Effect of Cardiac Resynchronization Therapy on Libido and Erectile Dysfunction

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ABSTRACT

Background: Chronic heart failure (HF) is a common, complex clinical syndrome characterized by dyspnea, fatigue and exercise intolerance. HF patients experience decreased libido and erectile dysfunction (ED). The effects of cardiac resynchronization therapy (CRT) on libido and erectile function have not been previously evaluated. We aimed to investigate the effects of CRT on libido and ED.

Hypothesis: Cardiac resynchronization therapy improves libido and ED.

Methods: Thirty-one male patients with advanced HF, scheduled for implantation of a CRT device, were included in the study. Left ventricular systolic function, New York Heart Association (NYHA) class, libido, and ED were assessed before and 6 months after CRT. Libido and ED were evaluated with the Aging Male Symptoms (AMS) rating scale and internationally validated Sexual Health Inventory for Men (SHIM) questionnaire, respectively.

Results: At the 6-month follow-up, the mean NYHA class improved from 3.4 ± 0.5 to 2.1 ± 0.6 ($P < 0.001$). On echocardiographic examination, an improvement in left ventricular ejection fraction (LVEF) from $18 \pm 5\%$ to $32 \pm 6\%$ was detected ($P < 0.001$). A significant increase in mean SHIM score and a significant decrease in mean AMS were noted. Changes in SHIM and AMS scores were correlated positively with the increase in LVEF ($r = 0.47$, $P = 0.007$ and $r = -0.36$, $P = 0.04$, respectively). Similarly, SHIM scores were correlated negatively ($r = -0.57$, $P = 0.001$) and AMS scores were correlated positively ($r = 0.73$, $P = 0.0001$) with the improvement in NYHA class.

Conclusions: CRT results in a significant improvement in libido and erectile function in patients with congestive HF. This improvement is related to the improvements in the LVEF and functional capacity.

Introduction

Chronic heart failure (HF) is a common, complex clinical syndrome characterized by dyspnea, fatigue and exercise intolerance. HF patients experience decreased libido and frequency of coitus, negative changes in sexual performance, and a general dissatisfaction related to their sexual function.¹ Erectile dysfunction (ED) is an increasingly common problem and is seen in HF patients with the effects of underlying atherosclerosis, neurologic pathology, hormonal deficiencies, drug side effects, psychological factors, and altered vasomotion leading to vasoconstriction.² Depression, anxiety, fear of death, usage of various drugs, decreased penial arterial flow, and endothelial dysfunction are common in HF and result in decreased libido and ED. Decreased left ventricular (LV) ejection fraction effects libido, sexual performance, and erectile function adversely.²

Also, it has been shown that functional capacity correlates with ejection fraction (EF). The safety of

engaging in sex, similar to other physical activities, depends on the cardiovascular reserve of the patient. The Second Princeton Consensus Conference provides guidelines for assessing the risk of sexual activity in all cardiac patients, including HF patients. Patients with New York Heart Association (NYHA) class I symptoms are not considered to be at increased risk of coitus-induced cardiovascular events. Patients whose symptoms are NYHA class II are considered in intermediate/indeterminate risk group. Patients with NYHA class III/IV symptoms are considered to be a high-risk group for coitus-induced cardiovascular events. According to these guidelines, sexual activity should be postponed in high-risk patients until the patient is treated and stabilized.^{2,3}

In clinical trials, cardiac resynchronization therapy (CRT) has been shown to improve HF symptoms, NYHA functional capacity, 6 minute walking distance, oxygen consumption in exercise, and quality of life in HF patients.^{4,5} Improvement in left ventricular ejection fraction (LVEF), cerebral blood flow, cognitive functions, and positive neurohormonal changes have been demonstrated in HF patients treated with CRT.^{6–8}

Although beneficial effects of CRT on clinical and hemodynamic status of patients are well known, the effects

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of CRT on libido and ED in HF patients have not yet been investigated. In this study, the effects of CRT on libido and ED in HF patients were investigated.

