Effect of high-intensity interval exercise on renal artery hemodynamics in healthy young adults

Urabe, Junji ; Ono, Kumiko ; Okagawa, Junya ; Nakayama, Yuto ; Yamau, Ryoga ; Ishikawa, Akira

(Citation)
The Journal of Sports Medicine and Physical Fitness,63(1):129-35

(Issue Date)
2023-01

(Resource Type)
journal article

(Version)
Accepted Manuscript

Effect of high-intensity interval exercise on renal artery hemodynamics in healthy young adults

Running title: Renal artery hemodynamics in HIIE

Junji Urabe[1], Kumiko Ono[1]*, Junya Okagawa[1], Yuto Nakayama[1], Ryoga Yamau[2], Akira Ishikawa[1]

[1]Kobe University Graduate School of Health Sciences, Hyogo, Japan; [2]Kobe University School of Medicine Faculty of Health Sciences, Hyogo Japan

*Corresponding author: Kumiko Ono, Kobe University Graduate School of Health Sciences, 7-10-2, Tomogaoka, Suma, Kobe, Hyogo, 654-0142, Japan.
E-mail: onoku@tiger.kobe-u.ac.jp

ABSTRACT

BACKGROUND: High-intensity interval exercise is useful for sustained exercise; however, its effect on renal artery hemodynamics is unclear. This study aimed to evaluate changes in renal artery blood flow velocity due to high-intensity interval exercise.

METHODS: Ten healthy adults (age, 23.5±1.2 years) completed high-intensity interval exercise and moderate-intensity continuous exercise protocols on separate days. The high-intensity interval exercise protocol (total duration, 26 min) comprised eight sets of high-intensity exercise sessions at 85% maximum oxygen uptake for 1 min, with intervals of 40% maximum oxygen uptake for 2 min between sets. The moderate-intensity continuous exercise protocol comprised 40 min of exercise at 40% maximum oxygen uptake. Renal artery blood flow velocity and natural log-transformed high frequency spectral power (an index of cardiac parasympathetic nervous system activity) were measured before and after exercise. Additionally, exercise enjoyment was measured using a questionnaire.

RESULTS: Renal artery blood flow velocity did not significantly differ between protocols or timepoints for either protocol. However, the natural log-transformed high frequency spectral power was significantly lower with high-intensity interval exercise than with

moderate-intensity continuous exercise ($p<0.001$, $F=25.97$) during exercise and at 10 min after exercise, and it did not return to pre-exercise levels with high-intensity interval exercise. Moreover, there was no significant difference in exercise enjoyment between the two protocols.

CONCLUSIONS: In healthy young adults, high-intensity interval exercise reduces parasympathetic activity; however, it does not produce any significant changes in renal artery hemodynamics after exercise.

Key words: High-Intensity Interval Exercise, Blood Flow Velocity, Parasympathetic Nervous System, Renal Artery

Introduction

Exercise has a significant impact on the maintenance of health. However, boredom and lack of time are the main reasons why individuals are unable to continue voluntary exercise. In contrast, exercise enjoyment has been shown as important for sustained exercise habits.[1,2] High-intensity interval exercise (HIIE), which has recently received a great deal of attention, is a repetitive exercise program in which short periods of exercise are performed at an intensity above the anaerobic metabolic threshold, in between intervals of low-intensity recovery exercise or recovery at rest.[3] HIIE can be performed for shorter periods of time than moderate-intensity continuous exercise (MICE), consuming energy, and also provides stronger physiological stimulation and adaptation. Previous studies have reported that HIIE improves exercise tolerance,[4] total fiber volume and type, skeletal muscle ratio, capillary density,[5] mitochondrial content and function,[6] and quality of life better than MICE.[7] In addition, HIIE has been reported to be as enjoyable or more enjoyable than MICE,[8] and has potential as an exercise modality of choice in one's exercise habits.

Renal blood flow is affected by exercise and is inversely correlated with exercise intensity and heart rate (HR).[9] Renal artery constriction due to increased renal sympathetic activity and catecholamine secretion can cause a decrease in renal blood flow.[10,11] The kidneys are blood flow-rich organs that receive 25% of the cardiac output, but are very hypoxic due to the presence of arteriovenous oxygen shunts.[12] Many cases of acute renal failure due to ischemia after vigorous exercise have been reported in healthy individuals.[13] It has also been reported that many patients with acute renal failure have a high probability of developing chronic renal failure in the future, leading to end-stage renal failure.[14] Therefore, it is important to prevent renal ischemia while exercising.

