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Original Research

Strength Training can Modulate Urinary Adipokine Levels in Healthy Young Males

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Abstract

International Journal of Exercise Science 18(2): 107-118, 2025. https://doi.org/10.70252/FXQY9475 Adipose tissue stores energy in fat-rich adipocytes, which can produce and release several adipokines and modulate body metabolism. Exercise may induce adipokine production in adipocytes; however, the relationship between the two remains unclear. Few studies have shown the relationship between adipokines and strength training. Thus, we aimed to evaluate the acute and chronic effects of strength training (ST) on urinary adiponectin, leptin, and resistin levels. Twelve untrained young men (23.42 ± 2.67 years) were included in this study. Body composition was evaluated at baseline and after completing of the training protocol using densitometry. Training protocol consisted of three exercises with three sets of 65% of one-repetition maximum (1MR) with a pause of 90 s between sets, each exercise lasting 5 s (2 s concentric / 3 s eccentric). The sessions were carried out three times a week for 10 weeks. Urine was collected during the pre- and post-training in the first and 30th session. Adipokine levels were determined by ELISA. Urinary levels of leptin acutely increased after the first ST session, and after the last ST session. Chronic changes in the leptin levels were also found when comparing the values before the last ST and before the first ST session. Urinary adiponectin levels changed in the comparison of values before and after the last session. There was a significant increase in the adiponectin levels when comparing values after the first and last ST sessions. The levels of resistin chronically increased. Strength training can induce acute and chronic changes in urinary levels of adipokines.

Keywords: Adiponectin, leptin, resistin, strength training, urinary adipokines

Introduction

Energy distribution to the organs is considered a vital mechanism in mammals, and nutritional status and body thermogenesis are crucial for the maintenance of life.[1] In this regard, the adipose tissue has a critical role in providing systemic energy. It is a calorie reservoir,[2] controls hormonal responses, and the adipocytes have specific characteristics.[3] Adipose tissue also contains fibroblasts and immune, vascular, endothelial, and stromal cells.[3]

A few decades ago, adipose tissue was thought to be an inert system with the primary function of storing triacylglycerol.[4] However, adipocytes mediate the interaction between adipose tissue and peripheral organs through blood circulation or in a paracrine manner.[5,6] In addition, adipose tissue has several endocrine functions and can produce and releasing adipokines.[6]

Since the discovery of leptin more than 25 years ago, other molecules have been discovered, including adiponectin and resistin, which are important in terms of increased adiposity and acute exercise.[7–9] Leptin has a molecular weight of 16 kilodaltons (kDa), and its serum level is proportional to adipocyte size; it inhibits appetite when stored energy is sufficiently stable.[10,11] Adiponectin has a molecular weight of 30 kilodaltons (kDa) and is secreted mainly from adipocytes. Its main functions are to stimulate glucose utilization and fatty-acid oxidation.[12–14] Resistin has a molecular weight of 12.5 kilodaltons (kDa) and has been named for its ability to interfere with insulin action.[15,16]

Adipokine levels can be measured in the serum and plasma and have been studied as they present a great clinical utility of providing a diagnosis.[17] However, studies analyzing the urinary levels of these molecules in response to exercise are scarce. Urinary measurements can reflect stable concentrations of a molecule much better than plasma or serum measurements can.[18] While plasma or serum measurements correspond to acute or short-term changes, urinary measurements include the molecules filtered by the glomerulus in addition to those produced in the renal tissue, resulting in more stable concentrations.[19]

Strength training (ST) has grown in popularity over the past several decades; it improves athletic performance by increasing strength, power, balance, and coordination. These protocols consist primarily of anaerobic exercises, which vary in intensity and duration.[20,21]In addition, it aims to increase muscle mass (hypertrophy),[22] mitigate the effects of aging on functional capacity and neuromuscular loss,[23] and is associated with adipose tissue metabolism.[7] However, the relationship between ST and adipokines requires further investigation.

