

Deterioration of heart rate recovery index in patients with erectile dysfunction

Şeref Ulucan, Zeynettin Kaya, Ahmet Keser, Hüseyin Katlandur, Mustafa Karanfil¹, İsmail Ateş²

Department of Cardiology, Faculty of Medicine, Mevlana University; Konya-Turkey

¹Department of Cardiology, Meram Faculty of Medicine, Necmettin Erbakan University; Konya-Turkey

²Division of Cardiology, Sema Hospital; Almaty-Kazakhstan

ABSTRACT

Objective: Heart rate recovery (HRR) after exercise is a function of vagal reactivation. This study aimed to evaluate HRR index in patients with erectile dysfunction.

Methods: Men over the age of 18 years who were diagnosed with erectile dysfunction were included in the study. Ninety patients with erectile dysfunction (mean age=56.1±8.3 years) and 50 healthy subjects as controls (mean age=53.1±10.4 years) were compared. The erectile status of patients was evaluated using the sexual health inventory for men questionnaire. Basal electrocardiography, echocardiography, and treadmill exercise testing were performed in all patients and controls. The HRR index was defined as the reduction in heart rate from the rate at peak exercise to the rate at the first minute (HRR₁), second minute (HRR₂), third minute (HRR₃), and fifth minute (HRR₅) after terminating exercise stress testing. An independent sample t-test, Pearson correlation coefficient test, linear multivariate regression analysis, and receiver operating characteristic curve analysis were used for statistical assessment.

Results: All HRR indices were found to be significantly decreased in patients with erectile dysfunction (p<0.001). Effort capacity was markedly lower (9.1±2.3 vs. 10.4±2.3 METs, p=0.002) among patients with erectile dysfunction. HRR₁ and HRR₃ were found to be an independent risk factor for erectile dysfunction (Beta=0.462, p<0.001; Beta=0.403, p<0.001; respectively) in linear regression analysis.

Conclusion: Decreased HRR index may be considered as one of the independent predictors of impaired autonomic function in patients with erectile dysfunction. (*Anatol J Cardiol* 2016; 16: 264-9)

Keywords: erectile dysfunction, heart rate recovery index, exercise test, autonomic nervous system

Introduction

Erectile dysfunction (ED) is the loss of ability to provide and maintain a satisfactory erection (1), and the frequency of ED increases in the elderly (2). ED has many organic and psychological contributors. Hormonal disorders, such as hypogonadism, cause ED (3), and there is also an evident association between ED and cardiovascular risk factors, including hypertension, dyslipidemia, diabetes mellitus, smoking, and metabolic syndrome, particularly with increasing age (4). Moreover, ED can be caused by psychological disorders and conditions, such as depression (5). The relationship between autonomic nervous system (ANS) dysfunction and ED has been investigated, and reports suggest that dysfunction of both the sympathetic and parasympathetic nervous systems could lead to ED (6, 7).

The autonomic nervous system plays a key role in the regulation of the cardiac and vascular systems; therefore, deterioration of

ANS function plays a vital role in cardiovascular morbidity and mortality (8, 9). The heart rate recovery (HRR) index is an important parameter for evaluating ANS cardiac effects and is a direct indicator of parasympathetic system activity (10, 11). HRR is defined as a decrease in peak heart rate that is observed during a cool-down period after a stress test (12). Arrhythmias, such as atrial fibrillation, are commonly observed in patients with ED, and previous reports have suggested that ANS dysfunction is a common pathophysiological mechanism for both disorders (1, 13). The deterioration of the HRR index may be a predictor of the arrhythmia-ED interaction.

Patients with ED have been reported to have ANS dysfunction by multiple techniques (13, 14). Doğru et al. (15) we aimed to investigate the relationship between heart rate recovery (HRR revealed that patients with ED exhibit HRR deterioration; however, HRR indices have not been separately evaluated. This study aimed to evaluate HRR indices and exercise test parameters in patients with ED.