The measurement of renal artery hemodynamics using ultrasound is useful. Blood flow can be visualized and evaluated non-invasively and repeatedly, allowing the observation of changes over time, before and after exercise. Blood flow is calculated as the product of blood flow velocity and vessel cross-sectional area. However, in the renal artery, drugs and exercise do not significantly change the vascular cross-sectional area, and the change in blood flow rate is dependent on blood flow velocity.[15,16] Therefore, it is possible to clarify blood flow rate in the renal artery by measuring blood flow velocity.

In healthy individuals, vigorous-intensity continuous exercise can decrease renal blood flow by >50% of the level at rest[17] and increase renal stress.[18] In contrast, MICE

does not significantly affect the renal arterial blood flow,[19,20] and the risk of hypoxia is low.[21] Thus, renal blood flow is known to decrease with continuous exercise in an intensity-dependent manner. However, the renal artery hemodynamics of interval exercise, which is discontinuous exercise, is unknown. Unlike vigorous-intensity continuous exercise, renal artery hemodynamics may not significantly change with HIIE. In HIIE, high-intensity exercise is performed for short periods of time, interspersed with recovery. Therefore, we hypothesized that there would be less decrease in renal blood flow with HIIE than with high-intensity continuous exercise. Additionally, we predicted that the same level of renal hemodynamics would be exhibited if the HIIE energy expenditure was equivalent to that of MICE.

The purpose of this study was to evaluate the changes in renal artery blood flow velocity induced by HIIE in young healthy individuals.

Materials and methods

Participants

Ten young healthy adults (age, 23.5±8.9 years) participated in this study. Their baseline characteristics are listed in Table I. Inclusion criteria comprised an ECG-free diagnosis on physical examination (based on the participant's self-report) and consent to participate in the study. Exclusion criteria comprised cardiovascular disease, renal disease, locomotor disease in the lower extremities rendering exercise difficult, current/past smoking, body fat percentage >20%, and an allergy to zinc. Participants refrained from vigorous exercise, alcohol intake, and caffeine intake for at least 24 h, and fasted for 8 h, before the test sessions. The study protocol was approved by the Kobe University Graduate School of Health Sciences, Health Sciences Ethics Committee (No. 967-1, March 29, 2021), and was conducted according to the ethical standards of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Testing procedures

On the first day, body composition was measured using a body composition monitor (DF 860, Yamato-scale Co., Ltd., Hyogo, Japan). Additionally, participants completed the Japanese version of the International Physical Activity Questionnaire short version (IPAQ short version).[22] Participants then performed an incremental exercise test on a cycle ergometer for maximum oxygen uptake ($\dot{V}O_2$ max) estimation. The incremental exercise

test was started at 15–40 Watts (W), followed by an increase of 10–20 W every 2 min, until the point of exhaustion. The pedal cadence was 60 rotations per minute (rpm) for the first four periods, and then was maintained at 90 rpm. $\dot{V}O_2$ max was calculated from the estimated HR max (220 - age) using the regression line obtained from the measured HR and $\dot{V}O_2$ values.

The main exercise tests were conducted in two sessions, separated by >2 days. As a control, we used MICE, which is commonly used for health maintenance and is less likely to alter renal hemodynamics. The HIIE and MICE protocols were performed in a random order. Participants rested in the supine position for 15 min after arriving at the laboratory. During this rest period, renal blood flow velocity was measured, as the pre-exercise reference value, using Doppler ultrasonography (F37; Hitachi Aloka Medical Co., Ltd., Tokyo, Japan). Participants then engaged in one of the two types of exercise (Figure 1). The HIIE protocol comprised a 2-min warm-up at 40% $\dot{V}O_2$ max, followed by eight sets of 1-min high-intensity exercise at 85% $\dot{V}O_2$ max, interspersed with 2-min active recovery periods at 40% $\dot{V}O_2$ max. The pedal cadence was 60 rpm during the warm-up and recovery periods and 90 rpm during high-intensity exercise. In the MICE protocol, participants performed continuous ergometer exercise at 40% $\dot{V}O_2$ max, with a pedal cadence of 60 rpm. The cycling exercise duration was 26 min in the HIIE protocol and 40 min in the MICE protocol. These exercise durations were set so that the energy expenditure (EE), calculated using Weir's equation,[23] was equal in the two protocols.