Our research group have been investigating the acute and chronic effects of ST on plasma and urinary levels of several endogenous molecules. Our first study investigated the effect of ST on molecules of the Renin Angiotensin System (RAS).[19] We collected plasma and urine samples before and after the first and last session of a 10-week ST protocol to measure RAS molecules.[19] We also measured adipokines in the same plasma and urine samples.[24] We consider that plasma and urine measurements reflect different physiological situations. The results obtained in plasma samples correspond to acute and temporary changes in the production of a molecule, considering the fast half-time and metabolism. On the other hand, urinary levels can reflect a

more stable production of the molecule at a constant rate. For this reason, we analyzed separately the results obtained in plasma and urine samples. Changes in the urinary levels of adipokines because of physical exercise should be explored not only because of the limited evidence currently available, but also because the different meaning of urinary measurements.

Therefore, this study aimed to evaluate the acute and chronic effects of ST on the urinary concentrations of adipokines in healthy male adults.

Methods

Participants

This study complied with all norms established by the National Health Council involving research with humans (Resolution 466/2012) and was approved by the Ethics Committee on Research in Human Beings (approval number: 1881.170). The written informed consent was obtained from all participants. This prospective study included 12 healthy young male adults aged 20-31 years, which provided informed consent for participation and completed this research. The inclusion criteria were healthy young male adults who had not practiced ST for at least 6 months prior to the study.[19] The Physical Activity Readiness Questionnaire (PAR-Q) was used to evaluate the individual's integrity and physical fitness.[25] Body mass was measured using an anthropometric scale (MARTE, Brazil). Height was measured using a stadiometer coupled with a scale (MARTE, Brazil). Pre-training body composition was measured on dual-energy X-ray absorptiometry (DXA) using the Discovery W equipment (Hologic, Bedford, MA, USA) software version 3.3.[26]

To estimate the training load, a one-repetition maximum (1MR) test was performed for the three types of exercise (leg press, leg extension, and leg curl), and was calculated using the Brzycki's equation.[27] The volunteers were allowed to warm up for 5 min on a bicycle by pedaling at low intensity. Thereafter, they were asked to position themselves as comfortably as possible on the device to record all the necessary adjustments for consistency throughout the study. After the initial tests, the volunteers participated in a training session. The protocols consisted of three exercises within three sets, performed 10–12 times at 65% of 1-MR.[21] Ninety-second breaks were intercalated between each set. The repetition duration was 2 s for concentric exercises and 3 s for eccentric exercises.[21] If the volunteer was able to perform 12 repetitions of the same exercise perfectly, the weight would be increased by approximately 10% in the next session.

Exercise was interrupted only when the volunteer was unable to either complete the established muscle action or perform exercises in the complete range of motion during the following two repetitions. A metronome was used to maintain a consistent duration of muscle action. The sessions were conducted three times a week on Mondays, Wednesdays, and Fridays, at the same time of the day. Before the start, during the training process, and on the day of samples collection, the volunteers were instructed to maintain their routine dietary habits. The training sessions were guided by trained professionals.

Protocol

Sample Collection.

Urine samples (15 mL) were collected in sterile containers at four time points: before (pre-S1) and after (post-S1) the first exercise session, and before (pre-S30) and after (port-S30) the last exercise session. The urine was centrifuged at 3000 rpm at 4°C for 10 min. Each sample was aliquoted (1 mL) into sterile tubes and stored in a freezer at -80°C. Blood samples (5 ml) were collected by venopuncture in sterile tubes with EDTA before the first ST. The venous blood was centrifuged at 3000 rpm at 4°C for 10 minutes to obtain plasma. Plasma samples were obtained, aliquoted, and stored in a freezer at -80°C.

Measurement of plasma creatinine and calculation of glomerular filtration rate (GFR).

Plasma levels of creatinine were measured using a standard kinetic colorimetric method (Creatinina PP, Gold Analisa Diagnóstica Ltda, Belo Horizonte, Brazil). GFR were estimated by the Chronic Kidney Disease Epidemiology (CKD-EPI) equation.[28]

Measurement of adipokines.