Address for Correspondence: Dr. Zeynettin Kaya, Mevlana Üniversitesi Tıp Fakültesi, Kardiyoloji Bölümü, Yeni İstanbul Cad. No: 235 42003 Selçuklu, Konya-Türkiye
Phone: +90 505 253 70 49 E-mail: zeynettinkaya@yahoo.com

Accepted Date: 18.06.2015 **Available Online Date:** 20.07.2015

©Copyright 2016 by Turkish Society of Cardiology - Available online at www.anatoljcardiol.com
DOI:10.5152/AnatolJCardiol.2015.6132



Table 1. Demographic and clinical features of patients and the controls (mean±SD)

	Patients with ED (n=90)	Healthy controls (n=50)	P
Age, years	56.1±8.3	53.1±10.4	0.08
Body mass index, kg/m ²	27.7±3.4	27.9±2.9	0.80
Heart rate, beats/min	85.1±11.9	84.9±13.4	0.91
Systolic blood pressure, mm Hg	131.5±12.3	131.9±19.1	0.92
Diastolic blood pressure, mm Hg	80.5±14.9	81.4±14.6	0.73
Fasting glucose, mg/dL	104.4±24.2	102.5±12.5	0.76
Total cholesterol, mg/dL	196.9±42.5	195.6±35.3	0.81
HDL cholesterol, mg/dL	40.9±8.8	42.2±7.9	0.37
LDL cholesterol, mg/dL	116.7±32.2	120.4±30.7	0.55
Plasma triglyceride, mg/dL	193.3±139.1	175.4±129.2	0.43
Independent samples t-test (mean±SD) ED- erectile dysfunction; HDL- high density lipoprotein; LDL- low density lipoprotein			

Methods

Study design

Ninety patients with ED (mean age=56.1±8.3 years) and 50 healthy control individuals without ED (mean age=53.1±10.4 years) were included in our cross sectional observational study. After the necessary cardiac examinations, patients admitted to the urology clinic of the Mevlana University Hospital between June 2013 and February 2014 who had been diagnosed with ED and who met all the criteria for inclusion were enrolled in the study. The erectile status of patients was evaluated using the sexual health inventory for men (SHIM) questionnaire. The SHIM questionnaire is also known as the International Index of Erectile Function (IIEF)-5. The SHIM questionnaire contains five items and is the shortened version of the 15-item IIEF questionnaire. Each item is scored from 0 or 1 to 5, yielding a global sexual function score of between 1 and 25. A SHIM score of <21 was defined as ED (16). Patient demographic data (age and gender), clinical features, and hematological and biochemical parameters were recorded at the time of admission. All patients were evaluated by a 12-lead electrocardiogram (ECG). Transthoracic echocardiography was performed in all patients to exclude heart failure and significant valvular heart disease. The left ventricle ejection fraction was obtained using the biplane modified Simpson's method (17).

The inclusion criteria were adult patients who were aged ≥18 years and diagnosed with ED. The exclusion criteria were as follows: diagnoses of coronary artery disease, peripheral artery disease, and overt diabetes mellitus (fasting blood glucose level ≥126 mg/dL); impaired glucose tolerance (fasting blood glucose level ≥110 mg/dL); advanced-stage renal (GFR <60 mL/

min) or liver dysfunction; hypertension; a micropenis; hypogonadism; hyper or hypothyroidism; Cushing's disease; heart failure (ejection fraction <50%); severe heart valve disease; cardiac rhythm and conduction disturbances; chronic obstructive pulmonary disease; severe anemia (hemoglobin <10 g/dL); malignancy; history of stroke; use of drugs that can cause ED, such as hypertensive agents, or affect HRR; psychiatric diseases, such as psychosis, major depression, or anxiety disorders; antidepressant or antipsychotic drug use; smoking; alcohol use; and ischemia during an exercise stress test.

Informed consent forms were obtained from all patients. The study protocol was approved by the local Ethics Committee.

