Heart rate recovery in hypertensive patients: relationship with blood pressure control

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Delayed heart rate recovery (HRR) post treadmill exercise testing reflects autonomic dysfunction and is related to worse cardiovascular outcome. The present study compared HRR in normotensive subjects and hypertensive patients taking anti-hypertensive medications with controlled blood pressure (BP) and uncontrolled BP. A total of 279 consecutive patients with \( n = 140 \), HP and without \( n = 139 \), N-HP essential hypertension who were hospitalized in our department during May 2012 to March 2016 were included in this study. All subjects underwent treadmill exercise testing. Hypertensive patients were divided into controlled BP \( n = 88 \) and uncontrolled BP \( n = 52 \) groups according to their BP prior to treadmill exercise testing. Body mass index, triglyceride level and incidence of diabetes mellitus (DM) were significantly higher in the HP group than in the N-HP group, and HDL-c and HRR were significantly lower. Male gender, higher creatinine value and lower cholesterol and HDL-c were associated with lower HRR in the N-HP group, and higher triglyceride, lower LDL-c, and HDL-c were associated with lower HRR in the HP group. More frequent, \( > 3 \), antihypertensive drug use, less monotherapy use and high incidence of smokers and lower HRR were found in hypertensive patients with uncontrolled BP compared to hypertensive patients with controlled BP. The present results demonstrate that uncontrolled BP following antihypertensive medication is associated with lower HRR in hypertensive patients.

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INTRODUCTION

Hypertension remains a major public health problem that is associated with considerable morbidity and mortality.\(^1\) The rate of decline in heart rate (HR) after exercise (HR recovery, or HRR) reflects the status of vagal tone activation and sympathetic tone withdrawal post exercise. Lower HRR represents an autonomous imbalance and is related to a worse cardiovascular outcome.\(^2\) Previous studies have shown reduced HRR in hypertensive patients.\(^3,4\) The impact of BP control on HRR in hypertensive patients is not fully understood. Beta-blockers are widely used to lower BP in hypertensive patients and exert a direct impact on HR. Previous studies have shown that HRR maintained its prognostic value in heart failure patients, regardless of beta-blocker use.\(^5\) Karnik et al.\(^6\) demonstrated that beta-blockers do not affect HRR in patients with a negative exercise stress echocardiography result and that HRR may be used for mortality prediction in these patients. HRR is improved in the presence of beta-blockers in patients with a positive exercise stress echocardiography result.\(^6\) The impact of beta-blockers on hypertensive patients has not been reported. The present study compared the HRR between hospitalized normotensive subjects and hypertensive patients and between hypertensive patients with controlled and uncontrolled BP in the absence and presence of beta-blockers.

PATIENTS AND METHODS

Study population
A total of 279 consecutive hospitalized patients with \( n = 140 \) and without \( n = 139 \) diagnoses of essential hypertension who underwent treadmill exercise tests and achieved the submaximal goal HR \( [(220−\text{age})×0.85] \) during May 2012 to March 2016 were included in this retrospective study. Patients with acute coronary syndrome, old myocardial infarction, complete left bundle branch block, WPW syndrome, atrial fibrillation, valvular heart disease and known non-ischemic cardiomyopathy were excluded. Patients treated with digitals were also excluded. The local hospital ethics committee approved the study protocol, and written consent was obtained from each participating patient. All hypertensive patients received antihypertensive medication. Venous blood samples were obtained for lipid measurements following an overnight fast.

Treadmill exercise test
The treadmill exercise test was performed as previously described on a GE T2100 treadmill machine equipped with CASE6.5 software and exercise ECG test system according to the ACC/AHA 2002 guideline update for exercise testing.\(^7\) Symptom-limited Bruce's protocol was used, and a surface 12-lead ECG was continuously monitored. BP was measured and recorded at rest, the end of each stress stage, peak stress, and recovery until six minutes after exercise or ST segment returned to the baseline level.\(^8,9\) The exercise was stopped at the time of submaximal goal HR \( [(220−\text{age})×0.85] \). The treadmill test was performed according to the Bruce plan: the initial speed was of the treadmill was 1.7 km h\(^{-1}\), slope 10°; the second speed was 2.5 km h\(^{-1}\), slope 12°; the third speed was 3.4 km h\(^{-1}\), slope 14°; and the fourth speed was 4.2 km h\(^{-1}\), slope 16°. The speed increased every 3 min. HR and BP at rest and after exercise were measured in a sitting position using the method proposed by the American Heart Association.\(^10\) HRR1 for the treadmill test was analyzed.