Adipokines (leptin, adiponectin, and resistin) were analyzed using enzyme-linked immunosorbent assay (ELISA) sandwich kits (R&D Systems, Minneapolis, MN, USA). The plates were incubated with urine samples for 3 h at room temperature and washed three times with 0.1% PBS-Tween. After washing, the plates were incubated with biotin-conjugated antibodies diluted in 1% PBS-BSA for one hour at room temperature. After washing the plates with 0.1% PBS-Tween again, peroxidase-conjugated streptavidin was added; the plates were incubated for 30 min at room temperature. After a final wash with 0.1% PBS-Tween, chromogen 3,3',5,5'-tetramethylbenzidine was added to the plates in the absence of light. After 30 min, the reaction was stopped using a solution containing 1M sulfuric acid. The intensity was marked using an ELISA reader at 450 nm (Agilent BioTek Epoch, Santa Clara, CA, USA). The detection limits for adiponectin, leptin, and resistin were 0.891 ng/ml, 7.8 pg/mL, and 6.59, respectively.

Statistical Analysis

Since we did not have objective parameters to calculate the sample size, we performed a post hoc power calculation using our sample, the plasma measurements of adipokines, and a type 1 error rate of 5%. The result showed that our study had a statistical power of 83%, so that the differences observed in plasma levels of adipokines were not due to chance alone (nQuerry Advisor 4.0 Statistical solutions, Saugus, MA, USA). Statistical analyses were performed using the SPSS software (version 22.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 6.0; GraphPad Software, Inc., La Jolla, California, USA). Figures were created using GraphPad Prism 6.0. Variables were initially checked for normal distribution using the Shapiro-Wilk test. For quantitative variables with a Gaussian distribution, the values are expressed as means and standard deviations. The median and interquartile range are used for non-parametric quantitative variables. Comparisons between the same individual at two time points (before versus after the exercise session, before the first versus last sessions, or after the first versus last

sessions) were performed using Wilcoxon's test (non-parametric variables). The significance level was set at $p < 0.05$.

Results

General characteristics and measurements

A total of 12 healthy, young, adult males aged 20–31 years old (23.4 ± 2.7) and height of 173.0 ± 0.7 cm were enrolled in the present study. The anthropometric characteristics measured on DXA of volunteers changed after the training intervention as following: average of body weight of 75.4 ± 10.4 kg to 76.0 ± 10.7 kg (p=0.1986), body fat 26.2 ± 4.6% to 25.3 ± 5.7% (p=0.0487), fat mass 19.8 ± 6.1 kg to 19.3 ± 5.5 (p=0.1835), total lean mass 51.7 ± 5.9 kg to 52.9 ± 6.6 kg (p=0.0057), and leg lean mass 17.9 ± 2.3 kg to 18.9 ± 2.8 (p=0.0037). The plasma levels of creatinine before the first ST session were within normal range in all volunteers (0.90 ± 0.20 mg/dl). The estimated glomerular filtration rate according to CKD-Epi formula confirmed normal renal function (132 ± 10 ml/min/1.73 m^2). We also measured plasma levels of creatinine in the other time-points. Plasma creatinine levels after the first ST remained very similar to values before the first ST (before: 0.90 ± 0.20 mg/dl vs. after: 0.89 ± 0.22 mg/dl, p= 0.58). The same occurred for the measurements of plasma creatinine levels before and after the last ST (0.89 ± 0.23 mg/dl vs. 0.90 ± 0.18 mg/dl, p=0.63).

