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Effects of Resistance Training on Autonomic Nervous Function in Older Individuals

Hidetaka Hamasaki

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Abstract

Skeletal muscle mass, strength, and function decline with aging are the symptoms that characterize sarcopenia, which has become a significant problem in aging societies. Aging is also associated with arterial stiffness and autonomic nervous dysfunction, leading to increase in the risk of cardiovascular disease (CVD) and mortality. Resistance training (RT) is effective for improving muscle fitness in older individuals as well as young healthy individuals. However, the effects of RT on autonomic nervous function (ANF) in the elderly have not been fully elucidated. The author reviewed the current evidence regarding RT and ANF in older individuals. Whole-body, high-intensity or progressive RT had either no effect on ANF or perhaps an unfavorable effect on ANF. On the other hand, local isometric, moderate-intensity RT may have a beneficial effect on ANF in older individuals. The combination of RT and aerobic exercise had a favorable effect on ANF in older patients with comorbidities. However, the optimal intensity, frequency, and duration of RT for improving ANF in older individuals remain unknown. Further studies with a large number of subjects are warranted.

Keywords: resistance training, sarcopenia, autonomic nervous function, heart rate variability

1. Introduction

Sarcopenia, age-related loss of muscle mass and/or decline in muscle strength and perform-ance [1] has become a significant problem in aging societies. Sarcopenia is associated with the increased risk of disability [2] and mortality [3], and resistance training (RT) should be performed in the elderly as well as healthy young individuals. A cohort study showed that

guideline-concordant RT reduced the risk of all-cause mortality (odds ratio 0.64) in older individuals over 65 years of age [4]. On the other hand, we should be careful when prescribing RT for older individuals with disabilities or diseases because such individuals may develop physical impairments due to their low physical fitness. Adverse effects of RT on the elderly have not been adequately reported in previous clinical studies [5]. Transient changes in blood pressure in response to exercise or environmental changes (e.g., posture, atmospheric pressure, temperature) are intricately regulated by the reciprocal action of the sympathetic and parasympathetic nervous systems. However, the incidences of orthostatic and postprandial hypotension increase with age [6], and systolic hypertension is caused by an increase in arterial stiffness and sympathetic nervous dysfunction in the elderly [7]. Aging is also a significant factor associated with reduced baroreflex sensitivity and increased blood pressure [7], and furthermore, baroreflex dysfunction in older subjects may be the underlying pathophysiological mechanism in vasovagal syncope [8]. Muscle sympathetic nerve activity (MSNA) increases with age in both men and women [9]. Higher sympathetic nerve activity causes hypertension with aging. Long-term endurance exercise (EE) decreases sympathetic nerve activity and increases parasympathetic nerve activity, which may reduce the risk of cardiovascular disease (CVD) [10]. However, the effect of RT on the cardiac autonomic nervous function (ANF) of younger individuals is controversial. Progressive RT with an emphasis on increasing the muscle strength of the lower limbs improved the vagal modulation of heart rate [11], whereas whole-body RT had no effect on vagal-cardiac control or cardiovagal baroreflex sensitivity [12] and heart rate variability (HRV) [13]. On the other hand, Taylor et al. [14] showed that isometric handgrip training at a moderate intensity could reduce resting blood pressure and increase vagal modulations in older individuals with hypertension. A previous review also showed that isometric exercise training reduces systolic and diastolic blood pressure in both young and older individuals [15]; however, the effects of RT on autonomic nervous function (ANF), especially in older individuals, are not fully elucidated. Thus, the aim of this review was to summarize and evaluate the current evidence of RT and ANF and to provide clinicians with knowledge on the role of RT in ANF among middle-aged and older individuals.

2. Methods

The author searched for English literature on RT and ANF by using the PubMed and MEDLINE databases. The search terms were "resistance training or resistance exercise," "autonomic nervous function," and "aged or elderly." The search returned 54 published articles. Studies were included if they met the following criteria: (1) it was a randomized controlled trial, (2) the participants' mean age ≥55 years, and (3) the study duration ≥12 weeks. Studies of experimental animals were excluded from this review. The titles and abstracts of the identified articles were reviewed to determine their relevance. A total of eight articles were eligible.