After completing the exercise protocol, participants were placed in a bed in the supine position for 10 min, and renal blood flow velocity was measured immediately and 10 min after exercise as "post 0" and "post 10," respectively. Measurements immediately after exercise were taken as soon as possible after the exercise was completed, after confirming that the patient was able to hold his or her breath for the measurement. Subsequently, participants completed the Physical Activity Enjoyment Scale (PACES)[24] to assess exercise enjoyment. The PACES comprises 18 items, with each item rated on a bipolar scale, from 1 to 7, in terms of how much one enjoyed the exercise; the total score ranges 18–126 points. Items 1, 4, 5, 7, 9, 10, 11, 13, 14, 16, and 17 were scored as follows: 7 points for 1, 6 points for 2, 5 points for 3, 4 points for 4, 5 points for 3, 6 points for 2, and 7 points for 1. Otherwise, the item was assigned points in accordance with the chosen number.

HR was monitored using an HR monitor (LRR-03, GMS Japan Co., Ltd., Tokyo, Japan). Additionally, cardiovascular autonomic activity was measured for 1 min before exercise (pre-exercise), for 3 min at the end of exercise (exercise), and for 1 min 9–10 min after exercise (post 10). The maximum entropy calculation method (MemCalc) was implemented using MemCalc/Tarawa (GMS, Tokyo, Japan) software for the real-time analysis of HR variability. Using this system, a frequency analysis of the R-R interval variability over the previous 30 s was performed, and the power of the low-frequency (0.04–0.15 Hz) and high-frequency (HF; 0.15–0.40 Hz) bands of the variability spectrum were calculated.[25] In addition, the HF component was converted to a natural logarithm scale (lnHF) to ensure a normal distribution, and was used as an indicator of the activity level of the cardiovascular parasympathetic nervous system. During the tests, the respiration rate was not controlled, as paced breathing could alter the normal autonomic activity during recovery from exercise. $\dot{V}O_2$ and carbon dioxide output ($\dot{V}CO_2$) were monitored during exercise using a gas analyzer (Aeromonitor AE 310s, Minato Medical Science Co., Ltd., Osaka, Japan). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were monitored during exercise, and were used to calculate the mean arterial pressure (MAP).

Assessment of renal blood flow velocity

To assess renal blood flow velocity, the time-averaged maximum flow velocity (MnV) in the right renal artery was measured by pulse Doppler using a 3.5-MHz convex electronic scanning probe of an ultrasound system. MnV was defined as the average of three pulsed Doppler waveforms, with the participant in the supine position and the probe applied to the abdomen. The focal zone was set to the depth of the renal artery, and the insonation angle was measured as within 60°. The participants held their breath during the 30-s measurement. The MnV indicates the rate of change, with “pre” set as the reference value. Renal vascular resistance (RVR) was calculated as MnV/MAP, and changes before and after exercise were examined.

Two examiners performed the measurements for each participant, and the two values were unified. To verify the reliability of the results using ultrasound echo, intraclass correlation coefficients (ICCs) were measured in a separate experiment, in which two examiners performed three measurements each in nine participants resting in

the supine position. ICC (1,1) and ICC (2,1) were calculated to verify the intra-examiner and inter-examiner reliabilities, respectively.

Statistical analysis

All data are presented as the mean±standard deviation (SD). Two-way repeated measures analysis of variance, with Tukey's Honest Significant Difference test for post hoc testing, was performed to evaluate the effects of exercise type (HIIE vs. MICE) and time on the MnV, RVR, MAP and lnHF. Data normality for HR, SBP, DBP, MAP, and MnV at baseline; peak HR, SBP, DBP, and MAP during exercise; EE; total energy expenditure weight ratio (EE/W); and PACES score were evaluated using the Shapiro-Wilk test, and the difference between exercise types was evaluated using the paired t-test or Wilcoxon signed-rank test, as appropriate. Based on the 95% confidence intervals of the mean, as recommended by Koo and Li,[26] ICC values were interpreted as follows: <0.5, poor reliability; 0.5–0.75, moderate reliability; 0.75–0.9, good reliability; and >0.90, excellent reliability. Reliability of the PACES score was evaluated by the Cronbach's alpha value. Statistical significance was set at $p<0.05$. All data were analyzed using JMP for Windows (version 12.0.1; SAS Institute Japan, Tokyo, Japan).