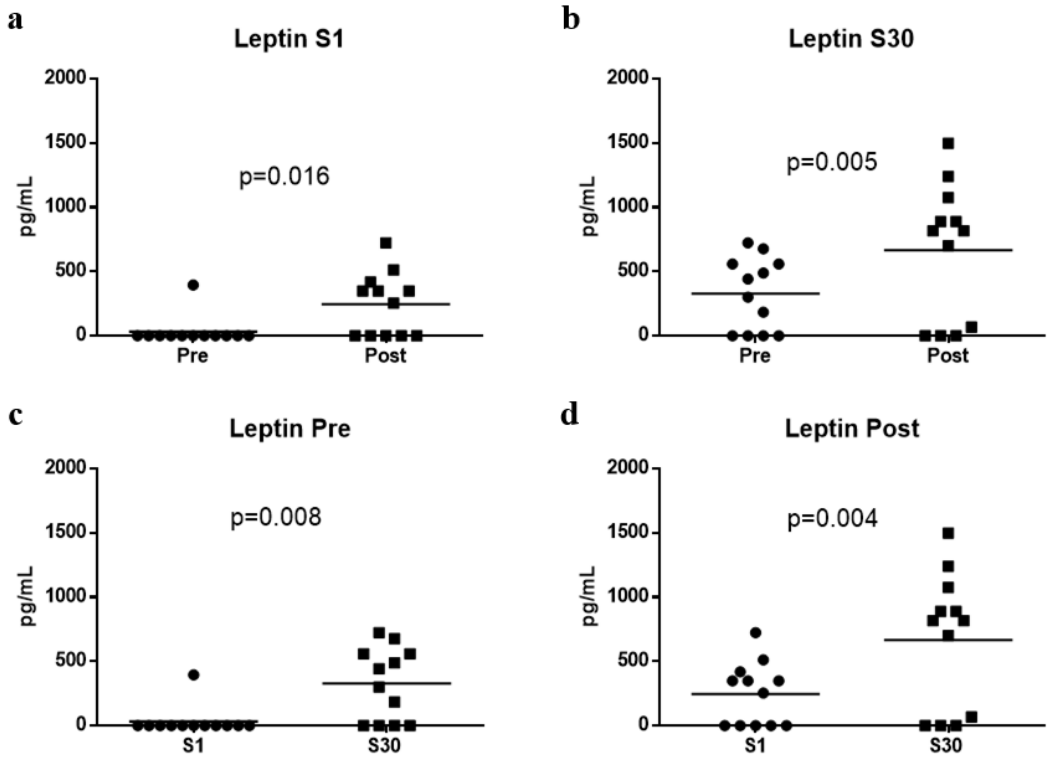

Figure 1. Urinary levels of leptin. **(a)** Urinary levels of leptin before and after the first exercise session (S1). **(b)** Urinary levels of leptin before and after the last exercise session (S30). **(c)** Urinary levels of leptin before the first (S1) versus the last exercise session (S30). **(d)** Urinary levels of leptin after the first (S1) versus the last exercise session (S30). Differences were considered significant at $p < 0.05$ (Wilcoxon test).

Urinary levels of adipokines

Changes in the urinary levels of adipokines are shown in Figures 1, 2, and 3, and were compared as follows: (a) before (pre-S1) and after (post-S1) the first training session; (b) before (pre-S30) and after (post-S30) the last training session; (c) before the first (pre-S1) and last training session (pre-S30); (d) after the first (post-S1) and last training session (post-S30).