Figure 1 shows HR and HRR changes after exercise.\(^4\) The overall kinetics of HR or HRR during the transition from exercise peak to rest 1–5 min was described using the following mono-exponential function:\(^4\)

\[
\text{HR( or HRR)}(t) = a_0 + a_1 \times \left(1 - e^{-t/T}\right)
\]

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where $\alpha_0$ is the pre-recovery value of HR (or HRR) of exercise peak and $\alpha_1$ is the amplitude of the change in HR (or HRR) from $\alpha_0$. $T$ is the recovery time constant (mean response time) and represents the time required to attain 63% of the steady-state amplitude. The model parameters were estimated using least-squares nonlinear regression, in which the best fit was defined by minimizing the residual sum of squares and minimal variation of residuals.

Follow-up
Patients were followed up for 3–48 months, with an average follow-up time of 18.8 ± 11.7 months, by phone call or home/clinic visit.

Statistical analysis
Continuous data are expressed as the mean ± standard deviation. Student’s $t$-test was used for comparisons between groups. The chi-square test was used to compare the rates. The risk factors for hypertension were determined using multivariate logistic regression model after adjusting for age and gender. $P$-values < 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS 19.0 software (Armonk, NY, USA).

RESULTS
Clinical features of patients in N-HP and HP groups
Table 1 shows the clinical characteristics between N-HP and HP patients. Body mass index (BMI), triglyceride level and incidence of DM were significantly higher in the HP group than in the N-HP group, and HDL-c and HRR were significantly lower. BP was significantly higher in the HP group than the N-HP group before treadmill exercise, at peak exercise and 1 and 5 min post exercise. HR was significantly higher and HRR was significantly lower in the HP group than the N-HP group at 1–5 min after exercise. The percent of manual labour was similar between the N-HP and HP patients.

**Figure 1.** (a, b) HR change and HRR change post-exercise for the HP and NHP groups; (c, d) HR change and HRR change post-exercise for the BP uncontrolled and BP controlled groups. $P$-values at individual data points represent the $P$-value between groups at that specific time point. The data are shown as the mean ± s.d.
groups, and education status was better in the HP group than in the N-HP group.

Multiple regression analysis showed that history of DM, higher BMI, TG values, education level, and reduced HRR post exercise were risk factors and that higher HDL-c was a protective factor of HP after adjusting for gender and age (Table 2). Figure 1a and b show the HR and HRR changes post exercise in the N-HP and HP groups.

Clinical features and risk factor comparison between N-HP and HP patients with normal and reduced HRR

Table 3 shows the clinical features of N-HP and HP patients with normal or reduced HRR. Male gender, smoking, BMI and creatinine values were higher in non-HP subjects, and CHOL and HDL-c values were lower in the reduced HRR group compared with the normal HRR group. TG was higher in HP subjects, while LDL-c and HDL-c were lower in the reduced HRR group compared to the normal HRR group.

Clinical features of hypertensive patients with or without beta-blockers

We divided the hypertensive patients into without beta-blockers group and with beta-blockers group to observe the potential impact of beta-blockers on HRR in hypertensive patients (Table 5). Our results demonstrated that the clinical characteristics, including HRR, were comparable between the groups, which suggest that HRR was not significantly affected by beta-blockers in hypertensive patients.

Follow-up results

Two patients were lost to follow-up, one patient in the HP group and the other in the N-HP group. There were no deaths or acute myocardial infarctions during the follow-up. Three of the 97 patients (3.1%) in the N-HP group with normal HRR and two of the 41 patients (4.9%) in the HP group with reduced HRR were hospitalized due to cardiac reasons. Three of the 74 patients (4.1%) in the HP group with normal HRR and three of the 65 patients (4.6%) in the HP group with reduced HRR were hospitalized due to cardiac reasons. The incidence of re-hospitalization due to cardiac reasons was similar among groups.