Methods

Patients

The study population consisted of 31 male patients with advanced symptoms of HF who were scheduled for implantation of a CRT device. Inclusion criteria were severe HF (NYHA class III or IV), LVEF $\leq 35\%$, sinus rhythm or atrial fibrillation, and QRS duration of >120 ms. Almost all of the patients had left bundle branch block. Twenty-four patients were nonischemic, and 7 patients were ischemic. Twenty-four patients were in sinus rhythm, and 7 patients were in atrial fibrillation. The etiology of HF was considered ischemic in the presence of significant coronary artery disease ($>50\%$ stenosis in ≥ 1 of the major coronary arteries) and/or a history of myocardial infarction or previous revascularization. The characteristics of the patients are shown in Table 1. Patients using any hormone therapy for erectile dysfunction, above 65 years old, and having urological diseases were excluded from the study. All patients were taking optimal pharmacological treatment for HF and the medical therapy was unchanged during the study period, including β -blockers. The percentage of patients taking β -blockers, angiotensin-converting enzyme inhibitors and diuretics were 90%, 87%, and 80%, respectively.

Written informed consent was obtained from all patients. The study was approved by the local ethical committee.

Table 1. Patient Characteristics (N = 31)

Age [y]	54 $\pm$ 8
Ischemic/nonischemic [n (%)]	7(23)/24(77)
NYHA [mean]	3.4 $\pm$ 0.5
NYHA III/IV [n (%)]	18(58)/13(42)
LVEF [%]	18 $\pm$ 5
Sinus/AF [n (%)]	24(77)/7(23)
QRS width [ms]	150 $\pm$ 15
LBBB [n/%]	29/94
RBBB [n/%]	2/6
HT [n/%]	15/48
DM [n/%]	4/13
β -blockers [n/%]	28/90
ACE inhibitors [n/%]	27/87
Diuretics [n/%]	25/80

Abbreviations: ACE, angiotensin-converting enzyme; DM, diabetes mellitus; HT, hypertension; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RBBB, right bundle branch block.

Echocardiographic Examination

Patients were examined with echocardiography before implantation of a CRT device. Patients were imaged in the left lateral decubitus position with a commercially available system (VIVID 7; General Electric-Vingmed Ultrasound, Horten, Norway). Images were obtained with a 2.5-MHz broadband transducer at a depth of 16 cm in the parasternal and apical views (standard long-axis, 2- and 4-chamber images). LVEF was calculated from the conventional apical 2- and 4-chamber images using the biplane Simpson's technique.⁹

Evaluation of ED and Decreased Libido

Before CRT implantation, ED and libido of the patients were evaluated. ED was evaluated with the internationally validated Sexual Health Inventory for Men (SHIM) questionnaire (Table 2).¹⁰ SHIM scores are classified as: 22–25, no ED; 17–21, mild ED; 12–16, mild-to-moderate ED; 8–11, moderate ED; and 1–7, severe ED.¹¹

The Aging Male Symptoms (AMS) rating scale is a standardized, commonly used scale for assessing health-related quality of life in men.¹² Psychological, somatovegetative, and sexual symptoms were identified in the 17-item scale. The psychological dimension describes psychological complaints in men: discouragement, depression, irritability, anxiety, and nervousness. The psychological dimension consists of 5 symptoms: pain in muscles or joints, sweating, increased need for sleep and sleep disturbances, impaired general well-being, decrease in muscular strength, and decreased energy. The sexual symptoms are: disturbances of potency, decrease in morning erections, decrease in libido and sexual activity, decrease in beard growth, and the impression of having "past the zenith of life." According to AMS scores, patients were diagnosed as mild (score, 27–36), moderate (score, 37–49), and severe (50 or more).¹³

We administered the SHIM questionnaire and AMS scale to 31 patients undergoing cardiac resynchronization therapy. Follow-up questionnaire and scale, and transthoracic echocardiography were repeated at the 6-month routine clinical follow-up visit.