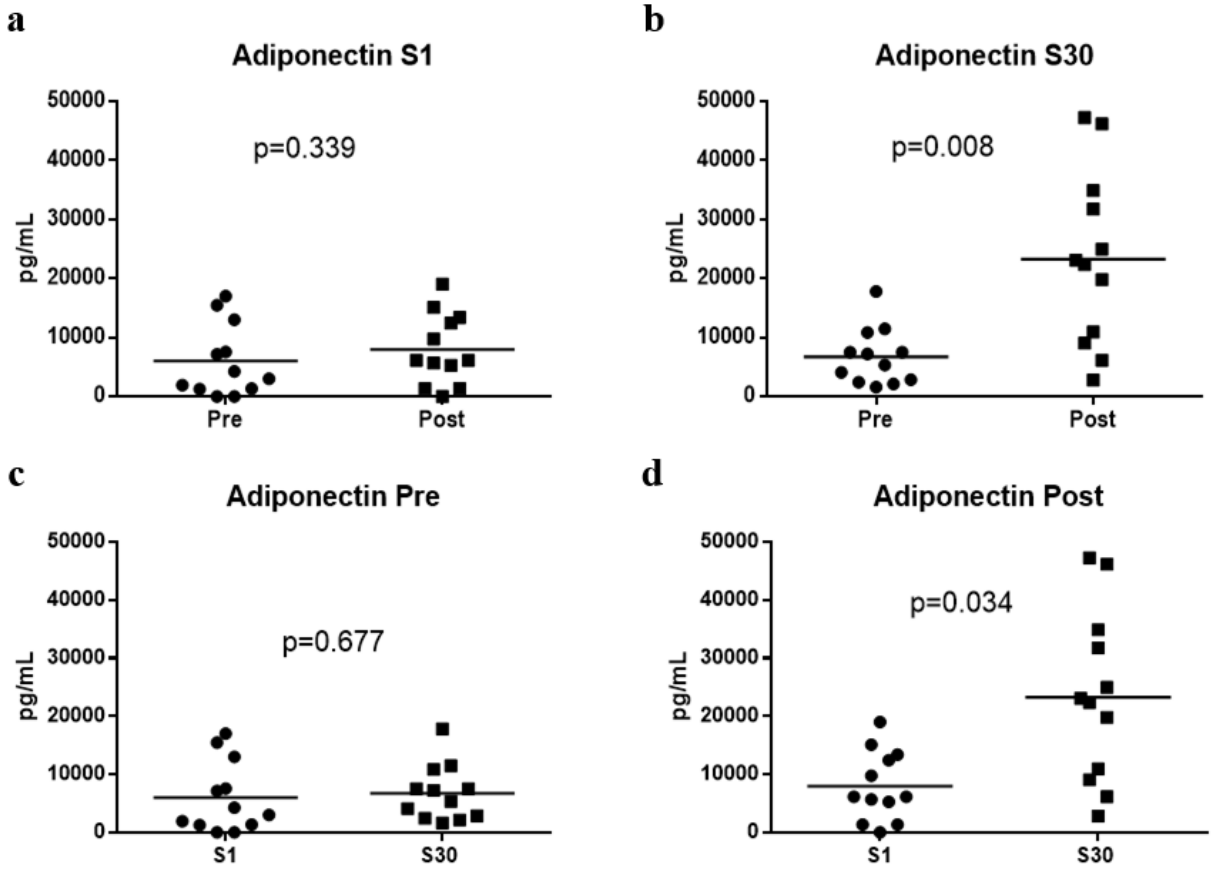

Figure 2. Urinary levels of adiponectin. **(a)** Urinary levels of adiponectin before and after the first exercise session (S1). **(b)** Urinary levels of adiponectin before and after the last exercise session (S30). **(c)** Urinary levels of adiponectin before the first (S1) versus the last exercise session (S30). **(d)** Urinary levels of adiponectin after the first (S1) versus the last exercise session (S30). Differences were considered significant at $p < 0.05$ (Wilcoxon test).

Urinary levels of leptin

Leptin levels significantly increased after the first ST session (pre-S1 0 pg/ml vs. post-S1 301.6 (0–401.4) pg/ml, p=0.016; Fig. 1a) and after the last ST session (pre-S30 372 (0–559.8) pg/ml vs. post-S30 818.1 (16.7–1029) pg/ml, p= 0.005; Fig. 1b). Significant increase in the leptin level was found before the last ST session than in the first ST session (pre-S1 0 pg/ml vs. pre-S30 372 (0–559.8) pg/ml, p= 0.008; Fig. 1c). Similar results were found when comparing the leptin levels after the first and last ST sessions (post-S1 301.6 (0–401.4) pg/ml vs. post-S30 818.1 (16.7 - 1029) pg/ml, p= 0.004; Fig. 1d).