Exercise testing

All patients underwent an exercise test with treadmill (Schiller Cardiovit AT-104, Reomed AG, Switzerland) using the Bruce protocol. The target heart rate was calculated by the following formula: 220-age. Stress exercise test qualification was determined if the heart rate reached 85% of the target rate. Patients walked for a 2-min cool-down period at a 1.5-mph speed and 2.5% grade (18). The decrease in heart rate from the peak rate (HRR indices) was measured during the cool-down period at the 1st, 2nd, 3rd, and 5th minutes after cessation of the stress test and are denoted as HRR₁, HRR₂, HRR₃, and HRR₅, respectively. EKG results were recorded within 5 min after the stress test. Hemodynamic parameters (heart rate and rhythm, blood pressure), symptoms, and estimated functional capacity in metabolic equivalents (METs; where 1 MET=3.5 mL/kg/min oxygen consumption) were also recorded by trained exercise technicians.

Statistical analysis

All statistical calculations were performed using the SPSS (version 20.0 for Windows; SPSS, Chicago, IL, USA) program. Normal distribution of the data was evaluated using the Kolmogorov-Smirnov test. Continuous variables are given as means±SD; categorical variables are defined as percentages. An independent sample t-test was used to compare the study variables between patients with ED and healthy controls. Correlation analyses were performed using the Pearson correlation coefficient test. A linear multivariate regression analysis and receiver operating characteristic (ROC) curve analysis were done. A probability value of p<0.05 was considered significant.

Results

The demographic and clinical features of were similar between the ED and control groups (Table 1). Both groups had blood pressures in the normal range, and there were no statistically significant differences between systolic or diastolic blood pressures. All subjects had a normal sinus rhythm, and there were no pathological alterations detected by ECG. All patients met the qualification criteria for the exercise tests. Arrhythmia,

Table 2. Comparison of echocardiographic and exercise stress test derived variables of patients and controls (mean±SD)

	Patients with ED (n=90)	Healthy controls (n=50)	P
Ventricular M-mode derived variables			
Left ventricular end-diastolic diameter, mm	49±4.2	50±3.7	0.12
Left ventricular end-systolic diameter, mm	31.9±5.7	32.6±4	0.40
Left ventricular ejection fraction, %	66.1±5.1	67.2±3.8	0.18
Systolic pulmonary artery pressure, mm Hg	30±3.2	29.2±3.7	0.21
Exercise stress test findings			
Exercise time, min	8.9±2.6	9.2±2.8	0.42
Maximal heart rate, beats/min	158.2±18.7	167.2±16	0.004
Maximal systolic blood pressure, mm Hg	152.4±17.7	152.2±13.6	0.92
Maximal diastolic blood pressure, mm Hg	84.1±13.8	84.2±13.8	0.94
Maximal metabolic equivalents, METs	9.1±2.3	10.4±2.3	0.002
HRR ₁	34.8±11.2	41.7±15.5	<0.001
HRR ₂	42.8±14.9	53.9±12.6	<0.001
HRR ₃	48.8±14.4	64.5±15.5	<0.001
HRR ₅	58.9±20.1	75.1±15.8	<0.001

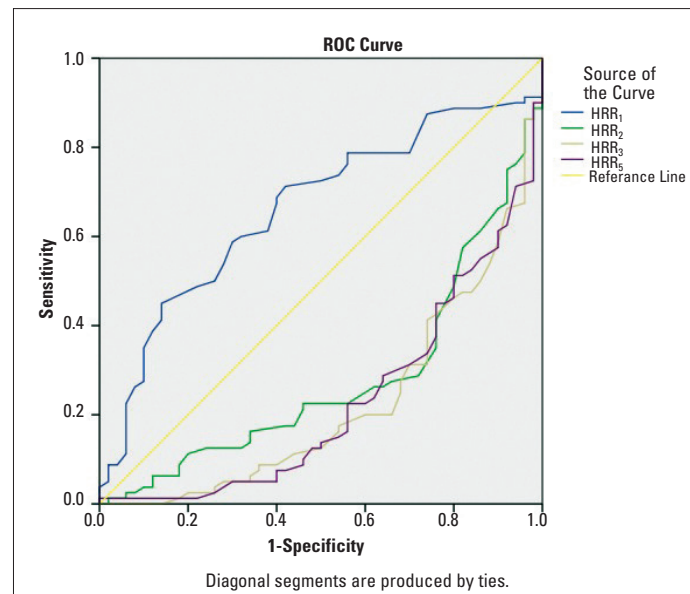
ED- erectile dysfunction; HRR- heart rate recovery index
METs- metabolic equivalents (1 MET=3.5 mL/kg per min of oxygen consumption)
Independent samples t-test (mean±SD)