**DISCUSSION**

This study found that HRR was significantly lower in hypertensive patients compared with non-hypertensive patients. HRR was also significantly lower in hypertensive patients with uncontrolled BP compared with hypertensive patients with controlled BP. Our data

**Table 1. Clinical characteristic of N-HP patients and HP patients**

|                     | N-HP (n = 139) | HP (n = 140) | P-value |
|---------------------|----------------|-------------|---------|
| Age (yr)            | 57.17 ± 6.14   | 58.72 ± 7.29 | 0.056   |
| Male gender (n, %)  | 49/139 (35.3%) | 58/140 (41.4%) | 0.289   |
| BMI (kg/m²)         | 23.16 ± 3.43   | 25.18 ± 3.48 | 0.000   |
| Smoker (n, %)       | 32/139 (23.0%) | 45/140 (32.1%) | 0.088   |
| Manual labour (n, %)| 84/139 (60.4%) | 90/140 (64.3%) | 0.056   |
| Education (n, %)    | 0.013          |             |         |
| Primary school and below (n, %)| 29/139 (20.9%) | 12/140 (8.6%) | 0.001   |
| Middle school (n, %)| 44/139 (31.7%) | 46/140 (32.9%) | 0.596   |
| High school (n, %)  | 56/139 (40.3%) | 62/140 (44.3%) | 0.687   |
| University and above (n, %) | 10/139 (7.2%) | 20/140 (14.3%) | 0.096   |
| CAD (n, %)          | 47/139 (33.8%) | 45/140 (32.1%) | 0.767   |
| DM (n, %)           | 12/139 (8.6%) | 27/140 (19.3%) | 0.010   |
| Dyslipidemia (n, %) | 102/139 (73.4%) | 116/140 (82.9%) | 0.056   |
| Creatinine (μmol)   | 64.89 ± 14.34  | 66.18 ± 14.71 | 0.459   |
| CHOL (mg/dl)        | 184.46 ± 69.3 | 140.46 ± 7.17 | 0.134   |
| HDL-c (mg/dl)       | 41/139 (29.5%) | 65/140 (46.4%) | 0.004   |
| HB (mg/dl)          | 91.63 ± 12.41  | 96.19 ± 13.3 | 0.003   |
| HRR2 (mg/dl)        | 50.09 ± 11.88  | 44.27 ± 11.49 | 0.000   |
| HRR3 (mg/dl)        | 31.19 ± 10.43  | 25.92 ± 7.86  | 0.000   |
| HRR4 (mg/dl)        | 57.96 ± 10.61  | 52.83 ± 10.80 | 0.000   |
| HRS (mg/dl)         | 83.72 ± 10.22  | 86.38 ± 11.97 | 0.000   |
| HRR5 (mg/dl)        | 58.01 ± 10.59  | 54.08 ± 10.80 | 0.000   |
| SBP before Ex (mm Hg)| 119.47 ± 12.27 | 130.49 ± 14.34 | 0.000   |
| DBP before Ex (mm Hg)| 75.43 ± 8.19  | 80.76 ± 8.93  | 0.000   |
| SBP peak (mm Hg)    | 156.30 ± 22.96 | 175.13 ± 20.20 | 0.000   |
| DBP peak (mm Hg)    | 73.50 ± 11.23  | 80.20 ± 11.33 | 0.000   |
| SBP at 1 min post Ex (mm Hg) | 134.66 ± 18.06 | 150.11 ± 21.39 | 0.000   |
| DBP at 1 min post Ex (mm Hg) | 75.42 ± 7.75  | 79.39 ± 10.09 | 0.016   |
| DBP at 5 min post Ex (mm Hg) | 124.65 ± 17.84 | 138.26 ± 16.77 | 0.000   |
| SBP at 5 min post Ex (mm Hg) | 76.25 ± 7.57  | 80.94 ± 9.50  | 0.000   |
| Time for Ex (minute)| 4.52 ± 1.86   | 4.24 ± 1.72  | 0.203   |
| Exercise tolerance (Mets)| 6.34 ± 1.69  | 6.36 ± 1.77  | 0.911   |
| Ejection fraction medication | 0.62 ± 0.06 | 0.63 ± 0.07 | 0.541   |

**Abbreviations:** ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BMI, body mass index; CAD, coronary artery disease; CCB, Calcium Channel Blockers; CHOL, cholesterol; DBP, diastolic blood pressure; DM, diabetes mellitus; Ex, treadmill exercise; HDL-c, high density lipoprotein cholesterol; HP, hypertensive; HR, heart rate; HRn, heart rate at n minute post exercise; HRR, heart rate recovery; HRRn, heart rate recovery at n minute post exercise; LDL-c, low density lipoprotein cholesterol; Mets, metabolic equivalents (1MET = 3.5 ml kg⁻¹ per minute of oxygen consumption); N-HP, normotensive; SBP, systolic blood pressure; TG, triglyceride; yr, year.
indicate that more intensive BP control is essential to improve the autonomous balance and outcome for hypertensive patients and HRR, which is an inexpensive and easily available biomarker. HRR should be monitored to guide anti-hypertensive therapy. To the best of our knowledge, this study is the first report describing the association between HRR and BP in hypertensive patients receiving anti-hypertensive therapy.