Urinary levels of adiponectin

Significant increases were observed in the adiponectin levels after the last session (pre-S30 6277 (2560–10013) vs. post-S30 22726 (9514–34122) pg/ml, p=0.008; Fig. 2b). There was also a significant increase in the adiponectin levels after the first and last ST sessions (post-S1 6132 (2332–13149) pg/ml vs. post-S30 22726 (9514–34122) pg/ml, p=0.034; Fig. 2d), compared the those before the sessions. This indicated the chronic effects of ST on urinary levels of adiponectin. No significant differences were observed between the pre-S1 and post-S1 (p=0.339; Fig. 2a), and pre-S1 and pre-S30 (p=0.677, Fig. 2c) urinary adiponectin levels.

Urinary levels of resistin

There was a significant increase in resistin levels before the last ST session than in the first ST session (pre-S1 0 (0 – 17) pg/ml vs. pre-S30 632.1 (383.7 - 1823) pg/ml, p=0.021; Fig. 3c). In addition, a significant increase occurred after the last ST session when compared with after the first ST session (post-S1 0 (0 – 252.9) vs. post-S30 1454 (313.9 – 4420) pg/ml, p=0.001; Fig. 3d). There was no difference between the pre-S1 and post-S1 (p=0.547, Fig. 3a) or the pre-S30 and post-S30 (p= 0.092; Fig. 3b) urinary resistin levels.

