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Original Article

The relationship between ProNT BNP levels and erectile dysfunction in patients with chronic congestive heart failure

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Abstract

Aim: Dysfunction and impairment of many organs occur in chronic congestive heart failure due to ischemia and stasis. Chronic congestive heart failure is frequently accompanied by erectile dysfunction since the two conditions have many etiologic factors in common. Our aim in the study was to investigate the potential relationship between ProNT BNP levels, which show the severity of cardiac failure, and erectile dysfunction in patients with an ejection fraction of 30-40%.

Materials and Methods: The study included 72 male patients followed-up for chronic congestive heart failure. for whom erectile dysfunction was investigated. International Erectile Function Index-5 (IIEF-5) questionnaire was questioned to the patients to evaluate erectile function.

Results: The mean age, total testosterone and lipids (low and high-density lipoprotein cholesterol triglyceride) levels did not significantly differ between the groups (P > 0.05). The mean ProNT BNP levels belonging to all subgroups showed statistically significant differences and correlated with the severity of erectile dysfunction according to the Kruskal-Wallis test (p<0.001).

Conclusions: In patients with chronic congestive heart failure, ProNT BNP was higher, and the severity of erectile disfunction was similarly increased.

Keywords: Chronic congestive heart failure; erectile dysfunction; ProNT BNP

INTRODUCTION

Chronic congestive heart failure (CCHF) is a chronic condition and a leading cause of morbidity and mortality. Heart failure (HF) has been defined as a clinical syndrome characterized by typical signs and symptoms resulting from the structural and/or functional abnormality of the heart in which intracardiac pressures are increased and/or the output volume is decreased during rest or effort (1). Etiologic factors include common morbidities in the study population, such as coronary artery disease and diabetes mellitus. In CCHF, blood volume and intercellular fluid are increased beyond physiologic ranges. This disorder is also associated with organ dysfunctions (2).

CCHF may lead to erectile dysfunction (ED) through many mechanisms. Thiazide diuretics, digoxin, aldosteron and β-blockers, and drugs used in cardiac failure have been considered to cause ED (3). Depression caused by decreased effort capacity has also been associated with ED (4). In addition, increased preload and afterload seen in CCHF may cause the occlusion of the arteries that supply blood to the corpus cavernosum, resulting in ED (5). Changes in the vascular penile structure, reduced penile circulation, decreased androgen levels, decreased number of penile smooth muscle myocytes, and lower production of nitric oxide have been demonstrated in adults diagnosed with CCHF (6). Schwarz et al. found that the mean age of male patients followed-up for chronic CCHF was 59 years, and the ED complaint was present in 84% of these patients (New York Heart Association [NYHA] classes 1-3) (7).

In particular, increased tension in the myocardium increases the release of N-terminal pro-brain natriuretic peptide (ProNT BNP) from cardiac myocytes to the circulation. ProNT BNP tries to maintain neurohumoral regulation through its cardiac and renal effects. The level of the N-terminal fragment of BNP is found to be an indicator of the prognosis and severity of cardiac failure in patients with CCHF (8-9). For this purpose, we aimed to investigate the relationship between ED and the ProNT BNP level that indicates the severity of CCHF.

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To the best of our knowledge, there are no studies in the literature investigating the relationship between ProNT BNP level and erectile function as an indicator of chronic heart failure. In this respect, our study is important in this sense.

MATERIALS and METHODS

This cross-sectional study retrospectively included male patients with HF that presented to the cardiology and urology outpatient clinics of Erzurum Education and Research Hospital from May 2014 to May 2017. The study was conducted in the tertiary cardiovascular unit of a university hospital and approved by the local University Ethics Committee (approval date: 18.06.2018; approval number: 2018/12-117). The study group consisted of 72 male HF cases with a similar left ventricular ejection fraction (LVEF) of 30-40%. All the patients included in the study were questioned about their ED problem. The patients describing ED indicated that they had problems in sexual activity within the last six months. According to the scores obtained with the International Erectile Function Index-5 (IIEF-5) questionnaire, the severity of ED was determined and divided into 4 groups (Table 1).

Participants with a IIEF-5 score of 5-7 were severe, 8-16 were moderate, 17-21 were mild and 22 and above were defined as non-ED. The echocardiographic investigations of the patients included in the study were completed with a Philips Epiq 7c device. LVEF was measured using the modified Simpson's method. All patients received the same dose of beta-blockers and statins. Patients with a psychological cause of ED or a history of major psychiatric disorders any thyroid and tumoral disease, neurological disorders or overt depression. Patients who received ED treatment in the last three months and received any medication that would affect the level of sex hormone were excluded from the study. For biochemical measurements, blood samples were taken from all 72 cases from the antecubital vein. ProNT BNP, total cholesterol, HDL, LDL, triglyceride, testosterone, routine biochemistry parameters, hemogram and sedimentation rate were measured.