Reduced HRR and hypertension

The present study found that HRR was reduced in hospitalized patients with hypertension compared with hospitalized patients without hypertension, which is consistent with previous studies. Multiple regression analysis demonstrated that besides history of DM, higher BMI and TG values, reduced HRR1 were also important risk factors of hypertension after adjusting for gender and age. Notably, our results showed that HRR1, HRR3 and HRR5 were significantly lower in hypertensive patients with uncontrolled BP than in hypertensive patients with controlled BP. This novel finding suggests that optimal BP after anti-hypertensive medication is related to an improved sympathetic/vagal balance in hypertensive patients. As expected, the percent of patients using a combined drug therapy regimen was higher in hypertensive patients with uncontrolled BP, and the percent of monotherapy use was more often seen in hypertensive patients with controlled BP. These results indicate that the sympathetic/vagal imbalance in patients with uncontrolled BP might serve as a reason for the uncontrolled BP despite the use of medications according to the current guideline. Strategies that aim to improve sympathetic/vagal imbalance might be important to treat patients with uncontrolled BP in addition to guideline-conforming antihypertensive medications.

Risk stratification for patients with severe cardiovascular diseases, such as in chronic heart failure patients (NYHA II or III) with left ventricular ejection fraction $\leq 40\%$ could be already made by lower HRR ($\leq 18$ per minute), and higher HRR might be applicable to patients with relatively ‘mild’ cardiovascular diseases, as in the case of uncomplicated essential hypertension shown in this study and in patients with stable heart failure ($\leq 24$/minute). The mean HRR in the present study cohort was $31 \pm 10$ for non-hypertensive patients with uncontrolled BP, and the percent of patients with controlled BP. These results indicate that the sympathetic/vagal imbalance in patients with uncontrolled BP might serve as a reason for the uncontrolled BP despite the use of medications according to the current guideline. Strategies that aim to improve sympathetic/vagal imbalance might be important to treat patients with uncontrolled BP in addition to guideline-conforming antihypertensive medications.

| Table 2. Multivariate logistic regression results for risk of HP |
|---------------------------------------------------------------|
| **B**  | **s.e.**  | **Wald**  | **P-value**  | **Exp**  | **95% CI lower limit**  | **95% CI upper limit**  |
| N: 360 |
|-----------------|---------|---------|------------|---------|---------------------|---------------------|
| BMI (kg/m$^{2}$) | 0.194  | 0.041  | 22.600  | 0.000  | 1.214  | 1.121  | 1.316  |
| Education       |         |         |          |         |         |         |        |
| Middle school (n, %) | 0.930  | 0.407  | 5.215  | 0.022  | 2.534  | 1.141  | 5.629  |
| High school (n, %) | 1.062  | 0.397  | 7.137  | 0.008  | 2.891  | 1.327  | 6.229  |
| University and above (n, %) | 1.613  | 0.534  | 9.116  | 0.003  | 5.018  | 1.761  | 14.296 |
| DM (n, %)        | 0.951  | 0.377  | 6.357  | 0.012  | 2.588  | 1.236  | 5.422  |
| TG (mM)          | 0.321  | 0.108  | 8.834  | 0.003  | 1.379  | 1.116  | 1.704  |
| HDL-c (mM)       | $-1.22$ | 0.405  | 9.116  | 0.003  | 0.295  | 0.133  | 0.651  |
| HRR1 (b.p.m.)    | 0.059  | 0.015  | 16.196 | 0.000  | 1.061  | 1.031  | 1.092  |
| HRR1 $\leq 24$ (%) | 0.653  | 0.258  | 6.389  | 0.011  | 1.921  | 1.158  | 3.188  |
| HRR2 (b.p.m.)    | 0.043  | 0.012  | 13.162 | 0.001  | 1.044  | 1.020  | 1.068  |
| HRR2 $\leq 24$ (%) | 0.959  | 0.278  | 11.860 | 0.001  | 2.608  | 1.512  | 4.501  |
| HRR3 (b.p.m.)    | 0.036  | 0.012  | 8.887  | 0.003  | 1.036  | 1.012  | 1.060  |
| HRR4 (b.p.m.)    | 0.033  | 0.012  | 7.221  | 0.007  | 1.034  | 1.009  | 1.059  |
| HRR5 (b.p.m.)    | 0.031  | 0.012  | 6.459  | 0.011  | 1.032  | 1.007  | 1.057  |

