lower in the S(+) group compared to the S(-) group (42.85% versus 82.89%, $P < 0.001$).

Table 1. The Demographics of the Study Population

Characteristic	Value
Age (years)	49 (40 - 57)
Etiology of heart failure	
Ischemic cardiomyopathy	111 (50)
Idiopathic dilated cardiomyopathy	111 (50)
LVEF (%)	15 (20 - 25)

Abbreviations: LVEF, left ventricular ejection fraction.

Data are presented as number (percentage) and median \pm interquartile range

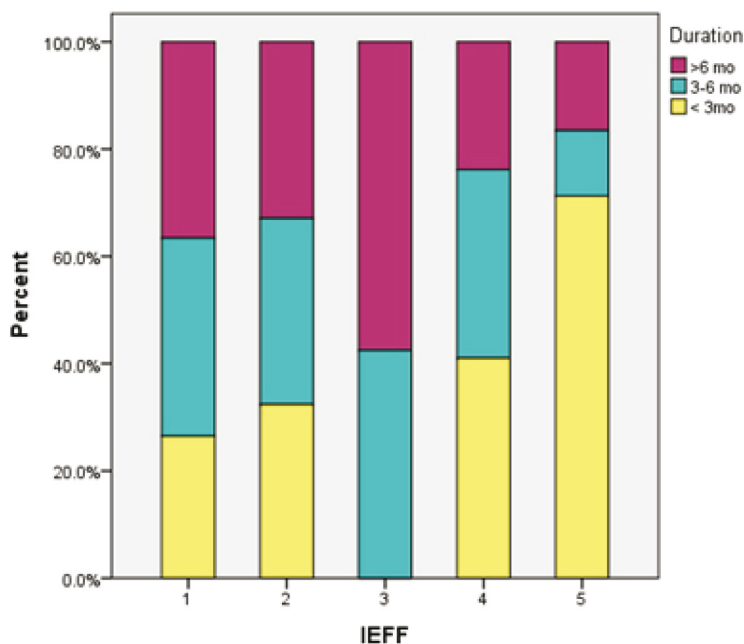


Figure 1. The Patients' Age Distribution in the Five Stages of ED

The results revealed a significant difference between the S(+) and S(-) groups regarding distribution of different ED stages ($P < 0.001$, Figure 2). However, the severity of ED was not significantly different in various durations of taking sildenafil, i.e., < 3 , $3 - 6$, or > 6 months ($n = 70$) ($P = 0.510$, Table 2). Distribution of various durations of taking sildenafil based on the severity of ED has been illustrated in Figure 3.

Moreover, distribution of different severities of ED was significantly different among the patients taking different

doses of sildenafil; i.e., < 125 , $125 - 250$, or > 250 mg per month ($P < 0.001$, Table 3).

Furthermore, ED was significantly more prevalent among the patients with ischemic HF compared to those with idiopathic DCM (55.85% versus 84.68%, $P < 0.001$). The median \pm interquartile range of LVEF was 15% (20% - 25%). In the S(-) group, but not in the S(+) group, LVEF was significantly correlated to the IIEF class (Spearman's $\rho = 0.19$, $P = 0.020$ and Spearman's $\rho = 0.06$, $P = 0.627$, respectively).