ischemia, hemodynamic instability, syncope, and other pathological conditions were not observed during exercise.

Transthoracic echocardiography and exercise test parameters were analyzed in the ED and control groups. Transthoracic echocardiography data were similar between the two groups (all p values >0.05) (Table 2).

Blood pressure, heart rate changes, maximal MET values, and HRR indices were compared between the groups. Exercise duration and peak systolic and diastolic blood pressures were similar between the groups (Table 2). The maximum heart rate was lower in patients with ED than healthy controls (158.2±18.7 vs. 167.2±16 beats/min; p=0.004). Similarly, exercise capacity, which was assessed in METs, was found to be statistically lower in the ED group than in the control group (9.1±2.3 vs. 10.4±2.3; p=0.002).

HRR indices, an indicator of ANS function, were analyzed in both the groups. After the 1st and 2nd minutes, HRR indices were significantly lower in the ED group than in the control group (34.8±11.2 vs. 41.7±15.5; p<0.001 and 42.8±14.9 vs.

**Figure 1. ROC curve analysis of HRR₁, HRR₂, HRR₃, and HRR₅ for ED**

53.9±12.6; p<0.001, respectively). Similarly, HRR indices after the 3rd and 5th minutes of the recovery phase were significantly lower in individuals with ED than in control individuals (48.8±14.4 vs. 64.5±15.5, p<0.001 and 58.9±20.1 vs. 75.1±15.8, p<0.001, respectively) (Table 2).

In linear multivariate regression analysis (including age, sex, smoking, body mass index, hyperlipidemia, maximal exercise heart rate, resting heart rate, maximal exercise systolic blood pressure, maximal exercise diastolic blood pressure, resting systolic blood pressure, resting diastolic blood pressure, fasting blood glucose, HRR₁, HRR₂, HRR₃, and HRR₅ as dependent parameters), only HRR₁ and HRR₃ were found to be independent risk factors for ED (Beta=0.462, p<0.001; Beta=0.403, p<0.001; respectively).

In ROC curve analysis, the optimal cut-off value of HRR₁ to predict ED was 35.5, with 68.8% sensitivity and 60.0% specificity (area under the curve 0.662, 95% confidence interval 0.567–0.756, p=0.02, Fig. 1).

Discussion

In this study, all HRR indices were found to be decreased in the ED group than in the control group. Furthermore, HRR₁ and HRR₃ were found to be independent risk factors for ED. The effort capacity was also significantly lower in patients with ED than in healthy controls.

Satisfactory erection occurs through an increase in parasympathetic activity and a decrease in sympathetic activity (6). In one study, autonomic nervous system dysfunction was indicated as an etiological factor responsible for ED (19); however, it is not always possible to identify the underlying cause. Other studies have demonstrated that an imbalance between parasympathetic and sympathetic activities, namely an increase in sympathetic activity and a decrease in parasympathetic activity, leads to ED (14, 20, 21).