Abbreviations: BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; HDL-c, high-density lipoprotein cholesterol; HP, hypertensive; HRR, heart rate recovery; HRRn, heart rate recovery at n minute post exercise; TG, triglyceride.
education level was slightly higher in the HP group compared to the N-HP group. The underlying reasons for higher hypertension in this small study cohort could not be explained, and it is beyond the scope of the present study. The percentage of labor occupation and education level were similar between hypertensive patients with controlled and uncontrolled BP. Therefore, these factors might not be related to the lower HRR found in hypertensive patients with uncontrolled BP.

Clinical implications

The present study suggests that reduced HRR, which is a simple and inexpensive biomarker, is related to hypertension and reflects suboptimal BP control in hypertensive patients. Therefore, monitoring HRR during antihypertensive therapy might be an essential strategy to improve the autonomous balance and outcome for hypertensive patients.

Study limitations

First, the present retrospective study results were derived from a small patient cohort based on a single center database. Our results need to be validated by a larger patient cohort from multi-center database. Second, the outcome during the short-term (18.8 ± 11.7 months) follow-up was similar among groups. A longer follow-up period is warranted to observe the impact of reduced HRR on outcomes in this patient cohort. Third, a
Table 4. Clinical characteristic of HP patients with controlled and uncontrolled BP

|                | BP controlled (n=88) | BP uncontrolled (n=52) | P-value |
|----------------|---------------------|------------------------|---------|
| Age (yr)        | 58.19±7.70          | 59.62±6.51             | 0.266   |
| Male gender (n, %) | 32/88 (36.4%)     | 26/52 (50.0%)          | 0.114   |
| BMI (kg m⁻²)    | 25.16±3.58          | 25.22±3.36             | 0.920   |
| Smoker (n, %)   | 22/88 (25.0%)       | 23/52(44.2%)           | 0.019   |
| Manual labour (n, %) | 56/88 (63.6%)   | 34/52(67.3%)           | 0.835   |
| Education (n, %) |                     |                        | 0.357   |
| Primary school and below (n, %) | 7/88 (8.0%)         | 5/92 (9.6%)            |         |
| Secondary and above (n, %) |                     |                        |         |
| School (n, %)   | 17/88 (19.3%)       | 14/52 (26.9%)          | 0.134   |
| School (n, %)   | 18/88 (20.5%)       | 13/52 (25.0%)          | 0.277   |
| Years (n, %)    | 27/88 (30.4%)       | 17/52 (32.7%)          | 0.491   |
| Year (n, %)     | 14/88 (16.1%)       | 9/52 (17.3%)           | 0.706   |
| Year (n, %)     | 16/88 (18.2%)       | 7/52 (13.5%)           | 0.447   |
| Year (n, %)     | 19/88 (21.6%)       | 8/52 (15.4%)           | 0.370   |
| Year (n, %)     | 22/88 (25.0%)       | 10/52 (19.2%)          | 0.223   |
| Year (n, %)     | 25/88 (28.4%)       | 11/52 (21.1%)          | 0.200   |
| Year (n, %)     | 28/88 (31.4%)       | 12/52 (23.1%)          | 0.146   |
| Year (n, %)     | 31/88 (35.2%)       | 14/52 (26.9%)          | 0.159   |
| Year (n, %)     | 34/88 (38.4%)       | 16/52 (30.8%)          | 0.090   |
| Year (n, %)     | 37/88 (41.5%)       | 18/52 (34.6%)          | 0.057   |
| Year (n, %)     | 40/88 (45.1%)       | 20/52 (38.5%)          | 0.031   |

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARBs, angiotensin receptor blocker; BP, blood pressure; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; CHOL, cholesterol; DBP, diastolic blood pressure; DM, diabetes mellitus; Ex, treadmill exercise; HDL-c, high density lipoprotein cholesterol; HP, hypertensive; HR, heart rate; HRn, heart rate at n minute post exercise; HRR, heart rate recovery; HRRn, heart rate recovery at n minute post exercise; LDL-c, low density lipoprotein cholesterol; Mts, metabolic equivalents (1MET = 3.5 ml kg⁻¹ per minute of oxygen consumption); SBP, systolic blood pressure; TG, triglyceride; yr, year.