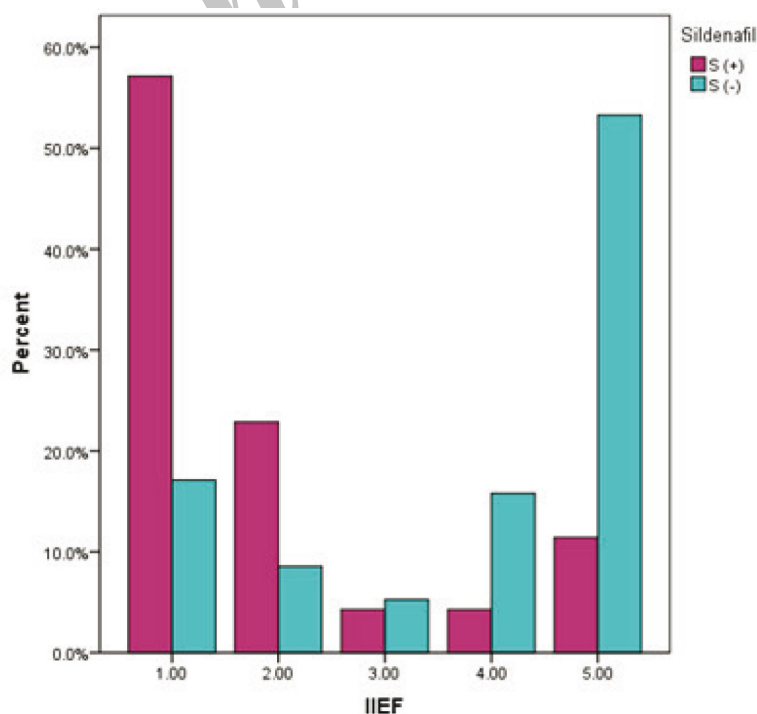


Figure 2. The Prevalence of Different ED Stages in the S(+) and S(-) Groups

Table 2. The Severity of ED among the Patients with Various Durations of Taking Sildenafil

Duration of taking sildenafil	Median IIEF-5 score (5 - 25)	P value	No	Stages of ED				Total
				Mild	Mild-to-moderate	Moderate	Severe	
< 3 months	11 (14 - 19)		8 (11.5)	4 (6)	0	1 (1.5)	5 (7)	18 (26)
3 - 6 months	15 (13 - 20)	0.510	13 (18.5)	5 (7)	1 (1.5)	1 (1.5)	1 (1.5)	21 (30.0)
6 months	19 (17-23)		19 (27.5)	7 (10)	2 (2.5)	1 (1.5)	2 (2.5)	31 (44)

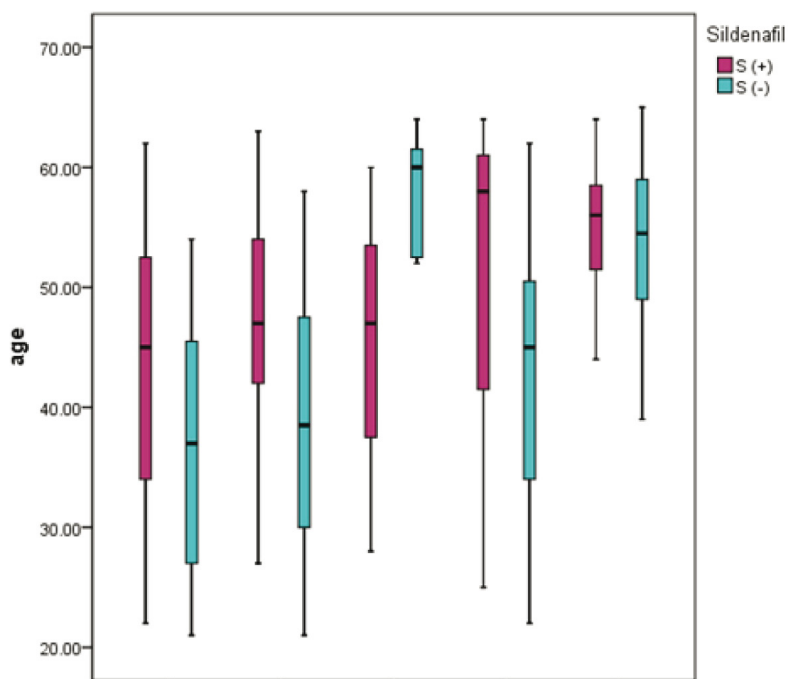


Figure 3. The Prevalence of Various Durations of Taking Sildenafil based on the Severity of ED