The autonomic nervous system is essential for normal functioning of the cardiovascular system. Heart rate is increased during exercise and then decreased upon exercise cessation, and this process is controlled by ANS. Previous studies have reported that sympathetic activity is increased during exercise and is responsible for the increase in heart rate; at the same time, parasympathetic activity is suppressed (22). Then, during the resting phase after exercise, when heart rate decreases, parasympathetic activity increases and sympathetic activity decreases (23). Previous studies have demonstrated that HRR indices are a direct indicator of parasympathetic activity (24, 25) and that an increase in parasympathetic activation along with a decrease in sympathetic activation occur during the first minutes of the recovery phase (25) Imai et al. (23) reported that HRR indices at 30 s and 2 min occurred because of the reactivation of the suppressed parasympathetic system. Kannankeril et al. (26) revealed that parasympathetic activity regulated heart rate. Together, these findings indicate that parasympathetic system activity is suppressed during exercise and during the first minute of recovery and then steadily increases until 4 min post-exercise and remains stable until 10 min post-recovery (23, 26). Alterations in HRR indices have been previously investigated in heart failure (27) albeit not fully recognized, in the development of vascular complications in diabetes mellitus (28), ischemic heart disease (18, 22), obstructive sleep apnea (29), pulmonary arterial hypertension (30), systemic lupus erythematosus (31) and its impairment is an independent prognostic indicator for cardiovascular and all-cause mortality. Dođru et al. (15) demonstrated decreased HRR values in patients with ED; however, HRR indices have not been separately evaluated. Patients with coronary artery disease, diabetes mellitus, neurological diseases, and ischemic changes during the stress test were excluded from our study because of the potential impacts on the HRR index values. Furthermore, the ED and control groups were similar to each other in terms of demographic and clinical features, indicating that the influence of other factors on HRR indices in this study was low. Our results demonstrate that exercise capacity, which was assessed in METs, was reduced in patients with ED than in the healthy control group. This is consistent with previous studies that have demonstrated that the frequency of ED is decreased in patients with good physical fitness (32). Moreover, the results of this study demonstrate that patients with ED have reduced HRR indices and thus, decreased parasympathetic reactivation. In addition, these results suggest that HRR indices that were evaluated by the exercise stress test can be used as measures of parasympathetic and sympathetic activation.

In this study, we found that individuals with good physical fitness had good parasympathetic system activation and thus, larger HRR indices. While this is true in a sense, when we think about the cause and effect relationship, it is obvious that both increased sympathetic activation and decreased parasympa-

thetic activation are reasons for ED in individuals with low physical fitness. Low physical fitness may be the reason for ED, and a decline in HRR indices can be an indication of both low physical fitness and ED. In this study, the results were expected, namely that patients with ED had lower HRR indices and reduced physical fitness than in the control group. Additional studies are required to completely ascertain the contribution of physical fitness to ED, and this could be achieved by performing the same experiments on subjects with the same level of physical fitness with or without ED.

Abnormal HRR has been defined as heart rate decreases of <12 beats/min, 1 min after post-exercise cool down; <18 beats/min, 1 min after immediately stopping exercise by laying in a supine position; and <42 beats/min after 2 min (8, 33). In many studies, HRR index decreases are interpreted as an indicator of cardiovascular morbidity and mortality (34). Similarly, in other studies, the extent of the decrease in heart rate during the first minute post-exercise has been suggested to predict the presence of myocardial diffusion defects and total mortality (35, 36). However, HRR is not an accurate diagnostic method for any disease.

Many complex methods exist to evaluate ANS function; however, they are difficult to use in daily practice because of the special training and equipment required. Therefore, HRR indices are a useful and beneficial tool to measure autonomic activation and have been used in many studies. In this study, we demonstrated that patients with ED had lower HRR indices than in the control group. Thus, autonomic dysfunction, which is observed as a decrease in HRR indices in ER patients, can be used to predict the risk of cardiovascular morbidity and mortality.

Study limitations

In this study, the HRR indices of patients with ED were examined and compared with a group of healthy controls. The design of the study is suitable, and the number of cases was sufficient to address the hypothesis. In contrast, the results cannot be applied to the general population because of the broad exclusion criteria. In addition, the effects of ED and decreased HRR indices on cardiovascular outcomes were not investigated. Furthermore, because the physical fitness of the ED group was lower than that of the control group, the prevalence of ED and HRR indices in groups with similar physical fitness is unknown. Furthermore, testosterone analysis could not be performed because of the cost, and the psychosocial aspects (e.g., anxiety, stress) of ED were not evaluated.