3. Heart rate variability (HRV)

HRV is the most common noninvasive analysis of cardiac autonomic nervous function. Time-domain measurements of HRV include the standard deviation of normal intervals, the root-mean-square of successive differences, and the proportion of R-R intervals that differ by >50 ms from the previous R-R interval [16]. A decrease in these measurements represents the impairment of ANF in CVD [17]. The total power of HRV is an indicator of autonomic nervous system activity. The low-frequency (0.04–0.15 Hz) component of HRV is mediated by sympathetic and parasympathetic nerve activities, and the high-frequency (0.15–0.40 Hz) component of HRV is a marker of cardiac parasympathetic nervous function. The ratio of low frequency to high frequency indicates the predominance of sympathetic nerve activity [16]. HRV decreases with age as a result of reduced parasympathetic nervous system activity and the predominance of sympathetic modulation [18]. Therefore, HRV is useful for assessing ANF in older individuals.

4. The effects of RT on ANF in healthy older subjects

ANF (cardiovascular sympathetic and parasympathetic modulations) is usually evaluated by the spectral analysis of R-R intervals of electrocardiogram and blood pressure variabilities [19]. Resting HRV is also useful in the diagnosis of cardiac autonomic neuropathy in patients with type 2 diabetes [20]. Previous studies have revealed that HRV can predict mortality in healthy middle-aged and older individuals [21, 22] and patients with heart failure [23].

Madden et al. [24] examined the effects of endurance exercise (EE) and RT on HRV in healthy older women on the hypothesis that RT had no effect on HRV, while EE had a beneficial effect on HRV. Forty-five female subjects (mean age 69.9 ± 0.9 years) participated in the trial. Subjects with histories of angina, myocardial infarction, stroke, hypertension, diabetes, chronic pulmonary disease, orthopedic impairment, and medications were excluded. Subjects were randomly assigned to one of three groups: a RT group ($n = 15$), a EE group ($n = 10$), and a sedentary group ($n = 15$). The mean body mass index (BMI) of each group was 26.8 ± 1.5, 28.5 ± 2.2, and $28.2 \pm 1.3 \text{ kg/m}^2$, respectively. The subjects engaged in each exercise intervention for 6 months. The RT program consisted of three sets with 8–12 repetitions of 10 exercises and was performed five times per week under the supervision of a certified trainer. The goal of the RT was to improve upper and lower muscle strength to 85% of a one-repetition maximum (1RM). On the other hand, the EE program consisted of moderate- to vigorous-intensity exercise on a cycle ergometer and was performed five times per week. The intensity of the EE was set to 50–60% of maximal heart rate for the first 2 months and progressed to 80–85% of maximal heart rate for the remaining 4 months. No significant change in VO_{2max} was found in the RT group, while VO_{2max} significantly increased in the EE group. After the 6-month intervention, the maximal heart rate did not change in both the RT and EE groups; however, the standard deviation of the 5-min mean R-R interval and the standard deviation of heart rate were significantly increased in the EE group. RT had no significant effect on measures of HRV. The authors speculated that the reason why RT did not affect HRV was that the increased

arterial stiffness induced by RT might have reduced arterial baroreceptor sensitivity, resulting in a reduction in HRV. Indeed, high-intensity RT is known to be associated with worsening arterial stiffness [25]. In addition, increased arterial stiffness is inversely associated with cardiac vagal modulation [26]. High-intensity RT with breath holding may cause both sympathovagal imbalance (sympathetic nerve ascendant) and a decrease in arterial compliance in older subjects. The intensity of RT (progressing to 85% of 1RM) might have been too high to have a beneficial effect on ANF in the elderly.

Neuroendocrinological system	Changes
Growth hormone	↓
Insulin-like growth factor-I	↓
Thyroid stimulating hormone	↓
Testosterone	↓
Estrogen	↓
Glucocorticoids	↑
Corticotropin-releasing hormone	↑
Sympathetic nerve activity	↑

Table 1. Changes in neuroendocrine hormone concentrations in older individuals.