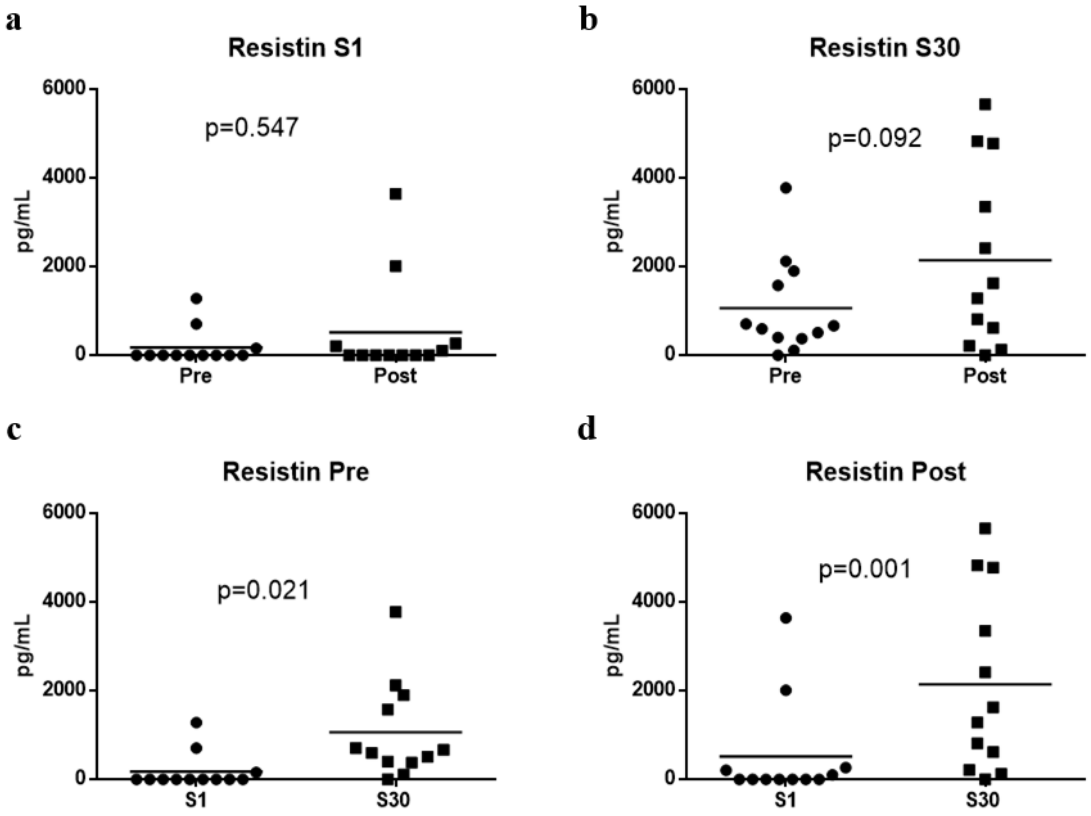

Figure 3. Urinary levels of resistin. **(a)** Urinary levels of resistin before and after the first exercise session (S1). **(b)** Urinary levels of resistin before and after the last exercise session (S30). **(c)** Urinary levels of resistin before the first (S1) versus the last exercise session (S30). **(d)** Urinary levels of resistin after the first (S1) versus the last exercise session (S30). Differences were considered significant at $p < 0.05$ (Wilcoxon test).

Discussion

This study investigated the acute and chronic effects of ST on urinary adipokine levels in healthy young men who underwent ST for 10 weeks. The main findings of this study were as follows: 1) ST acutely increased the urinary levels of leptin and adiponectin, and 2) ST chronically increased the urinary levels of leptin, adiponectin, and resistin.

In addition to the training intervention time, our protocol comprised three exercises for the lower limbs. However, other variables such as muscle action time and intensity were strictly controlled, which ensured that our protocol could generate the stimulus needed for such metabolic changes. To date, few studies have analyzed the effects of exercise on urinary levels of biological markers, either acutely or chronically.[19] This is the first study to evaluate the urinary levels of adipokines in response to ST.

Tests involving the collection of urinary samples offer two important advantages: one, they are non-invasive and avoid pain or discomfort to the volunteer, and two, urine testing produces a wide range of diagnostic targets.[29] The analysis of molecules in urine is important for diagnosing and monitoring kidney function, renal diseases, viral infections, and certain types of cancer.[29] Many biomarkers have been identified in human urine, that are sensitive and specific for a diagnosis.[30] No previous study has investigated the acute and chronic effects of ST on urinary levels of adipokines. However, we have previously measured renin-angiotensin system molecules in the plasma and urine following different protocols of physical exercise.[18,19] It should also be mentioned that the measurements in plasma and urinary samples provided different information. Plasma measurements show acute and short-term changes in circulating levels of molecules. In turn, urine measurements reflect the glomerular filtrated molecules released in the circulation plus the molecules produced in kidney tissue. Therefore, urine measurements are able to show more stable changes in the plasma levels of the molecules. Since the participants had plasma levels of creatinine stable and within normal range, we believe that the changes in urinary levels of adipokines were probably due to the modulation of systemic production as a response to ST.

Circulating leptin levels show circadian fluctuations and changes with nutritional status, and is associated with the size of adipose tissue, which is responsible for its production and secretion.[11] The free form of leptin is rapidly removed from the serum with a half-life of 3-4 minutes, and its urinary excretion is constant.[31] Our study showed an increase in urinary levels of leptin in healthy young adults after an ST session, both acutely (immediately after S1 and S30) and chronically (pre-S1 vs. pre-S30 and post-S1 vs. post-S30). Generally, physical exercise is considered a stressor for the body. Thus, the determination of urinary concentrations of leptin is important to understand the effect of exercise on body physiology. The molecules excreted in the urine result from glomerular filtration subtracted by the amount reabsorbed and added by the quantity secreted by tubular cells. We consider that urinary levels of the molecules may reflect more stable changes in the systemic production and excretion of each molecule in individuals with normal renal function. Thus, if pre-exercise levels are low and post-exercise levels are high, it indicates that ST might modulate the systemic production at a more constant rate that resulted in increased excretion in urine.[11] Furthermore, the chronic increase in urinary

leptin levels may represent a beneficial effect of progressive and monitored ST since it was able to maintain increased leptin levels after 10 weeks of intervention.