Data availability

The data associated with this study are not publicly available, but are available from the corresponding author on reasonable request.

Results

Baseline data for HR, SBP, DBP, MAP, and MnV are shown in Table II. The physiological responses according to exercise protocol are shown in Table III. Peak HR ($p=0.002$, $r=0.98$), SBP ($p<0.001$, $r=0.92$), and MAP ($p=0.006$, $r=0.76$) were significantly higher with HIIE than with MICE. In contrast, the EE/W did not significantly differ between HIIE (2.56±0.43 kcal/kg) and MICE (2.64±0.45 kcal/kg) ($p=0.12$, $r=0.49$). Additionally, ICC (1,1) indicated good to excellent intra-examiner reliability (0.916 and 0.879, respectively), and ICC (2,1) indicated excellent inter-examiner reliability (0.956).

The renal blood flow velocity, measured immediately after the end of exercise, was 166.0±82.2 seconds for HIIE and 141.8±40.4 seconds for MICE. The MnV did not show significant differences between protocols or across time for either protocol (Figure

2). The MAP was significantly increased after exercise compared to the pre-exercise level for HIIE (from 85.3±5.9 to 98.3±11.5, p=0.003), but not for MICE (from 83.3±7.8 to 88.0±9.0). In contrast, the RVR did not significantly change with exercise for HIIE (from 0.71±0.10 to 0.65±0.13) and for MICE (from 0.73±0.09 to 0.69±0.10). The lnHF power was significantly lower with HIIE than with MICE, during exercise and at post 10 ($p<0.001$, $F=25.97$) (Figure 3). For both protocols, the lnHF decreased during exercise and increased during recovery, relative to the pre-exercise level ($p<0.001$, $F=189.17$). For HIIE, the lnHF was significantly lower during exercise and at post 10 than before exercise (pre). For MICE, the lnHF was significantly lower during exercise than before exercise (pre).

The internal consistency of the PACES score in the present study was high ($\alpha=0.9541$). PACES scores did not significantly differ between HIIE (101.1±12.8) and MICE (93.3±20.9). A detailed analysis revealed that PACES scores were higher for HIIE than for MICE in 5 of 10 participants and lower for HIIE than for MICE in 2 of 10 participants, indicating that the exercise style perceived as more enjoyable varied.

Discussion

To the best of our knowledge, the current study is the first to use Doppler ultrasonography to investigate changes in renal artery hemodynamics due to HIIE. We found that the renal artery blood flow velocity did not decrease immediately after exercise for both HIIE and MICE protocols. Furthermore, there was no difference in renal artery blood flow velocity between the protocols. However, there was greater suppression of parasympathetic activity during and at 10 min after exercise with HIIE than with MICE.

In the present study, the exercise load in the MICE protocol was at 40% VO_2 max, and there was no change in the renal blood flow velocity. A previous study reported no significant change in renal arterial blood flow and renal arterial blood flow velocity for exercise at an intensity below the anaerobic threshold,[17,18] which is consistent with the present results. In terms of HR variability, in the current MICE protocol, cardiac parasympathetic activity was suppressed during exercise compared with that at rest, and had fully recovered within 10 min after exercise. However, in the HIIE protocol, cardiac parasympathetic activity was suppressed to a greater extent than that in the MICE protocol and did not recover to the pre-exercise level within 10 min after exercise. A previous study indicated that HF power immediately after exercise is significantly lower with high-

intensity interval training than with endurance exercise,[27] which is consistent with the results of the current study. In addition, cardiac sympathetic activity increases, and cardiac parasympathetic activity decreases, during exercise, and the recovery of cardiac parasympathetic activity precedes that for cardiac sympathetic activity.[28] This suggests that cardiac sympathetic hyperactivity in the HIIE protocol continued beyond 10 min after exercise. Although previous studies have reported that renal blood flow decreases with renal sympathetic hyperactivity, there was no decrease in renal artery blood flow velocity immediately after exercise in the current study, despite expected renal sympathetic hyperactivity.