Melo et al. [27] showed that high eccentric RT reduced HRV. Twenty-eight healthy older men were recruited, but only nine subjects (mean age 62 ± 2.0 years) completed the study protocol. The mean BMI was 25.43 ± 1.92 kg/m². The subjects carried out 2–4 sets of bilateral eccentric knee flexion and extension 2 days per week for 12 weeks. The subjects performed 8–12 repetitions at an intensity of 75–80% of peak torque. After 12 weeks of training, systolic blood pressure decreased from 123.78 ± 8.3 mmHg to 117.67 ± 10.2 mmHg. The knee flexion and extension peak torque also increased by 13 and 20%, respectively. No changes in heart rate and log [root-mean-square of successive differences] were observed; however, the ratio of low frequency to high frequency significantly increased after training. In this study, there was a considerable discrepancy between the decrease in systolic blood pressure and the increase in HRV by 12-week RT. The authors described that the increase in HRV might have been caused by increased catecholamine levels [28, 29] and not by increased arterial stiffness [30]. However, it is unclear whether the change in catecholamine levels alone could explain the unfavorable effect on ANF. Although sympathetic nerve activity increases with age, tissue responsiveness to catecholamine decreases with age. Older individuals respond differently to exercise stress compared to younger individuals [31]. Growth hormone, insulin-like growth factor-I, thyroid stimulating hormone, testosterone, and estrogen production decline with advancing age [31–33]. In contrast, aging is associated with elevated basal levels of circulating glucocorticoids and central levels of corticotropin-releasing hormone, which are secreted in response to stress via activation of the hypothalamic pituitary adrenal axis [33]. Recent studies have suggested that leptin also induces the activation of the sympathetic nervous system [32]. Because various

neuroendocrine hormones are altered in the elderly (**Table 1**) and they have mutual relationships with each other, it is difficult to conclude that increased catecholamine levels due to RT are responsible for the reduction in HRV.

Takahashi et al. [34] reinvestigated whether eccentric strength training affected HRV because their previous study [27] showed that eccentric strength training had an unfavorable effect on HRV. A total of 22 healthy elderly male subjects participated in the study. Subjects who had hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular, respiratory and neurological disease, and musculoskeletal disease were excluded. Three subjects in the training group and two subjects in the control group dropped out. The strength training program consisted of 2–4 sets of bilateral knee eccentric flexion and extension. The subjects in the training group performed RT with 8–12 repetitions per set at the intensity of 70–80% of the peak torque value 2 days per week for 12 weeks. The heart rate response and HRV were evaluated during submaximal isometric contraction of knee extension (15, 30, and 40% of the peak torque value). The mean ages of the subjects in the training group and the control group were 62 ± 2 and 64 ± 4 years, respectively. The mean BMIs of subjects in the training group and the control group were 25.5 ± 1.8 and 26.6 ± 2.6 kg/m^2, respectively. After 12 weeks of training, peak eccentric torque (extensor and flexor) significantly increased, and group effects were also observed. On the other hand, no significant time or group effects on heart rate change during submaximal isometric contraction were found; RT did not modify heart rate change. Moreover, no significant time or group effects were observed on HRV (the root-mean-square of successive differences index) during the submaximal isometric exercise. The heart rate response pattern and HRV in the training group were similar to those in the control group. Eccentric strength training did not modify HRV or the heart rate response during isometric exercise in older men. The authors described that HRV in older subjects may be less sensitive to RT because HRV decreases with advancing age [35]. However, the effects of eccentric RT on ANF cannot be affirmed. The difference between these two studies, Melo et al. and Takahashi et al., is the measurement method of heart rate and HRV. In the former study, HRV was measured at rest, whereas in the latter study, heart rate and HRV response were measured during isometric exercise. HRV during isometric exercise and after eccentric RT includes not only a chronic effect of eccentric RT but also an acute effect of isometric exercise. Isometric handgrip exercises at 30% of the maximal isometric voluntary contraction increase vagal modulation in older hypertensive subjects [14]. Taken together, isometric RT at a moderate intensity has a beneficial effect on ANF; however, eccentric RT at a high intensity has no effect or some unfavorable effects on ANF in older individuals.