Table 3. The Severity of ED among the Patients Taking Various Doses of Sildenafil

Dose of sildenafil (per month)	Median IIEF-5 score (5 - 25)	P value	No	Mild	Stages of ED			Total
					Mild-to-moderate	Moderate	Severe	
< 125 mg	9 (11 - 14)		4 (6)	3 (4.5)	2 (2.5)	3 (4.5)	6 (8.5)	18 (26)
125 - 250 mg	15 (10 - 17)	< 0.001	12 (17)	5 (7)	1 (1.5)	0	2 (2.5)	20 (28.5)
250 mg	21 (19 - 23)		24 (34.5)	8 (11.5)	0	0	0	32 (46)

5. Discussion

In the present study, analysis of IIEF-5 questionnaires applied to 222 men with CHF showed that around 70% of the patients with systolic HF had erectile complaints which led to severe ED in more than half of them. The prevalence of ED mostly depends on the study population as well as on the used definitions and instruments (2, 12-14). Nonetheless, the prevalence of ED in the present study was comparable to the previously reported prevalence rates which ranged from 74% to 85% (15-18).

In this study, we compared two groups of subjects; patients with or without concurrent sildenafil therapy. Our findings demonstrated that the prevalence of ED was considerably lower in the S(+) patients compared to those in the S(-) group.

The study results also showed that duration of taking sildenafil had statistically borderline effects on response to sildenafil. However, the patients taking higher doses of sildenafil per month were more likely to have lower severity of ED. These findings were in accordance with the

previous literature that evaluated the effects of sildenafil on ED in patients with CHF. In an uncontrolled, open-label study conducted on 20 CHF patients with various etiologies, 1-month sildenafil therapy at an average dose of 58 mg was shown to improve erectile function and patient satisfaction compared to baseline values (19). Similar findings were also obtained in a 12-week, open-label, placebo-controlled, crossover study on 35 male patients with NYHA classes II to III CHF (20). That study demonstrated that 6 weeks of treatment with 50-mg dose of sildenafil significantly improved sexual function, assessed by IIEF score, compared to the placebo (20). In another study, evaluation of 132 CHF patients with ED revealed higher sexual satisfaction in the sildenafil-treated group compared to the placebo group (16).

Furthermore, the current study findings indicated a significant correlation between the patients' age and the degree of sexual dysfunction; ED was more severe in higher ages. This result was in agreement with the previous reports which found advancing age as an independent risk

factor for disturbed erectile performance (4, 8, 21, 22). The effects of aging on erectile function were also noted in other chronic diseases. For instance, Cerqueira (23) et al. found an association between age and ED in patients with chronic renal failure. Yet, physical activity could lower the risk of ED in men over 50 years of age (8, 9), which would be limited by the presence of HF.

According to the previous literature, about 5 metabolic equivalents are expended during the “average” sexual intercourse, which is also comparable to a brisk walk up to two flights of stairs (24). The ability to increase heart rate and stroke volume during exercise is impaired in patients with CHF (25). On the other hand, increased vasoconstriction with decreased exercise-induced vasodilation is seen in HF patients (26). Additionally, neurohormonal activation in CHF contributes to lack of preload response, impaired autonomic regulation, and increased vascular resistance. These mechanisms may be responsible for the blunted hemodynamic response to exercise which is the characteristic of systolic HF. Moreover, severely impaired left ventricular function further reduces physical capacity which is required for satisfactory sexual activity. The effect of left ventricular systolic function on ED was evaluated in the investigation by Mandras et al. (18). Their results showed that a reduced ejection fraction might further impair sexual performance. However, Jaarsma et al. found no association between sexual function and LVEF (15). The results of the present study showed that lower LVEF was associated with higher stages of ED in the S(-) group, while this association was not seen in the patients receiving sildenafil. On the other hand, LVEF had equal distribution among the patients with or without sildenafil therapy. Accordingly, it might be concluded that although LVEF can adversely affect erectile function in patients with HF, sildenafil therapy may be able to overcome the negative effects of low LVEF on sexual performance.