In healthy kidneys, autoregulation against a decrease in perfusion pressure may be involved in the physiological response to exercise. Autoregulation ensures that the renal blood flow remains nearly constant, even when the MAP fluctuates between 70 and 180 mmHg.[29] Autoregulation may be due to muscular regulation, autonomic regulation, or regulation by fluid factors. In the current study, there was a decrease in cardiac parasympathetic nervous system activity after exercise, which was expected to lead to an increase in renal sympathetic nervous system activity, i.e., constriction of the renal arteries and a decreased in renal blood flow. Despite this, MAP fluctuations were in the range of 70-180 mmHg, suggesting that renal blood flow is maintained by muscle and fluid factor regulation. When blood pressure rises and the vessel wall expands, smooth muscle contractility increases; conversely, when blood pressure decreases and the vessel wall relaxes, smooth muscle contractility decreases. This muscular regulation by smooth muscles maintains the blood flow. In addition, renal blood flow is regulated in response to changes in renal arterial pressure via vasodilator (e.g., prostaglandins) and vasoconstrictor effects (e.g., angiotensin II).[30] In older adults and in patients with atherosclerosis, hypertension, and chronic renal failure, autoregulation may be impaired, resulting in vulnerability to hypoperfusion. However, as the participants in the present study comprised healthy young adults, renal autoregulation functioned normally, and blood flow to the glomerulus was maintained; accordingly, the renal artery blood flow velocity was not decreased significantly immediately after exercise. Another substance involved in the regulation of renal blood flow is nitric oxide (NO), which is produced by the vascular endothelium as a result of increased shear stress caused by blood flow. In the renal circulation, NO is secreted continuously and acts to maintain renal blood flow and renal vascular resistance.[31]

In the current study, the duration of HIIE was 35% shorter than the duration of MICE, and there was no significant difference in the enjoyment of exercise between the HIIE and MICE protocols. Although several previous studies reported HIIE as more, or equally, enjoyable than MICE, the results vary according to the study protocol and population.[32] HIIE is considered more enjoyable in high physical activity populations.[33] Consistent with this, the PACES score for HIIE was either equal to or higher than that for MICE in the three participants with high physical activity in the current study. However, in populations with a wide range of physical activity levels, the results have been mixed. Thus, HIIE should be actively recommended for people with regular exercise habits and high activity levels. We also recommend that people with no exercise habit or low activity level experience both HIIE and MICE and choose their favorite exercise type to support sustained exercise.

Improved exercise tolerance with continued exercise is associated with a better prognosis.[34] Especially in patients with renal disease, the renal protective effects of exercise therapy have been reported to play a major role in the prevention of dialysis.[35] Exercise that does not alter renal hemodynamics is recommended for patients with renal disease.[36] The present study suggests that HIIE does not significantly alter renal hemodynamics in healthy individuals, providing a basis for the use of HIIE in renal rehabilitation.

Limitations

In the current study, we could not measure renal artery hemodynamics “during” exercise, but only observed changes before and after exercise, as obtaining stable measurements during exercise is difficult because of the large abdominal movements due to breathing. Therefore, the observation of renal artery hemodynamics during HIIE is a challenge for future studies. In addition, we were not able to measure catecholamine levels and renin-angiotensin system factors in the blood because we were unable to perform biochemical tests using blood samples. Finally, since renal artery hemodynamics may differ significantly between healthy young people with normal renal function and patients with renal dysfunction or older adults, studies in patients with mild renal dysfunction and different age groups are required. Nevertheless, our study of young, healthy adults establishes a baseline for comparison with other populations.

Conclusions

In healthy young adults, HIIE is associated with the suppression of cardiac parasympathetic activity; however, as with MICE, HIIE may not reduce renal artery blood flow velocity after exercise. This finding suggests that HIIE could be used for establishing exercise habits without greatly reducing renal artery blood flow. These results not only promote continued exercise habits in healthy individuals, but also provide a basis for the future use of HIIE in rehabilitation for elderly individuals and patients with chronic kidney disease.