Table 5. Clinical characteristic of HP patients with and without beta-blockers

|                | Without beta-blockers (n=70) | With beta-blockers (n=70) | P-value |
|----------------|------------------------------|---------------------------|---------|
| Age (yr)       | 58.29±7.41                  | 59.16±7.20               | 0.482   |
| Male gender (n, %) | 28/70 (40.0%)            | 30/70 (42.9%)             | 0.731   |
| BMI (kg m⁻²)   | 25.85±3.25                  | 24.51±3.61               | 0.022   |
| Smoker (n, %)  | 21/70 (30.0%)               | 24/70 (34.3%)             | 0.587   |
| Manual labour (n, %) | 46/70 (65.7%)        | 44/70 (62.9%)             | 0.724   |
| Education (n, %) |                           |                           | 0.316   |
| Primary school and below (n, %) | 7/70 (10.0%)          | 5/70 (7.1%)               |         |
| Middle school (n, %) | 18/70 (25.7%)          | 28/70 (40.0%)             |         |
| High school (n, %) | 35/70 (50.0%)            | 27/70 (38.6%)             |         |
| University and above (n, %) | 10/70 (14.3%)         | 10/70 (14.3%)             |         |
| CAD (n, %)     | 12.70±18.6%                | 33.00±47.1%              | 0.000   |
| DM (n, %)      | 17.00±24.3%                | 10.00±14.3%              | 0.134   |
| Dyslipidemia (n, %) | 60/70 (85.7%)         | 56/70 (80.0%)             | 0.370   |
| Creatinine (µmol) | 66.73±13.83               | 65.63±15.61              | 0.659   |
| CHOL (mmol)    | 4.78±0.94                  | 4.71±1.19                | 0.706   |
| TG (mmol)      | 2.31±1.59                  | 2.18±1.92                | 0.822   |
| HDL-c (mmol)   | 2.88±0.77                  | 2.80±1.15                | 0.637   |
| LDL-c (mmol)   | 5.28±1.56                  | 5.12±1.37                | 0.052   |

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARBs, angiotensin receptor blocker; BP, blood pressure; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; CHOL, cholesterol; DBP, diastolic blood pressure; DM, diabetes mellitus; Ex, treadmill exercise; HDL-c, high density lipoprotein cholesterol; HP, hypertensive; HR, heart rate; HRn, heart rate at n minute post exercise; HRR, heart rate recovery; HRRn, heart rate recovery at n minute post exercise; LDL-c, low density lipoprotein cholesterol; Mts, metabolic equivalents (1MET = 3.5 ml kg⁻¹ per minute of oxygen consumption); SBP, systolic blood pressure; TG, triglyceride; yr, year.

Prospective study is needed to explore the impact of intensive BP control on HRR and outcome in hypertensive patients. Notably, HRR could be affected by aerobic fitness, and the lower HRR in hypertensive patients with uncontrolled BP compared to hypertensive patients with controlled BP might reflect differences in aerobic fitness. The present study could not clarify this issue because of the lack of some data, such as VO₂ peak derived from...
cardiopulmonary exercise tests. Future studies are warranted to clarify this issue using cardiopulmonary exercise tests. The resting HR was relatively high (~80 per minute) in the N-HP and HP groups, although beta-blockers were prescribed to approximately 30% of the patients without hypertension and 50% of the hypertensive patients. Mental stress before the treadmill exercise test might play a minor role in these subjects, but this factor could not be confirmed in this study. Medication compliance might be another difficult-to-confirm issue for the relatively high resting HR in the study subjects. Although all patients confirmed their prescribed medications by answering the questionnaire sheets, we could not confirm whether individual patients actually took their prescribed medication.

CONCLUSIONS

The present results show that uncontrolled BP post antihypertensive medication is associated with lower HRR in hypertensive patients. Monitoring HRR might be an important strategy to optimize therapeutic efficacy by focusing on improving autonomous balance and outcome for hypertensive patients.