Karavirta et al. [36] examined the effects of concurrent EE and RT on heart rate dynamics compared with EE or RT alone. They measured not only conventional HRV but also fractal heart rate dynamics, utilizing detrended fluctuation analysis. This method is considered to be more suitable for evaluating heart rate dynamics during exercise [37]. A total of 105 male subjects were randomly allocated to an EE group (n = 23), a RT group (n = 25), a combined EE and RT group (n = 29), and a control group (n = 16). Ninety-three subjects (mean age 55.6 ± 7.4 years) completed the 21-week intervention program. EE was performed twice a week, and all the sessions were supervised. The subjects trained for 30 min on a bicycle ergometer

under the aerobic threshold during the first 7 weeks, and both the duration of each session and the percentage above the anaerobic threshold were increased during the weeks from 8 to 14 and from 15 to 21. RT was also carried out twice a week, and all the sessions were supervised. The RT program included 7–10 exercises per session. The subjects carried out RT with light loads (40–60% of 1RM) and a high number of repetitions (15–30) with three sets during the first 7 weeks. During weeks 8–14, the loads were increased up to 60–80% of 1RM with 6–12 repetitions per set. The subjects carried out RT with higher loads (70–85% off 1RM) and 5–8 repetitions per set to optimize the muscle strength during the last 7 weeks. The combined training group performed both twice weekly endurance and resistance trainings. After 21 weeks of training, VO_{2max} increased by $11.9 \pm 11.0\%$ in the EE group and $10.1 \pm 9.8\%$ in the combined training group, whereas no significant improvement in VO_{2max} was observed in the RT group. The 1RM of the bilateral leg extension significantly increased by $21.1 \pm 7.9\%$ in the RT group and by $22.1 \pm 9.5\%$ in the combined training group compared with the increase of $7.1 \pm 5.1\%$ in the EE group. Only subjects in the combined training group showed a decrease in fractal heart rate behavior during exercise, and the group effects were significant. The short-term fractal scaling exponent decreased from 1.18 ± 0.20 to 1.11 ± 0.21 in the combined training group during supine rest, whereas no significant change was observed in the EE or RT group. In addition, the relative change in the short-term fractal scaling exponent was inversely correlated with age at an exercise intensity of 90% of the maximal aerobic work rate. As for spectral measures of HRV, the decrease in resting heart rate was correlated with the changes in low-frequency power (0.04–0.15 Hz) and high-frequency power (0.15–0.40 Hz) in only the combined training group. This study showed that RT alone did not change heart rate dynamics. The ability to adapt to physiological changes is impaired in older individuals [38]. However, the improvement in adaptability to physiological stress, including exercise, is important because older individuals are at a high risk of CVD. Although no effects of RT on heart rate dynamics were found, the synergetic effect between EE and RT on fractal heart rate behavior was detected. The authors stated that the underlying mechanism was unknown; however, the change in MSNA due to exercise might be associated with the improvement in ANF. A previous study showed that MSNA response increased 1 week after RT using a handgrip exercise with maximal effort; however, the MSNA returned to the baseline level at 4 weeks post-training in healthy young individuals [39]. The enhanced MSNA response to strength exercise may be caused by the activation of the central nervous system rather than the muscle metaboreflex [39], indicating that sympathetic nerve hyperactivity is diluted by the repetition of RT. Long-term exercises, including RT, decreased MSNA and systolic arterial pressure and increased baroreflex sensitivity in patients with myocardial infarction [40], which suggests that the combination of EE and RT ameliorates blood vessel elasticity and arterial baroreflex control. MSNA may be a more useful and reliable indicator of ANF in the elderly than measures of HRV because it is representative of sympathetic nerve activity that innervates not only the heart but also the kidney and skeletal muscle, and the reproducibility of age and gender is very high [9].