REFERENCES

1. Simek EM, McPhate L, Hill KD, Finch CF, Day L, Haines TP. What are the characteristics of home exercise programs that older adults prefer?: A cross-sectional study. Am J Phys Med and Rehabil 2015;94:508-21.

2. Arakawa S, Watanabe T, Sone H, Kobayashi M, Kawamori R, Atsumi Y, *et al*. Current situation of diet and exercise therapy in terms of medical consultations in patients with diabetes mellitus in Japan: A nationwide survey. J Japan Diab Soc 2015;58:265-78.

3. Laursen PB, Jenkins DG. The scientific basis for high-intensity interval training: optimising training programmes and maximizing performance in highly trained endurance athletes. Sports Med 2002;32:53-73.

4. Beetham KS, Howden EJ, Fassett RG, Petersen A, Trewin AJ, Isbel NM, *et al*. High-intensity interval training in chronic kidney disease: A randomized pilot study. Scand J Med Sci Sports 2019;29:1197-204.

5. Guadalupe-Grau A, Fernández-Elías VE, Ortega JF, Dela F, Helge JW, Mora-Rodriguez R. Effects of 6-month aerobic interval training on skeletal muscle metabolism in middle-aged metabolic syndrome patients. Scand J Med Sci Sports 2018;28:585-95.

6. de Matos MA, Vieira DV, Pinhal KC, Lopes JF, Dias-Peixoto MF, Pauli JR, *et al*. High-intensity interval training improves markers of oxidative metabolism in skeletal muscle of individuals with obesity and insulin resistance. Front Physiol 2018;9:1451.

7. Conraads VM, Pattyn N, De Maeyer C, Beckers PJ, Coeckelberghs E, Cornelissen VA, *et al*. Aerobic interval training and continuous training equally improve aerobic exercise capacity in patients with coronary artery disease: The SAINTEX-CAD study. Int J Cardiol 2015;179:203-10.

8. Niven A, Laird Y, Saunders DH, Phillips SM. A systematic review and meta-analysis of affective responses to acute high intensity interval exercise compared with continuous moderate- and high-Intensity exercise. Health Psychol Rev 2021;15:540-573.

9. Poortmans JR. Exercise and renal function. Exerc Sport Sci Rev 1977;5:255-94.

10. Schneider DA, McLellan TM, Gass GC. Plasma catecholamine and blood lactate responses to incremental arm and leg exercise. Med Sci Sports Exerc 2000;32:608-13.

11. Tidgren B, Hjemdahl P, Theodorsson E, Nussberger J. Renal neurohormonal and vascular responses to dynamic exercise in humans. J Appl Physiol 1991;70:2279-86.

12. Brezis M, Rosen S. Hypoxia of the renal medulla--its implications for disease. N Engl J Med 1995;332:647-55.

13. Ishikawa I. Acute renal failure with severe loin pain and patchy renal ischemia after anaerobic exercise in patients with or without renal hypouricemia. Nephron 2002;91:559-70.

14. Okusa MD, Chertow GM, Portilla D; Acute Kidney Injury Advisory Group of the American Society of Nephrology. The nexus of acute kidney injury, chronic kidney disease, and World Kidney Day 2009. Clin J Am Soc Nephrol 2009;4:520-2.

15. Manoharan G, Pijls NH, Lameire N, Verhamme K, Heyndrickx GR, Barbato E, *et al*. Assessment of renal flow and flow reserve in humans. J Am Coll Cardiol 2006;47:620-5.

16. Marraccini P, Fedele S, Marzilli M, Orsini E, Dukic G, Serasini L, *et al*. Adenosine-induced renal vasoconstriction in man. Cardiovasc Res 1996;32:949-53.

17. Suzuki M, Sudoh M, Matsubara S, Kawakami K, Shiota M, Ikawa S. Changes in renal blood flow measured by radionuclide angiography following exhausting exercise in humans. Eur J Appl Physiol Occup Physiol 1996;74:1-7.

18. Apeland T, Danielsen T, Staal EM, Åsberg A, Thorsen IS, Dalsrud TO, *et al*. Risk factors for exertional rhabdomyolysis with renal stress. BMJ Open Sport and Exerc Med 2017;3:e000241.