This study also revealed a higher prevalence of ED in the patients whose etiology of CHF was ischemic heart disease compared to those with DCM. This can be explained by the fact that patients with ischemic cardiomyopathy have underlying systemic atherosclerosis, which accounts for approximately 40% of ED in men above 50 years of age (27). Intimal hyperplasia and plaque deposition result in focal stenosis in the common iliac, hypogastric, and pudendal arteries (28) which in turn leads to reduced arterial inflow into the penile corpora cavernosa, as the major contributor to ED (28). Additionally, patients with ischemic cardiomyopathy commonly exhibit other chronic diseases that are independently associated with ED, such as hypertension and diabetes mellitus. Moreover, systemic atherosclerosis is associated with endothelial dysfunction, and data are growing regarding the role of endothelial dysfunction in the pathophysiology of ED (10, 29, 30). In the S(+) group in the current study, 70% of the patients with any degree of ED had ischemic cardiomyopathy. On the other hand, around 62% of the patients with ischemic cardiomyopathy exhibited ED complaints. In the S(-) group, 58% of the patients with ED had ischemic HF, whereas about 95% of the patients with ischemic cardiomyopathy

had ED. Thus, etiology of HF might cause differences in the response to sildenafil treatment. Our findings also showed that the risk of ED was 7 folds higher in the S(-) group in comparison to the S(+) group (OR = 7.22, 95% CI = 2.29 - 17.83). In the DCM patients, however, absence of sildenafil therapy resulted in an 11-fold increase in the risk of ED compared to sildenafil therapy state (OR = 11.29, 95% CI = 3.31 - 38.31). Therefore, it might be reasonable to conclude that sildenafil seems to be more effective in improving erectile function in patients with ischemic HF compared to those with non-ischemic CHF. In other words, patients with idiopathic DCM are less likely to retrieve normal sexual function with sildenafil therapy. However, these results must not be interpreted as such therapy should not be prescribed in DCM patients with ED since the results of the present study and the previous literature have shown that sildenafil is apparently effective enough which could help improve sexual dysfunction in DCM patients.

5.1. Study Limitations

The data presented here were derived from IIEF-5 questionnaires applied to a non-selected group of patients with stable HF. By virtue of the outpatient setting of the study and the subsequent time limitation during the interviews, we did not have a chance to evaluate comprehensive information regarding the patients' status (such as NYHA groups), detailed history, and medical or mechanical therapy. Likewise, we did not have laboratory and echocardiographic data of the study population. Moreover, we did not use random sampling methods; therefore, the selection bias could not be completely ruled out. Additionally, we did not retrieve a non-heart failure population as the control group. Hence, the study was more descriptive rather than analytical, which might raise more questions rather than providing answers.

5.2. Conclusions

HF is strongly associated with male sexual dysfunction. The prevalence of ED among CHF patients has been in a steady magnitude since the initial published reports. This shows that despite the improvements introduced in treatment of CHF, the prevalence of ED has remained high. Consequently, improving the quality of life in this high proportion of CHF patients only requires special attention to application of appropriate diagnostic approaches and treatments. Herein, sildenafil appears to provide satisfactory results in patients with both idiopathic and ischemic cardiomyopathy. However, blinded randomized controlled trials with larger sample sizes are required to confirm these findings.

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Authors' Contribution

Niloufar Samiei: Study concept and design, data collection, critical revision of the manuscript, and approval of the article, Sepideh Taghavi And Mohammad Safarian: Data collection and approval of the article, Ahmad Amin: Study concept and design, Data collection, drafting, critical

revision of the manuscript, and approval of the article, Mitra Chitsazan: Analysis and interpretation, statistics, drafting, critical revision of the manuscript, and approval of the article.

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The authors declare that there is no conflict of interest.

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