Kanegusuku et al. [41] investigated the effects of high-intensity progressive RT on cardiovascular function and autonomic neural regulation in older individuals. Among the 83 subjects, 37 subjects were randomized into the RT group ($n = 18$) and the control group ($n = 19$). However,

six subjects dropped out in each group, and a total of 25 subjects completed the study. Subjects in the RT group performed seven supervised exercises (horizontal leg press, bilateral knee flexion, plantar flexion on the horizontal leg press, unilateral hip extension, chest press, lat pull down, and upright row on the isoinertial machines) twice a week for 16 weeks. During the first 4 weeks, subjects carried out two sets of RT with 10 repetitions, and the training sets and repetitions were progressively increased every 4 weeks. The mean ages of subjects in the RT and control group were 63 ± 4 and 64 ± 4 years, respectively. The mean BMIs of subjects in the RT and control group were 26.8 ± 4.7 and 25.7 ± 4.2 kg/m², respectively. The quadriceps cross-sectional area and the strengths of the leg press and chest press significantly increased after the 16-week high-intensity, progressive RT compared with controls. However, cardiovascular and autonomic nervous variables, such as blood pressure, systemic vascular resistance, cardiac output, heart rate, the variance of R-R intervals, high frequency, low frequency, and spontaneous baroreflex sensitivity, did not have any significant effect or interaction, and no differences between groups existed. High-intensity, progressive RT could increase muscle mass and strength in healthy older individuals without a decrease in autonomic control. In older subjects, ANF might be less responsive to exercise stress [42] because their sympathetic nerve activity is already increased at rest [9]. Even if it is high intensity, whole-body RT may not worsen ANF, even though it cannot improve ANF in the elderly.

References	Subjects	RT	Results
Madden et al. [24]	40 female subjects Age: 69.9 ± 0.9 years Dropout: five subjects	10 exercises for both upper and lower body utilizing free weights 8–12 repetitions × 3 sets, 5 times per week for 6 months Progressed to 85% of 1RM	No effects on measures of HRV
Melo et al. [27]	Nine healthy male subjects Age: 62 ± 2.0 years Dropout or excluded: 19 subjects	Bilateral eccentric knee flexion and extension 8–12 repetitions with an intensity of 75–80% peak torque × 2–4 sets, twice a week for 12 weeks	No effects on resting heart rate and log RMSSD Low-frequency/high-frequency index↓ Systolic blood pressure↓
Takahashi et al. [34]	17 healthy male subjects Age: 62 ± 2 years in the training group and 64 ± 4 years in the control group Dropout: five subjects	Bilateral eccentric knee flexion and extension 8–12 repetitions with an intensity of 70–80% peak torque × 2–4 sets, twice a week for 12 weeks HRV was evaluated during submaximal isometric contraction of knee extension	No effects on heart rate response and RMSSD during submaximal isometric contraction of knee extension
Karavirta et al. [36]	93 untrained male subjects Age: 55.6 ± 7.4 years Dropout: 12 subjects	7–10 exercises for all the main muscle groups Twice a week for 21 weeks, First 7 weeks: 15–30 repetitions with 40–60% of 1RM Second 7 weeks: 6–12 repetitions	HRV↓ in the combined RT and EE group No effects on HRV in the RT alone group

References	Subjects	RT	Results
		with 60–80% of 1RM The last 7 weeks: 5–8 repetitions with 70–85% of 1RM	
Kanegusuku et al. [41]	25 subjects (seven men and 18 women) Age: 63 ± 4 years in the training group and 64 ± 4 years in the control group Dropout: 12 subjects	Seven exercises (horizontal leg press, bilateral knee flexion, plantar flexion on the horizontal leg press; unilateral hip extension, chest press, lat pull down, and upright row on the isoinertial machines) Twice a week for 16 weeks, 10 repetitions × 2 sets, overload was progressively increased; however, the exact intensity of each session was not described in detail(only training repetitions and sets were described)	No effects on blood pressure, systemic vascular resistance, cardiac output, heart rate, the variance of R-R intervals, high frequency, low frequency, and spontaneous baroreflex sensitivity
Wanderley et al. [43]	50 subjects (11 men and 39 women) Age: 67.3 ± 4.9 years in the RT group, 69.9 ± 5.7 years in the EE group, and 67.8 ± 5.5 years in the control group Dropout: 35 subjects	Nine exercises (leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, biceps curl, low-back extension, and triceps extension) Three times per week for 8 months, 12–15 repetitions × 2 sets with an intensity of 50–60% of 1RM→resistance was progressively increased to 80% of the re-evaluated 1RM	Blood pressure↓ and resting heart rate↓ in the EE group No effects on HRV in both the EE and RT groups

RT, resistance training; ANF, autonomic nervous function; HRV, heart rate variability; 1RM, one-repetition maximum; RMSSD, root-means-square of successive differences; EE, endurance training.