19. Kawakami S, Yasuno T, Matsuda T, Fujimi K, Ito A, Yoshimura S, *et al*. Association between exercise intensity and renal blood flow evaluated using ultrasound echo. Clin Exp Nephrol 2018;22:1061-8.

20. Kotoku K, Yasuno T, Kawakami S, Fujimi K, Matsuda T, Nakashima S, *et al*. Effect of exercise intensity on renal blood flow in patients with chronic kidney disease stage 2. Clin Exp Nephrol 2019;23:621-8.

21. Hiraki K, Kamijo-Ikemori A, Yasuda T, Hotta C, Izawa KP, Watanabe S, *et al*. Moderate-intensity single exercise session does not induce renal damage. J Clin Lab Anal 2013;27:177-80.

22. Murase N, Katsumura T, Ueda C, Inoue S, Shimomitsu T. Validity and reliability of Japanese version of International Physical Activity Questionnaire. J Health Welfare Stat 2002;49:1-9.

23. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.

24. Kendzierski D, DeCarlo KJ. Physical activity enjoyment scale: Two validation studies. J Sport Exerc Psychol 1991;13:50-64.

25. Pomeranz B, Macaulay RJ, Caudill MA, Kutz I, Adam D, Gordon D, *et al*. Assessment of autonomic function in humans by heart rate spectral analysis. Am J Physiol 1985;248:H151-3.

26. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155-63.

27. Andrade DC, Arce-Alvarez A, Parada F, Uribe S, Gordillo P, Dupre A, *et al*. Acute effects of high-intensity interval training session and endurance exercise on pulmonary function and cardiorespiratory coupling. Physiol Rep 2020;8:e14455.

28. Niewiadomski W, Gasiorowska A, Krauss B, Mróz A, Cybulski G. Suppression of heart rate variability after supramaximal exertion. Clinical Physiol Funct Imaging 2007;27:309-19.

29. Shipley RE, Study RS. Changes in renal blood flow, extraction of inulin, glomerular filtration rate, tissue pressure and urine flow with acute alterations of renal artery blood pressure. Am J Physiol 1951;167:676-88.

30. Abuelo JG. Normotensive ischemic acute renal failure. N Eng J Med 2007;357:797-805.

31. Salom MG, Lahera V, Miranda-Guardiola F, Romero JC. Blockade of pressure natriuresis induced by inhibition of renal synthesis of nitric oxide in dogs. Am J Physiol 1992;262:F718-22.

32. Jung ME, Bourne JE, Little JP. Where does HIT fit? An examination of the affective response to high-intensity intervals in comparison to continuous moderate- and continuous vigorous-intensity exercise in the exercise intensity-affect continuum. PLOS ONE 2014;9: e114541.

33. Bartlett JD, Close GL, MacLaren DP, Gregson W, Drust B, Morton JP. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: Implications for exercise adherence. J Sports Sci 2011;29:547-53.

34. Forman DE, Fleg JL, Kitzman DW, Brawner CA, Swank AM, McKelvie RS, *et al*. 6-min walk test provides prognostic utility comparable to cardiopulmonary exercise testing in ambulatory outpatients with systolic heart failure. J Am Coll Cardiol 2012;60:2653-61.

35. Kohzuki M, Kamimoto M, Wu XM, Xu HL, Kawamura T, Mori N, *et al*. Renal protective effects of chronic exercise and antihypertensive therapy in hypertensive rats with chronic renal failure. J Hypertens 2001;19:1877-82.

36. Yamagata K, Hoshino J, Sugiyama H, Hanafusa N, Shibagaki Y, Komatsu Y, *et al*. Clinical practice guideline for renal rehabilitation: systematic reviews and recommendations of exercise therapies in patients with kidney diseases. Ren Replace Ther 2019;5:28.

Conflicts of interest.— The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding.— This work was partially supported by JSPS KAKENHI, Grant-in-Aid for Scientific Research(C), Grant Number JP21K11389. The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

Authors' contributions.— All authors contributed substantially to the conception and design of the study. Junji Urabe and Kumiko Ono contributed to the acquisition, analysis, and interpretation of the data. All authors participated in drafting the manuscript. Junji Urabe critically revised the manuscript. All authors read and approved the final version of the manuscript.