Conclusion

HRR indices and effort capacity are decreased in patients with ED. Decreased HRR after a stress test can be considered an indicator of impaired autonomic function in patients with ED.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - Ş.U.; Design - Ş.U., Z.K.; Supervision - S.Ü.; Materials - A.K.; Data collection &/or processing - H.K., H.Ö.; Analysis &/or interpretation - Ş.U., Z.K.; Literature search - M.K.; Writing - Ş.U.; Critical review - S.Ü., M.K.

References

1. Dong JY, Zhang YH, Qin LQ. Erectile dysfunction and risk of cardiovascular disease: meta-analysis of prospective cohort studies. *J Am Coll Cardiol* 2011; 58: 1378-85.
2. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. *Am J Med* 2007; 120: 151-7.
3. Isidori AM, Buvat J, Corona G, Goldstein I, Jannini EA, Lenzi A, et al. A critical analysis of the role of testosterone in erectile function: from pathophysiology to treatment-a systematic review. *Eur Urol* 2014; 65: 99-112.
4. Pastuszak AW. Current Diagnosis and Management of Erectile Dysfunction. *Curr Sex Health Rep* 2014; 6: 164-76.
5. Perelman MA. Erectile dysfunction and depression: screening and treatment. *Urol Clin North Am* 2011; 38: 125-39.
6. Jung J, Jo HW, Kwon H, Jeong NY. Clinical neuroanatomy and neurotransmitter-mediated regulation of penile erection. *Int Neurourol J* 2014; 18: 58-62.
7. Hecht MJ, Neundörfer B, Kiesewetter F, Hilz MJ. Neuropathy is a major contributing factor to diabetic erectile dysfunction. *Neurol Res* 2001; 23: 651-4.
8. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med* 1999; 341: 1351-7.
9. Lauer MS, Okin PM, Larson MG, Evans JC, Levy D. Impaired heart rate response to graded exercise. Prognostic implications of chronotropic incompetence in the Framingham Heart Study. *Circulation* 1996; 93: 1520-6.
10. Shetler K, Marcus R, Froelicher VF, Vora S, Kalisetti D, Prakash M, et al. Heart rate recovery: validation and methodologic issues. *J Am Coll Cardiol* 2001; 38: 1980-7.
11. Okutucu S, Karakulak UN, Aytémir K, Oto A. Heart rate recovery: a practical clinical indicator of abnormal cardiac autonomic function. *Expert Rev Cardiovasc Ther* 2011; 9: 1417-30.
12. Ardiç I, Kaya MG, Yarlioglu M, Dođdu O, Büyükođlan H, Kalay N, et al. Impaired heart rate recovery index in patients with sarcoidosis. *Chest* 2011; 139: 60-8.
13. Pop-Busui R, Hotaling J, Braffett BH, Cleary PA, Dunn RL, Martin CL, et al. Cardiovascular Autonomic Neuropathy, Erectile Dysfunction and Lower Urinary Tract Symptoms in Men with Type 1 Diabetes: Findings from the DCCT/EDIC. *J Urol* 2015; 193: 2045-51.
14. Pagani M. Hypertension, stress and erectile dysfunction: potential insights from the analysis of heart rate variability. *Curr Med Res Opin* 2000; 16(Suppl 1): s3-8.
15. Dođru MT, Bařar MM, Hacıslamođlu A. The difference of heart rate recovery between males with and without erectile dysfunction. *Ann Noninvasive Electrocardiol* 2010; 15: 223-9.
16. Arıbař A, Kayrak M, Ulucan S, Keser A, Demir K, Alibasić H, et al. The relationship between uric acid and erectile dysfunction in hypertensive subjects. *Blood Press* 2014; 23: 370-6.
17. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; 2: 358-67.
