SEXUAL MEDICINE ORIGINAL RESEARCH

ERECTILE DYSFUNCTION

Deterioration of Chronotropic Responses and Heart Rate Recovery Indices in Men With Erectile Dysfunction

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ABSTRACT

Introduction: Erectile dysfunction (ED) and cardiovascular (CV) diseases share common risk factors and ED has been accepted as an early manifestation of CV disease. Exercise stress testing (EST) is used to evaluate CV functions in men with ED. Low exercise workload, a slower heart rate recovery (HRR) after exercise, and inability to increase heart rate during EST (chronotropic incompetence) are independent negative predictors of adverse CV outcomes.

Aim: To assess the association among EST parameters, ED, and testosterone levels.

Methods: The study population consisted of 41 patients with ED and 40 controls. All participants underwent treadmill EST to assess cardiac autonomic functions. HRR indices were calculated by subtracting 1st (HRR1), 2nd (HRR2), and 3rd (HRR3) minute heart rates during the recovery period from maximal heart rate. Total exercise duration, exercise capacity and chronotropic response, and plasma testosterone levels were evaluated. Erectile functions were evaluated with the Sexual Health Inventory for Men. Patients were divided into subgroups according to severity and duration of ED.

Main Outcome Measures: Mean HRR1 (30.6 ± 11.9 vs 36.9 ± 9.9; $P = .01$), HRR2 (44.9 ± 12.4 vs 54.9 ± 7.8; $P < .001$), and HRR3 (50.1 ± 11.7 vs 63.0 ± 7.9; $P < .001$) were significantly lower in the ED than in the control group. Total exercise duration (9.4 ± 1.9 vs 10.9 ± 1.7 minutes; $P < .001$), exercise capacity (12.5 ± 1.9 vs 13.6 ± 1.4 metabolic equivalents; $P = .004$), and chronotropic response (0.88 ± 0.1 vs 1.0 ± 0.1; $P < .001$) were worse in the ED group. However, we found no association between severity and duration of ED and EST parameters. In addition, serum testosterone levels were significantly correlated with HRR1 ($r = 0.36$, $P = .02$) in men with ED.

Conclusion: Our data suggested that cardiac autonomic functions are impaired in patients with ED. A weak correlation between cardiac autonomic dysfunction and low testosterone levels in patients with ED was noted. However, further studies are needed to elucidate the prognostic significance and clinical implications of impaired autonomic functions and testosterone replacement therapy in patients with ED. **Kucukdurmaz F, Agar G, Resim S. Deterioration of Chronotropic Responses and Heart Rate Recovery Indices in Men With Erectile Dysfunction. Sex Med 2017;X:XXX–XXX.**

Key Words: Erectile Dysfunction; Heart Rate Recovery; Chronotropic Response; Testosterone

INTRODUCTION

Erectile dysfunction (ED) is described as the inability to attain and maintain an erection that is sufficient for satisfactory sexual performance.[1] Epidemiologic studies have shown that prevalence rates vary from 20% to 50% in men 40 to 70 years old, with a steep age-related increase.[2,3] ED can disturb physical and psychological health and result in significant lowering of quality-of-life scores of men and their partners.[4] Moreover, increasing evidence shows that ED can be an early manifestation of coronary artery and peripheral vascular diseases. Therefore, it can be hypothesized that ED is not only a quality-of-life issue but also an early marker of cardiovascular (CV) diseases (CVDs).[5,6] However, it is not affordable to evaluate all patients with ED for cardiac diseases. Priority for cardiac evaluation of patients with ED can be given to those who live in regions with prevalence toward CVD or share more than a few common risk factors for ED and CVD.

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ED and CVD share unmodifiable and modifiable common risk factors, such as obesity, diabetes mellitus, dyslipidemia, hypertension, metabolic syndrome, smoking, and lack of exercise.[7–9] In addition, autonomic nervous system (ANS) dysfunction is considered another common pathophysiologic mechanism linking the 2 diseases. The relation between ANS and erectile function is well known. In normal physiologic conditions, activation of the parasympathetic system is mandatory to provide penile erection. Studies have reported that ANS dysfunction can lead to ED.[10,11]

The ANS has a pivotal role in the regulation of cardiac and vascular systems and its disruption can lead to CV events, which can result in morbidity and mortality.[12,13] Cardiac autonomic functions can be evaluated by exercise stress testing (EST). Of EST parameters, heart rate (HR) recovery (HRR) index is important for investigating cardiac effects of ANS and is accepted as an indicator of parasympathetic reactivation.[14] In addition, chronotropic responses (CRs) can reflect changes in ANS behavior.