Statistical Analyses

All data were analyzed using the statistical package SPSS version 13.0 (SPSS Inc., Chicago, IL). Continuous data were expressed as mean $\pm$ standard deviation. EF, NYHA functional class, SHIM, and AMS score in the preimplantation period and at 6 months were compared using Wilcoxon signed rank test. Correlations between NYHA functional class, EF, SHIM, and AMS score were examined by Pearson correlation analysis. A *P* value <0.05 was accepted as statistically significant.

Results

Twenty-four patients had an SHIM score of 21 or less, indicative of mild to moderate ED, and 3 patients had a SHIM score of 7 or less, indicative of severe ED before CRT. At 6 months of follow-up after CRT, 23 patients reported no ED, and only 2 patients had moderate ED. Severe ED was not found in any patient. After CRT,

Table 2. The Sexual Health Inventory for Men

Over the past 6 months:			
1. How do you rate your confidence that you could get and keep an erection?			
Very Low	1	High	4
Low	2	Very High	5
Moderate	3		
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?			
No sexual activity	0	Sometimes (about half the time)	3
Almost never or never	1	Most times (much more than half the time)	4
A few times (much less than half the time)	2	Almost always or always	5
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) you partner?			
Did not attempt intercourse	0	Sometimes (about half the time)	3
Almost never or never	1	Most times (much more than half the time)	4
A few times (much less than half the time)	2	Almost always or always	5
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?			
Did not attempt intercourse	0	Difficult	3
Extremely difficult	1	Slightly difficult	4
Very difficult	2	Not difficult	5
5. When you attempted sexual intercourse, how often was it satisfactory for you?			
Did not attempt intercourse	0	Sometimes (about half the time)	3
Almost never or never	1	Most times (much more than half the time)	4
A few times (much less than half the time)	2	Almost always or always	5
Score: Add the numbers corresponding to questions 1 through 5.			

a significant increase of mean SHIM scores was noted. The mean SHIM score before CRT and after CRT was 14.2 ± 5.6 and 21.2 ± 3.9 , respectively ($P < 0.001$).

Six patients had an AMS score of 27 or more, indicative of mildly decreased libido, 14 patients had an AMS score of 37 or more, indicative of moderately decreased libido, and 8 patients had a AMS score of 50 or more, indicative of severe decreased libido before CRT. At 6 months of follow-up after CRT, a significant increase in patients with normal libido was found ($P < 0.001$). The mean AMS score before CRT and after CRT was 40.9 ± 10.1 and 23.0 ± 5.6 , respectively, and the decrease in AMS score was also significant ($P < 0.001$) (Table 3).

At 6 months of follow-up after CRT, the clinical status and functional capacity of the patients were improved. The mean NYHA class improved from 3.4 ± 0.5 to 2.1 ± 0.6 ($P < 0.001$). On echocardiographic examination, an improvement in LVEF from $18 \pm 5\%$ to $32 \pm 6\%$ was detected ($P < 0.001$).

At follow-up, SHIM scores and AMS scores were improved significantly with the increase in LVEF. Changes in SHIM scores were correlated positively with the increase in LVEF ($r = 0.47$, $P = 0.007$). Again, changes in AMS scores were correlated negatively with the increase in

LVEF ($r = -0.36$, $P = 0.04$). Similarly, SHIM scores were correlated negatively with the improvement in NYHA class ($r = -0.57$, $P = 0.001$). AMS scores were correlated positively with the improvement in NYHA class ($r = 0.73$, $P = 0.0001$).

Discussion

Normal sexual function requires the coordination of psychological, hormonal, vascular and neurological factors.² Erection is a vascular event and begins with increased arterial blood flow into the corpora cavernosa and spongiosum.²

HF results in decreased libido and ED due to depression, performance anxiety, fear of death, use of drugs, decreased penile arterial flow, and endothelial dysfunction.² It has been suggested that HF should be stabilized first before starting to treat decreased libido and ED.³ Currently, there are no randomized controlled studies showing improvement of ED except sildenafil citrate in mild to moderate HF patients.^{14–16} Improvement of ED in a patient with HF following CRT has been reported in a case report.¹⁷ This study investigated the effects of CRT on libido and ED in patients with NYHA functional class III/IV.