Table 1. International Index of Erectile Function (IIEF-5)

	1 point	2 point	3 point	4 point	5 point
How do you rate your Confidence that you couuld get and keep an erection?	Very Low	Low	Moderate	High	Very High
When you had erections with sexual stimulation, how often were your erection hard enough for partner?	Never	A few times	Sometimes	Most times	Almost/ always
During sexual intercourse, how often were you able to maintain your erection after you had penetraed your partner?	Never	A few times	Sometimes	Most times	Almost/ always
During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely	Very difficult	Difficult	Slightly difficult	Not difficult
When you attempted sexual intercourse, how often was it satisfactory for you?	Never	A few times	Sometimes	Most times	Almost/ always

IIEF-5 scores range from 5 to 25: severe (5-7), moderate (8-16), mild (17-21), and no ED (22-25)

Statistical analysis

The distribution of normality was assessed using the D'Agostino-Pearson test. Nominal categorical variables were assessed with the chi-square test. The analysis of variance and Kruskal-Wallis tests were used to compare the variables between more than two groups for the normally and non-normally distributed data, respectively. Pairwise comparisons were performed via the Scheffé test. The data were presented as box-and-whisker plots. The differences were considered statistically significant at $p < 0.05$. MedCalc statistical software was used for statistical analysis (version 12.2.1.0, Mariakerke, Belgium).

RESULTS

The study included 72 male patients with CCHF. The mean age of the study population was 66.01 ± 7.22 years. The mean age, smoking status, prevalence of hypertension and diabetes mellitus. and the serum total testosterone and cholesterol levels of the four ED groups did not significantly differ. Table 2 presents the clinical data and the results of fasting serum glucose, testosterone, lipid profile and ProNT BNP levels. The LVEF percentage was 38.51± 2.10, 37.21 ± 2.27, 34.83 ± 3.64, and 30.65 ± 3.04 for the ED groups with an IIEF score of 22-25, 17-21, 8-16 and 5-7 respectively. A correlation was found between reduced LVEF and the severity of ED ($r = 0.527$, $p < 0.001$).

The mean serum ProNT BNP level was found to be 6408.14 ± 938.74, 1233.12 ± 322.01, 712.11 ± 161.02 and 289.01 ± 82.21 pg/ml in the severe, moderate, mild and non ED groups, respectively. Figure 1 shows the box-and-whisker plot for the ProNT BNP levels of the different IIEF subgroups. The ProNT BNP levels belonging to all subgroups showed statistically significant differences according to the Kruskal-Wallis test ($p < 0.001$). Central lines mark the medians, terminal lines represent the ranges, and rectangles represent the 25th and 75th percentiles.

Table 2. Clinical and hematochemical parameters of patients with chronic congestive heart failure and corresponding p values

	No ED (n = 18)	Mild ED (n = 18)	Moderate ED n = 18)	Severe ED (n = 18)	p value
Clinical Values					
Age (years)	63.62 ± 6.21	66.54 ± 6.92	68.30 ± 8.04	65.61 ± 7.72	0.272
Diabetes (%)	1 (5.55%)	6 (33.33%)	2 (11.11%)	4 (22.22%)	0.136
Smoking (%)	8 (44.44%)	8 (44.44%)	7 (38.88%)	8 (44.44%)	0.982
Hypertension (%)	4 (22.22%)	3 (16.66%)	3 (16.66%)	2 (11.11%)	0.849
Left ventricular ejection fraction	38.51±2.10	37.21±2.27*	34.83±3.64*	30.65±3.04*	**<0.001**
Hematochemical values					
LDL (mg dl^{-1})	115.51 ± 16.11	115.14 ± 22.45	113.97 ± 25.98	115.31 ± 24.94	0.997
HDL (mg dl^{-1})	39.14 ± 3.61	41.00 ± 3.61	41.21 ± 3.92	40.51 ± 4.74	0.419
TG (mg dl^{-1})	230.72 ± 47.27	222.20 ± 53.37	225.24 ± 47.25	211.00 ± 54.94	0.614
Total cholesterol (mg dl^{-1})	184.81 ± 18.43	202.44 ± 21.52	187.74 ± 27.55	190.95 ± 16.06	0.080
Total testosterone (mg dl^{-1})	393.11 ± 61.42	387.35 ± 63.37	396.57 ± 67.02	383.07 ± 63.11	0.923
ProNT BNP (pg/ml)	289.01 ± 82.21**	712.11 ± 161.02**	1233.1 ± 322.0**	6408.1 ± 938.7**	**<0.001**
Medications					
Aspirin (%)	10 (55.5%)	11 (61.1%)	10 (55.5%)	13 (72.2%)	0.314
Beta blocker	16 (88.9%)	17 (94.4%)	16 (88.9%)	17 (94.4%)	0.876
ACE inhibitors/ARB (%)	15 (83.3%)	16 (88.9%)	16 (88.9%)	15 (83.3%)	0.835
Calcium channel blocker (%)	3 (16.6%)	2 (11.1%)	2 (11.1%)	3 (16.6%)	0.765