Table 2. Clinical studies that investigated the effects of RT on ANF in older individuals.

Wanderley et al. [43] examined the effectiveness of EE and RT on body fat, ANF, and low-grade inflammation in community-dwelling older individuals. Eighty-five subjects were randomly allocated into an EE group, a RT group, or a control group. Subjects with acute illness, severe or uncontrolled hypertension, cardiovascular and/or respiratory disease, and pharmacological therapies that could affect cardiovascular function were excluded. Thirty-five subjects dropped out from the protocol, and a total of 50 subjects were analyzed: EE (n = 20), RT (n = 11), and control (n = 19). The subjects trained three times per week for 8 months. Each exercise session was performed for approximately 50 min under supervision. The subjects in the EE group performed a walking aerobic exercise in addition to stepping and dancing with 10 min of warm-up and cool-down. The intensity of exercise was 50–60% of heart rate reserve during the first month and increased up to 70–80% of heart rate reserve. The RT consisted of nine exercises (leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, biceps curl, low-back extension, and triceps extension) and was performed with 12–15

repetitions per set. The subjects carried out two sets of 12–15 repetitions at 50–60% of 1RM for the first month, and resistance increased to 80% of the reevaluated 1RM every 2 months. The mean age of subjects was 67.3 ± 4.9 (RT), 69.9 ± 5.7 (EE), and 67.8 ± 5.5 (control) years. The mean BMI of subjects was 29.5 ± 5.0 (RT), 28.1 ± 4.1 (EE), and 27.2 ± 3.5 (control) kg/m^2. Fifty-six percent of subjects had hypertension, 42% had dyslipidemia, and 18% had diabetes. Body fat significantly decreased in the EE and RT group after the 8-month training. The EE group demonstrated significant decrease in systolic and diastolic blood pressure and resting heart rate. RT did not affect blood pressure, heart rate, lipid profile, inflammation markers, such as hs-CRP, TNF-α, and IL-6, and 6-min walk distance. No significant change in HRV was observed in all the groups. Whole-body RT had no effects on ANF. This study is important because the study participants were not limited to healthy older individuals. The study population is more similar to that of the real world compared with previous clinical studies. The number of chronic diseases, such as hypertension, diabetes, stroke, heart disease, and cancer, increases with age. Although the prevalences of chronic diseases vary substantially by country, more than 15% of older individuals have six or more diseases in the US [44]. Therefore, clinicians should consider the influence of comorbidities in the elderly patients on ANF. This review also focuses on clinical studies that investigated the effects of RT on ANF in older subjects with heart disease. **Table 2** shows a list of published articles that investigated the effects of RT on ANF in healthy older subjects.

5. The effects of RT on ANF in older subjects with heart failure and diabetes

Few studies have investigated the effects of RT alone on ANF in older subjects with comorbidities. Although they did not evaluate the isolated effects of RT, two studies assessed the effects of cardiac rehabilitation on autonomic control in patients with heart failure [45] and the effects of combined aerobic/resistance training in patients with type 2 diabetes [46]. Ricca-Mallada et al. [45] evaluated the effects of cardiac rehabilitation on deceleration and acceleration capacity, new indicators of autonomic control of the cardiovascular system [47], in patients with heart failure with reduced left ventricular ejection fraction. Patients who were diagnosed as having chronic heart failure with New York Heart Association class I or II, who had a left ventricular ejection fraction ≤40%, and who took an optimal pharmacological therapy for heart failure were included. Twenty-four patients were randomly assigned to participate in the cardiac rehabilitation group and the control group. However, two patients in each group dropped out from the study. A total of 20 patients (10 in the training group and 10 in the control group) completed the study protocol. The mean ages of the training and control groups were 59 ± 7.92 and 56.5 ± 8.43 years, respectively. The mean BMIs of the training and control groups were 27.17 and 28.57 kg/m^2, respectively. Patients in the training group engaged in supervised training three times a week for 24 weeks. The training session consisted of 10 min of warm-up walking, 20 min of breathing exercises and nonresistance arm and leg movements, 20 min of circuit RT using a mechanical bicycle, and 5 min of cool-down stretching. The initial intensity of the bicycle ergometer was 50% of the peak workload in the exercise test, and it was gradually