Table 3. Sexual Health Inventory for Men and Aging Male Symptoms Scores of the Patients Before and After Cardiac Resynchronization Therapy

	Before CRT	After CRT	P
SHIM, n			
No ED (n)	4	23	<0.001
Mild ED (n)	10	5	0.09, NS
Mild–moderate ED	5	1	0.04
Moderate ED	9	2	0.02
Severe ED	3	0	0.08, NS
SHIM mean score	14.2 ± 5.6	21.2 ± 3.9	<0.001
AMS, n			
Normal libido	3	25	<0.001
Mildly decreased libido	6	4	0.48, NS
Moderately decreased libido	14	2	0.001
Severely decreased libido	8	0	0.005
AMS mean score	40.9 ± 10.1	23.0 ± 5.6	<0.001
Abbreviations: AMS, Aging Male Symptoms; CRT, cardiac resynchronization therapy; ED, erectile dysfunction; NS, not significant; SHIM, Sexual Health Inventory for Men.			

Baumhäkel et al evaluated 192 cardiovascular high-risk patients regarding onset and severity of ED. Patients were classified into 3 groups with severe (EF ≤ 40%), moderate (EF 41%–60%), and preserved LV dysfunction (EF > 60%). Patients with severe and moderate LV dysfunction had a significant increase of ED. LV dysfunction was found to be an independent risk factor for ED independent of HF symptoms. Functional capacity was classified according to NYHA into 3 groups as 2.1 ± 0.8, 1.7 ± 0.7 and 1.5 ± 0.7, and there was no association of functional class with ED. Patients with LV dysfunction were shown to have a decreased libido, sexual performance, and erectile function.¹⁸ Jaarsma et al studied sexual function in HF patients. A significant but weak relation between patients' sexual function, 6-minute walk, and NYHA functional class, and a significant relation between EF and ED had been reported. Also, decreased libido, satisfaction from sex, and number of coitus and negative changes in sexual functioning had been reported.¹ Our study showed that patients with decreased EF and NYHA functional class III/IV experience severe ED and decreased libido. Although improvement in LVEF and NYHA functional class was associated with increased libido and improved erectile function after CRT, the most powerful relationship was found between NYHA functional class improvement and increased libido ($r = -0.73$, $P = 0.0001$). The more decreased functional classes of our patients, compared to patients evaluated in the above-mentioned studies, may result in our finding of a significant relationship between NYHA functional class and libido and ED. A significant improvement in erectile function, libido, and sexual performance with CRT was found after 6 months of follow-up. It is thought that this

powerful relationship may be associated with improved functional capacity, exercise tolerance, self confidence, and decreased fear of death.

Altered vasomotion is an important factor for erectile dysfunction in HF patients. Impaired endothelial function results in vasculogenic ED.¹⁹ Decreased EF is associated with endothelial dysfunction due to neurohormonal changes in HF patients.^{18,20} Positive effects of CRT on functional capacity, arterial blood flow and circulation, vasoconstriction, vasomotion, and no adverse effects on libido and erectile function like drugs used in the management of HF, increases sexual performance of patients.

Adverse effects of diuretics on libido and erectile function are well known. As the medical treatment of the patients was not changed significantly before and after CRT, we thought that the improvement in sexual performance is only related to CRT.

Although a significant relationship has been shown between age and ED,¹⁸ we did not find any relationship between age and ED. This might result from the lower average age of our patients than other studies. Although diabetes mellitus (DM) is an independent risk factor of ED, 4 patients in our study had DM, and there was not any relationship between ED and DM in our study. The low prevalence of DM in our study population may be the reason.

Conclusion

HF patients experience decreased libido and frequency of coitus, erectile dysfunction, negative changes in sexual performance, and a general dissatisfaction related to their sexual function. CRT results in significant improvement in libido, erectile function, and sexual performance as a consequence of the improvement in functional capacity and EF. One limitation of our study was the single-center, nonrandomized design. Second, the study sample was small. Last, the patient group was relatively young. CRT has a significant placebo effect. Therefore, the improvement in libido and ED can be influenced by placebo effect. Further studies are needed to confirm our findings.

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