IEF-5, International Index of Erectile Function-5; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.
*Significantly different from the other ED groups according to the post-hoc analysis following the Kruskal-Wallis test.
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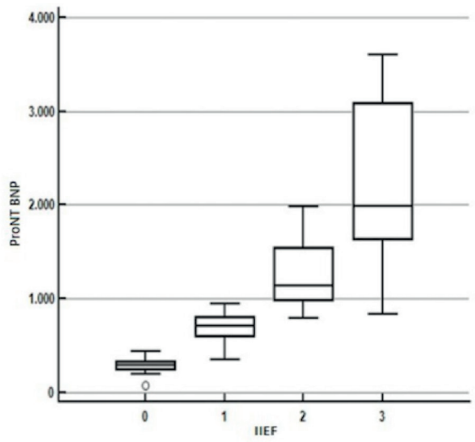

Figure 1. Box-and-whisker plot for the ProBNP levels of different IIEF subgroups

DISCUSSION

The relationship between ED and cardiovascular diseases have been investigated in many studies (10-11). Both CCHF and ED have many common etiologic causes, such as diabetes mellitus, smoking, obesity, hypertension, and immobilization. However, ED in CCHF has not been adequately studied despite being among the most frequent consequences of cardiovascular diseases.

The clinical outcomes of CCHF lead to many systemic impairments and organ dysfunctions. In patients with CCHF, multiple factors play a role at the microvascular level, such as reduced arterial compliance, endothelial dysfunction, and generalized or focal atherosclerosis (12). The prevalence of ED in patients with CCHF appears to be significantly higher; 80% of patients with CCHF had ED, which was associated with age, medical conditions, comorbidities, drugs used for treatment, and psychological disorders. In patients with CCHF, ED has a negative impact on their quality of life (13). Agents, such as beta-blockers or RAAS blockers that are used in the treatment of cardiac insufficiency may lead to ED due to their effect on the level of peripheral circulation. HF also leads to ED as a clinical consequence of pumping defects and restricted peripheral circulation. These consequences can be avoided with an optimal CCHF treatment. In patients with CCHF presenting with ED complaints, many physicians associate the latter with the medication used for CCHF. In this study, differences were found between different ED severity groups although equivalent doses of CCHF medication had been prescribed for all patient groups. We observed that the severity of ED had a positive correlation with ProNT BNP as a prognostic indicator of CCHF.

ED is described as not being able to reach or maintain an erection in the desired time for a proper sexual intercourse (14). Erection is a function regulated through hormones and neurovascular mechanisms both at cerebral or peripheral levels (15). ED can occur as a result of hormonal imbalance, neural disorders, or insufficient

blood supply to the penis (16). Insufficient blood supply may be a consequence of impaired endothelial function associated with HF. A substantial proportion of patients with HF suffer from ED, and the administration of an optimal treatment can substantially increase the exercise capacity in patients with HF. The increased efor capacity of patients will make them feel ready for sexual activity psychologically (17).

ProNT BNP levels have been associated with many cardiovascular diseases and their consequences, including coronary artery disease, acute ischemic stroke, chronic renal failure, and cardiac cachexia. ProNT BNP has been suggested as a diagnostic and prognostic marker of CCHF (18). The ProNT BNP release is stimulated by ventricular tension and is strongly correlated with left ventricular dysfunction and structural abnormalities (19). Congestion is responsible for many clinical consequences of CCHF. Changes in the level of BNP during the follow-up are associated with the level of congestive condition and clinical consequences (20).

In recent years biomarkers have emerged as important tools for diagnosis, risk stratification and therapeutic decision making in cardiovascular diseases. Currently, ProNT BNP is widely used as diagnostic biomarkers for heart failure and has proven its diagnostic usefulness in studies and thus have progressed from bench to clinical application (21). This study demonstrated whether the treatment of ED should focus on cardiac failure or impotence in patients diagnosis with HF. The level of ProNT BNP will guide us in the prevention of other potential complications, as well as treatment effectiveness. In this study, we identified a positive correlation between ED and ProNT BNP levels.

CONCLUSION

Patients with CCHF may exhibit different ProNT BNP levels. Therefore, we believe that in the evaluation of ED, which is a pathology that can be considered as end-organ damage in heart failure, ProNT BNP levels may give valuable diagnostic information and serve as a rapid screening tool to evaluate ED in patients with CCHF. We consider that high levels of ProNT BNP measured in patients with CCHF may conduce to enhanced treatment of the disease, resulting in the improvement of ED as a clinical consequence of CCHF. The limitations of our study include having a low power derived from small patient groups and the lack of an objective ED diagnosis based on penile Doppler ultrasound.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The study was conducted in the tertiary cardiovascular unit of a university hospital and approved by the local University Ethics Committee (approval date: 18.06.2018; approval number: 2018/12-117).

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