increased up to the maximum workload achieved in the initial exercise test or 80% of maximum heart rate. After the 24-week cardiac rehabilitation, in the training group patients, the mean resting R-R interval was prolonged, the high- and low-frequency band of the power spectral HRV analysis had increased, and the magnitudes of deceleration and acceleration capacity had also increased, whereas the low-frequency/high-frequency index and the standard deviation of the R-R intervals did not change. In the control group patients, no significant changes in HRV-derived measures were observed. The reduction in deceleration and acceleration capacity, which are regulated by the balance between the sympathetic and parasympathetic nervous activity, is a good predictive value for mortality in patients with heart failure [47] and type 1 diabetes [48]. Cardiac rehabilitation, including circuit RT, could improve ANF in patients with chronic heart failure. Sacre et al. [46] investigated the efficacy of exercise training to improve cardiac autonomic function in type 2 diabetic patients with non-ischemic subclinical left ventricular dysfunction. Patients with valvular disease, ischemic heart disease, cardiovascular disease, psychiatric disorder, symptomatic macro- or micro-vascular complications, and low ejection fraction (<50%) were excluded. A total of 49 patients were randomly allocated to the exercise intervention group ($n = 25$) and the control group ($n = 24$). Two subjects were lost to follow-up, and 49 patients were included in the intention-to-treat analysis. The exercise program was based on the recommendation for type 2 diabetes. The patients performed 20–40 min of aerobic exercise and 6–12 RTs twice a week for 24 weeks. The exercise intensity was monitored using rating of perceived exertion and targeted to a moderate to vigorous intensity. Unfortunately, the details of the RT were not described in the paper. The mean ages of patients in the exercise and control groups were 59 ± 10 and 60 ± 9 years, respectively. The mean BMIs of the patients in the exercise and control groups were 32 ± 6 and 32 ± 5 kg/m², respectively. The study participants had fair glycemic control; i.e., their hemoglobin A1c levels were approximately 7.7%. Diastolic blood pressure was significantly higher in the exercise group at baseline. Waist circumference was significantly decreased in the exercise group with a significant difference between groups. The VO_{2peak} increased by 11% in the exercise intervention group compared with −1% in the control group. Patients in the exercise group also showed a significant increase in metabolic equivalents (+29%) compared with controls (+2%). The improvement in exercise capacity was not accompanied with a change in HRV (coefficient of variation of normal R-R intervals). Exercise elicited a significant decrease in resting heart rate and an increase in the reciprocal mean R-R interval. The standard deviation of normal R-R intervals and the total spectral power increased in the exercise intervention group, and total spectral power had a significant group effect. However, baroreflex sensitivity did not change in both groups. Ejection fraction and left ventricular mass were also unchanged in both groups. Although the coefficient of variation of the normal R-R interval did not change in this study, other markers of HRV improved without changes in cardiac function, suggesting that the recommended exercise improved cardiac sympathovagal balance in patients with type 2 diabetes. Exercise improves HRV in healthy individuals [42]; specifically, EE decreases sympathetic nerve activity and increases parasympathetic nerve activity, leading to a risk reduction in CVD [10]. This study showed that exercise also improves ANF in patients with type 2 diabetes and that RT probably contributes to it. However, the effect of RT alone on ANF in type 2 diabetic patients has not been elucidated. The autonomic nervous system concomitant

with vascular smooth muscle cells and endothelial cells plays a pivotal role in vascular recruitment in skeletal muscle. The impairment of ANF may affect muscle contraction by reducing blood flow in exercising muscle [49]. On the other hand, diabetic neuropathy impairs muscle performance by lowering motor nerve conduction, and microvascular complications induce muscle dysfunction by oxidative stress, inflammation, and decreased blood flow [49]. Therefore, investigating whether RT improves ANF as well as muscle function in patients with type 2 diabetes is quite important for the prevention of diabetic complications. Further studies are strongly needed.