Adiponectin is a hormone secreted mainly by adipocytes and is related to insulin regulation, glucose utilization, fatty acid oxidation, and inflammation control.[12,13] A previous study reported that urinary levels of adiponectin are increased in patients with diabetic nephropathy in comparison to healthy controls, indicating a potential role of this molecule as a marker of renal function deterioration.[14] In our study, the ST protocol increased the urinary levels of adiponectin immediately after the last session, but not immediately after the first session. These results indicate the need for a longer time adjustment for the systemic production and urinary excretion of adiponectin in response to ST. Our long-term results (post-S1 vs. post-S30) showed that a period of 10 weeks was necessary to increase adiponectin production, with a consequent higher urinary excretion. We hypothesized that our ST protocol could acutely and chronically stimulate adiponectin production under conditions associated with low levels of this molecule.

Resistin was initially identified as a factor that is associated with insulin resistance. Other studies have linked this molecule to the development of atherosclerosis, cardiovascular disease, asthma, and chronic kidney disease.[16] Additionally, the plasma levels of resistin are proportional to the degree of adiposity and can be considered a pro-inflammatory marker.[32,33] In our study, we found a chronic increase in urinary resistin levels after 10 weeks of ST, but without acute changes. Our results suggest that enhanced urinary excretion of resistin is a probable consequence of increased production of this molecule at a more constant rate rather than an acute effect of a single ST session.

It is well known that there is an impact of fasting and feeding on adipose tissue metabolism. Adipokines have a major role in the regulation of metabolism during feeding and fasting.[33] However, very few studies evaluated the effect of diet on adipokines and most of them measured plasma levels of the molecules. In this regard, and co-workers compared plasma levels of adiponectin and leptin in patients with chronic kidney disease randomized to four conditions: caloric restriction of 10%–15%, exercise three times per week, combined caloric restriction and exercise, and control.[32] The authors found that plasma adiponectin levels significantly increased in patients randomized to the caloric restriction and usual activity but not to exercise, while circulating leptin did not change.[32] Considering the potential effect of dietary changes on the production and urinary excretion of adipokines, our volunteers were instructed to maintain their routine eating habits before the start, during the training process, and on the day of sample collection.

This study had several limitations. First, the relatively small sample size precludes generalization of our findings. Second, the inclusion of only healthy young males does not allow us to make inferences regarding changes in diseased conditions. Third, our study did not evaluate the mechanisms by which ST affects the urinary levels of adipokines. If the kidney function is compromised, the interpretation of our results may change. These molecules are filtrated by the glomerulus. If the glomerular filtration rate is reduced, the urine levels of the molecules will probably decrease, and the plasma concentration will consequently increase. However, these changes depend on the intensity of renal dysfunction, the reduction of

glomerular filtration rate, and the mechanism of kidney damage. For example, if inflammatory cells infiltrate the kidney, adipokines can be locally produced by these cells and excreted in the urine, leading to high urinary levels that do not correspond to systemic production of the molecule. However, plasma levels creatinine measurements of the study participants were within normal range and remained unchanged in all time-points of the study. Therefore, we consider that our results were not related to changes in glomerular filtration rate. In addition, we previously reported that urinary osmolality measurements remained stable in all time-points.[19] The stability of plasma creatinine levels and urinary osmolality support the hypothesis that the changes produced in adipokines in the present study were not due to renal function alterations. It should be mentioned that the use of the analysis of adipokines in urine is still not possible in clinical practice. However, we consider that these measurements are of interest for research as an attempt to understand the effect of the exercise in the synthesis of adipokines in individuals with normal renal function. In addition, the originality of our findings, the use of urine samples, and the strict ST protocol were strengths of our study.

Acute and chronic ST changed the urinary adipokine levels in young male adults. Urinary levels of leptin and adiponectin increased acutely and chronically, whereas that of resistin only increased chronically. Our study shows the importance of analyzing the adipokines levels not only in serum or plasma, but also in urine; urine collection is non-invasive and urinary measurements reflect stable concentrations of the molecules. Further studies are necessary to investigate the significance and mechanisms of adipokine changes in response to physical exercise.

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