Congresses.— This paper was presented at the 76th Japanese Society of Physical Fitness and Sports Medicine Congress held online on September 17-30, 2021.

Acknowledgements.— I would like to express my deepest appreciation to the members of the Akira Ishikawa Laboratory for their helpful suggestions. I would like to give special thanks to the people who participated in this study.

TABLES

Table I.— Participants' characteristics

Participants, n	10
Height (cm)	166.2±10.7
Body weight (kg)	56.2±8.9
Body mass index (kg/m^2)	20.2±1.4
Body fat percentage (%)	21.3±8.2
Age (years)	23.5±1.2
Sex (male, %)	5 (50)
Physical activity (IPAQ short version)	high: 3, moderate: 3, low: 4
Estimated VO_2 max (mL/kg/min)	37.1±6.1
Exercise load at 40% VO_2 max (Watt)	48.5±16.6
Exercise load at 85% VO_2 max (Watt)	108.7±30.1

Data are expressed as the mean±standard deviation. IPAQ, Japanese version of the International Physical Activity Questionnaire short version; VO_2, oxygen uptake

Table II.— Comparisons between the two protocols at baseline

	HIIE protocol	MICE protocol	P value
HR (bpm)	69.0±7.8	70.4±5.2	0.44
Systolic blood pressure (mmHg)	111.4±11.1	112.8±13.9	0.65
Diastolic blood pressure (mmHg)	72.2±5.2	68.6±7.4	0.11
Mean arterial pressure (mmHg)	85.3±5.9	83.3±7.8	0.30
MnV (cm/s)	61.3±11.1	60.8±9.9	0.87

Data are expressed as the mean±standard deviation. HIIE, high-intensity interval exercise; MICE, moderate-intensity interval exercise; HR, heart rate; MnV, the time-averaged maximum flow velocity

Table III.— Comparisons between the two protocols in terms of physiological responses

	HIIE protocol	MICE protocol
Mean HR (bpm)	152.7±8.1 (high intensity) 125.7±8.1 (interval)	104.2±6.5
Peak HR (bpm)	164.9±7.5*	115.9±8.1
Mean HR (%HR max)	77.7±3.9 (high intensity) 63.9±4.0 (interval)	53.0±3.3
Mean VO_2 (mL/kg/min)	26.0±4.2 (high intensity) 17.0±2.9 (interval)	13.6±2.2
Mean VO_2 (%VO_2 max)	70.2±4.7 (high intensity) 45.9±3.1 (interval)	36.7±2.2
Systolic blood pressure (mmHg)	149.2±18.8*	125.6±14.7
Diastolic blood pressure (mmHg)	72.8±11.0	69.2±7.5
Mean arterial pressure (mmHg)	98.3±11.5*	88±9.0
Energy expenditure (kcal)	144.8±37.0	150.0±42.1
Energy expenditure weight ratio (kcal/kg)	2.56±0.43	2.64±0.45

Data are expressed as the mean±standard deviation. HIIE, high-intensity interval exercise; MICE, moderate-intensity interval exercise; HR, heart rate; VO_2, oxygen uptake
*$p<0.01$ for HIIE vs. MICE

TITLES OF FIGURES

Figure 1.— The main test protocol. The exercises comprised high-intensity interval exercise (HIIE) and moderate intensity continuous exercise (MICE). The time-averaged maximum flow velocity (MnV) was measured before, immediately after, and 10 min after exercise. The natural logarithm of the high-frequency spectral power (lnHF) was measured before exercise (for 1 min), at the end of exercise (for 3 min) and 10 min after exercise (for 1 min). PACES, Physical Activity Enjoyment Scale

Figure 2.— Rate of change in the time-averaged maximum flow velocity (MnV) before and after high-intensity interval exercise (HIIE) and moderate intensity continuous exercise (MICE). There were no significant differences between exercise type or time, and no significant interaction. pre, before exercise; post 0, immediately after exercise; post 10, 10 min after exercise

Figure 3.— Natural logarithm of the high-frequency spectral power (lnHF) before and after high-intensity interval exercise (HIIE) and moderate intensity continuous exercise (MICE). *$p<0.001$ for HIIE vs MICE: †$p<0.001$ vs. pre; pre, before exercise; post 10, 10 min after exercise