6. Conclusions

Whole-body progressive RT can increase muscle mass, strength, and function in older individuals [5], which may prevent sarcopenia. However, high-intensity RT could induce arterial stiffness or a neuroendocrinological response, reduce arterial baroreceptor sensitivity, and not improve ANF in older individuals. On the other hand, local isometric RT, such as handgrip exercises, may improve ANF (**Figure 1**). Limited evidence is available on the effects of RT on ANF in older patients with comorbidities; however, RT in conjunction with EE has a favorable effect on ANF.
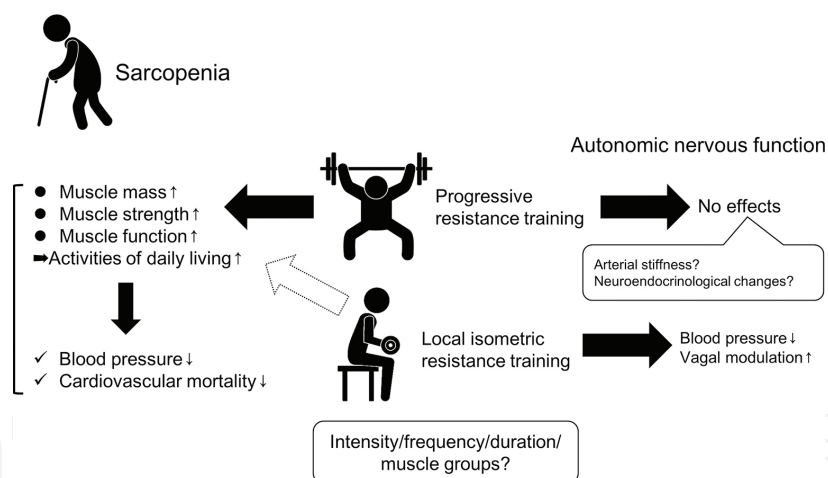

Figure 1. Whole-body progressive resistance training (RT) had no effects on autonomic nervous function (ANF), whereas local isometric RT may improve ANF in older individuals. However, to prevent and/or improve sarcopenia and to reduce the risk of cardiovascular disease and mortality, whole-body progressive RT may be required.

The clinical studies that the author reviewed were well designed; however, the sample sizes were small and many subjects dropped out of the studies (approximately 10–40% of study participants). It is still questionable whether RT is a tolerable intervention for elderly subjects. Moreover, the optimal intensity, frequency, and duration of RT to improve ANF in older individuals remain unknown. The muscle groups that should be trained are also unknown. However, progressive RT with an intensity of approximately 80% of 1RM performed 2–5 times per week for 12–24 weeks seems to have no effect on ANF. Such progressive training may be

too hard to improve ANF in older individuals. We should also assess the efficacy of light- (i.e., 10–40% of 1RM) to moderate-intensity (i.e., 40–60% of RM) RT on ANF in the elderly. A systematic review and meta-analysis suggested that RT should be performed twice a week to promote muscular hypertrophy [50]; thus, the frequency should probably be twice a week or more. However, the optimal intensity, frequency, and duration of RT to gain muscle mass and strength may be inconsistent with the RT needed to improve ANF in older individuals.

Clinicians should be prepared for the aging of society. RT can improve activities of daily living as well as muscle strength and function in very elderly people [51]. Older individuals usually suffer from physical disturbances/deconditioning or non-communicable diseases, such as diabetes, hypertension, dyslipidemia, and cardiovascular disease. RT may reduce blood pressure, heart disease, and stroke mortality in subjects with metabolic syndrome [52]. This indicates that RT also improves the prognosis of older individuals with comorbidities. On the other hand, autonomic imbalance (resting heart rate and HRV) is predictors of hypertension, diabetes, the development of cardiovascular disease, and early mortality [53]. If we can determine the parameters of RT to improve ANF, then this would certainly contribute to the health of the elderly. Further studies are warranted in the future.

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