18. Akyüz A, Alpsoy S, Akkoyun DC, Deđirmenci H, Güler N. Heart rate recovery may predict the presence of coronary artery disease. *Anatol J Cardiol* 2014; 14: 351-6.
19. Çelik O, İpekçi T, Akarken I, Ekin G, Köksal T. To evaluate the etiology of erectile dysfunction: What should we know currently? *Arch Ital Urol Androl* 2014; 86: 197-201.
20. Cheitlin MD. Sexual activity and cardiac risk. *Am J Cardiol* 2005; 96: 24M-28M.
21. Giuliano F, Rampin O. Neural control of erection. *Physiol Behav* 2004; 83: 189-201.
22. Vivekananthan DP, Blackstone EH, Pothier CE, Lauer MS. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. *J Am Coll Cardiol* 2003; 42: 831-8.
23. Imai K, Sato H, Hori M, Kusuoka H, Ozaki H, Yokoyama H, et al. Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure. *J Am Coll Cardiol* 1994; 24: 1529-35.
24. Arai Y, Saul JP, Albrecht P, Hartley LH, Lilly LS, Cohen RJ, et al. Modulation of cardiac autonomic activity during and immediately after exercise. *Am J Physiol* 1989; 256: H132-41.
25. Savin WM, Davidson DM, Haskell WL. Autonomic contribution to heart rate recovery from exercise in humans. *J Appl Physiol* 1982; 53: 1572-5.
26. Kannankeril PJ, Le FK, Kadish AH, Goldberger JJ. Parasympathetic effects on heart rate recovery after exercise. *J Investig Med* 2004; 52: 394-401.
27. Lipinski B. Pathophysiology of oxidative stress in diabetes mellitus. *J Diabetes Complications* 2001; 15: 203-10.
28. Jae SY, Carnethon MR, Heffernan KS, Fernhall B, Lee MK, Park WH. Heart rate recovery after exercise and incidence of type 2 diabetes in men. *Clin Auton Res* 2009; 19: 189-92.
29. Maeder MT, Münzer T, Rickli H, Schoch OD, Korte W, Hürny C, et al. Association between heart rate recovery and severity of obstructive sleep apnea syndrome. *Sleep Med* 2008; 9: 753-61.
30. Ramos RP, Arakaki JSO, Barbosa P, Treptow E, Valois FM, Ferreira EVM, et al. Heart rate recovery in pulmonary arterial hypertension: relationship with exercise capacity and prognosis. *Am Heart J* 2012; 163: 580-8.
31. Dođdu O, Yarlioglu M, Kaya MG, Ardiç I, Ođuzhan N, Akpek M, et al. Deterioration of heart rate recovery index in patients with systemic lupus erythematosus. *J Rheumatol* 2010; 37: 2511-5.
32. Kařka D, Domagařa Z, Dworak J, Womperski K, Rusiecki L, Marciniak W, et al. Association between physical exercise and quality of erection in men with ischaemic heart disease and erectile dysfunction subjected to physical training. *Kardiol Pol* 2013; 71: 573-80.

33. Cole CR, Foody JM, Blackstone EH, Lauer MS. Heart rate recovery after submaximal exercise testing as a predictor of mortality in a cardiovascularly healthy cohort. *Ann Intern Med* 2000; 132: 552-5.
34. Mora S, Redberg RF, Cui Y, Whiteman MK, Flaws JA, Sharrett AR, et al. Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the lipid research clinics prevalence study. *JAMA* 2003; 290: 1600-7.
35. Pierpont GL, Stolpman DR, Gornick CC. Heart rate recovery post-exercise as an index of parasympathetic activity. *J Auton Nerv Syst* 2000; 80: 169-74.
36. Louthrenoo W, Ruttanaumpawan P, Aramrattana A, Sukitawut W. Cardiovascular autonomic nervous system dysfunction in patients with rheumatoid arthritis and systemic lupus erythematosus. *QJM Mon J Assoc Physicians* 1999; 92: 97-102.



From Prof. Dr. Siber Göksel's collections