What is known about the topic?

- Reduced heart rate recovery (HRR) post-treadmill exercise testing reflects autonomic dysfunction.
- Reduced HRR is related to worse cardiovascular outcome.

What this study adds?

- HRR was significantly lower in the HP group than the N-HP group.
- HRR was also significantly lower in hypertensive patients with uncontrolled BP than hypertensive patients with controlled BP post antihypertensive medication.

Table 6. Multivariate logistic regression results for risk of uncontrolled BP

| HRR1 (b.p.m.) | B     | s.e.   | Wald  | P-value | Exp 95% Cl lower limit | 95% Cl upper limit |
|---------------|-------|--------|-------|---------|------------------------|-------------------|
| 0.040         | 0.027 | 2.157  | 0.142 | 1.041   | 0.987                  | 1.096             |
| HRR1 ≤ 24 (%) | 0.801 | 0.388  | 4.250 | 0.039   | 2.227                  | 1.040             |
| 0.032         | 0.020 | 2.713  | 0.100 | 1.033   | 0.994                  | 1.074             |
| HRR4 (b.p.m.) | 0.028 | 0.021  | 1.816 | 0.178   | 1.028                  | 0.987             |
| HRR5 (b.p.m.) | 0.026 | 0.021  | 1.529 | 0.216   | 1.026                  | 0.985             |

Abbreviations: BP, blood pressure; CI, confidence interval; HRR, heart rate recovery; HRRn, heart rate recovery at n minute post exercise.

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REFERENCES

1. Chobanian AV. Time to reassess blood-pressure goals. N Engl J Med 2015; 373:2093–2095.
2. Ramos RP, Arakaki JS, Barbosa P, Trepotow E, Valois FM, Ferreira EV et al. Heart rate recovery in pulmonary arterial hypertension: relationship with exercise capacity and prognosis. Am Heart J 2012; 163:580–588.
3. Erdogan D, Gonul E, Icli A, Yucel H, Arslan A, Akcay S et al. Effects of normal blood pressure, prehypertension, and hypertension on autonomic nervous system function. Int J Cardiol 2011; 151:50–53.
4. Best SA, Bivens TB, Dean Palmer M, Boyd KN, Melyn Galbreath M, Okada Y et al. Heart rate recovery after maximal exercise is blunted in hypertensive seniors. J Appl Physiol (1985) 2014; 117:1302–1307.
5. Arena R, Myers J, Abella J, Peberdy MA, Bensimhon D, Chase P et al. The prognostic value of the heart rate response during exercise and recovery in patients with heart failure: influence of beta-blockade. Int J Cardiol 2010; 138:166–173.
6. Kamnik RS, Lewis W, Miles P, Baker L. The effect of beta-blockade on heart rate recovery following exercise stress echocardiography. Prev Cardiol 2008; 11:26–28.
7. Gibbons RJ, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 2002; 106:1883–1892.
8. Yu Y, Peng D, Liu T, Bai Y, Zou W, Gao B et al. Diagnostic value of combined exercise-induced ST segment changes and heart rate recovery post treadmill exercise for the detection of coronary artery disease in the real world: a single center experience. IRJPEH 2015; 2:232–237.
9. Ghaffari S, Kazemi B, Alakbarzadeh P. Abnormal heart rate recovery after exercise predicts coronary artery disease severity. Cardiol J 2011; 18:47–54.
10. Perloff D, Grim C, Flack J, Frohlich ED, Hill M, McDonald M et al. Human blood pressure determination by sphygmomanometry. Circulation 1993; 88:2460–2470.
11. Gharacholou SM, Scott CG, Borlaug BA, Kane GC, McCully RB, Oh JK et al. Relationship between diastolic function and heart rate recovery after symptom-limited exercise. J Card Fail 2012; 18:34–40.
12. Jaques H. NICE guideline on hypertension. Eur Heart J 2013; 34:406–408.
13. Bilisel T, Terzi S, Akbulut T, Sayar N, Hobikoglu G, Yesilcimen K. Abnormal heart rate recovery immediately after cardiopulmonary exercise testing in heart failure patients. Int Heart J 2006; 47:431–440.
14. Yilmaz A, Erdem A, Kucukdurmaz Z, Karapinar H, Gul I, Sarikaya S et al. Abnormal heart rate recovery in stable heart failure patients. Pacing Clin Electrophysiol 2013; 36:591–595.

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