In a previous study, younger patients with ED were found to have decreased functional capacity and CR compared with men without ED.[15] More recently, Ioakeimidis et al[16] reported that abnormal HRR and chronotropic incompetence (ChI) were associated with endothelial dysfunction and were lower in men with ED. Furthermore, severity of ED correlated with the worsening of those parameters. Ulucan et al[17] also noted that HRR indices and effort capacity were remarkably decreased in patients with ED. These 2 studies suggest that these findings might indicate possible pathophysiologic links and could help predict CV risk in patients with ED.

Therefore, the aim of the present study was to further investigate the association of EST parameters with the presence, severity, and duration of ED. We also evaluated the relation between serum testosterone levels and EST parameters in men with ED.

METHODS

Study Populations

This case-control study was carried out in the cardiology and urology clinics of a tertiary university hospital in Kahramanmaras, a province located at the intersection of the southeast and Mediterranean regions of Turkey, from December 2016 through February 2017. Patients admitted to the andrology outpatient clinic with the complaint of ED were referred to the cardiology department for EST to investigate cardiac autonomic functions. Participants were selected from those who were admitted to the hospital without considering their place of birth or ethnic or religious origins to provide a generalized study population. Initially, 59 men underwent EST. However, 18 were not enrolled in the study because of the following exclusion criteria: 6 used medications that could lead to arrhythmia, 4 had thyroid dysfunction, 3 had peripheral vascular disease, and 2 had bundle branch block. Also excluded were 3 patients who showed ischemic changes during EST. Therefore, 41 men who were diagnosed with ED according to the 5-item International Index of Erectile Function (IIEF-5) participated in the study. 40 controls were recruited from the hospital staff. In the beginning, 65 men were selected for the control group. Those subjects were asked about previous cardiac events or presence of relatives with known cardiac diseases, history of ED, and use of erectogenic drugs or supplements including testosterone. Subsequently, 13 men were excluded owing to a history of angina and presence of first-degree relatives with known cardiac diseases. 5 and 7 patients were excluded owing to the use of erectogenic drugs and testosterone supplements, respectively. Inclusion criteria of cases were age older than 18 years and the diagnosis of ED. Exclusion criteria were the presence of diagnoses of coronary artery disease, peripheral vascular disease, ejection fraction less than 50%, atrial fibrillation, renal or liver dysfunction, chronic obstructive pulmonary disease, psychological diseases including depression and anxiety disorders, drug abuse, malignancy, moderate to severe valvular heart disease, bundle branch block and atrioventricular conduction abnormalities on electrocardiogram, thyroid dysfunction, anemia, electrolyte imbalance, use of medications that could lead to arrhythmia or ED, hormonal therapy for ED, pelvic surgery, or trauma. In addition, participants who showed ischemic changes during EST were excluded. Although we provided strict exclusion criteria to control for possible confounders, cases and controls could have had some unmeasured confounders such as stress, duration of smoking, dietary habits, and daily exercise patterns.

Clinical and laboratory characteristics of the participants including age and hematologic and biochemical parameters were obtained. All patients underwent a 12-lead electrocardiographic and transthoracic echocardiographic examination (Vivid 7 System, GE-Vingmed Ultrasound AS, Horten, Norway) to rule out rhythm disorders, heart failure, and valvular heart diseases. Written informed consent was obtained from each subject and the institutional ethics committee approved the study protocol.

Evaluation of Erectile Function

Participants' erectile function was evaluated according to comprehensive medical and sexual history, physical examination, IIEF-5 score, and morning testosterone levels. The IIEF-5 is a validated and widely used questionnaire in clinical settings and was used to evaluate sexual function within the past 6 months.[18] Responses to each of the 5 items on the IIEF-5, which are based on a rating scale from 0 to 5 or from 1 to 5 (depending on the item), are summed to arrive at a total score that can range from 1 to 25, with higher scores indicating better sexual health. Patients with a score no higher than 21 might have evidence of ED. For men in a stable relationship (ie, men who had an opportunity for sexual activity), ED was categorized as mild (score = 12−21), moderate (score = 8−11), or severe (score = 1−7). We also classified duration of ED as shorter than 1 year, 1 to 5 years, or longer than 5 years.