

Acute glycemic outcomes along the aerobic training in deep water in patients with type 2 diabetes

Rodrigo Sudatti Delevatti^{1,2}, Nathalie de Souza Netto¹, Ana Carolina Kanitz^{1,3}, Cristine Lima Alberton⁴, Carolina Dertzbocher Feil Pinho¹, Elisa Corrêa Marson¹, Luciana Peruchena Bregagnol¹, Salime Chedid Lisboa¹, Luiz Fernando Martins Kruehl¹

¹Exercise Research laboratory, Department of Physical Education, Universidade Federal do Rio Grande do Sul, Brazil. ²Faculdade Sogipa de Educação Física, Brazil. ³Department of Physical Education, Universidade Federal de Uberlândia, Brazil. ⁴Department of Physical Education, Universidade Federal de Pelotas, Rio Grande do Sul, Brazil.

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Summary

Aims: The present study aimed to analyze the acute glucose responses in the first and last sessions of four mesocycles along an aquatic aerobic training periodization.

Methods: Fourteen patients (6 men and 8 women; 54.3 ± 9.0 years; body mass index of 34.5 ± 3.9 kg/m²) with type 2 diabetes underwent a 12-week training program involving deep-water running. This exercise training was performed by an interval training method, with a frequency of 3 times a week, session duration of 35 minutes and intensity progressing from 85 to 90% to 95 to 100% of the anaerobic threshold heart rate (ATHR) along the periodization. Capillary glucose was assessed before and immediately after the first and last session of each mesocycle. A generalized estimated equation (time x session x mesocycle) was used to assess reductions in glucose levels in different sessions (first and last) along four mesocycles ($\alpha = 0.05$).

Results: All sessions resulted in a reduction in glucose levels (time effect: $p < 0.001$), without differences between the first and last session of each mesocycle (session effect: $p = 0.738$). With regard to the mesocycles (mesocycle effect: $p = 0.003$), significant differences were found between mesocycles 2 and 3. In time*mesocycle interaction ($p = 0.002$), in most comparisons, post-session values were lowest than pre-session values, regardless of mesocycle, except for the post-session value of mesocycle 3, which was similar to the pre-values of mesocycles 2 and 4.

Conclusion: Aerobic training in deep water with crescent linear periodization over 12 weeks is able to reduce glucose levels in patients with type 2 diabetes.

Key words:

Aquatic environment.
Exercise.
Diabetes mellitus.
Glycemia.

Respuestas de la glucemia aguda a lo largo del entrenamiento aeróbico en aguas profundas en pacientes con diabetes tipo 2

Resumen

Objetivo: Analizar las respuestas de glucemia aguda en las primeras y últimas sesiones de cuatro mesociclos a lo largo de una periodización de entrenamiento aeróbico acuático.

Métodos: Catorce pacientes (6 hombres y 8 mujeres; 54,3±9,0 años; índice de masa corporal de 34,5±3,9 kg/m²) con diabetes tipo 2 fueron sometidos a un programa de entrenamiento de 12 semanas de carrera en aguas profundas. Se realizó un entrenamiento aeróbico de intervalos, realizado 3 veces por semana, con sesiones de 35 minutos y la intensidad progresando a lo largo de la periodización desde 85% - 90% a 95% - 100% de la frecuencia cardíaca del umbral anaeróbico (FCUA). La glucosa capilar fue evaluada antes e inmediatamente después de la primera y la última sesión de cada mesociclo. Se utilizó una ecuación generalizada estimada (tiempo x sesión x mesociclo) para evaluar las reducciones en los niveles de glucosa en las diferentes sesiones (primera y última) a lo largo de cuatro mesociclos ($\alpha = 0.05$).

Resultados: todas las sesiones resultaron en una reducción en los niveles de glucosa (efecto tiempo: $p < 0,001$), sin diferencias entre la primera y la última sesión de cada mesociclo (efecto de sesión: $p = 0,738$). Con respecto a los mesociclos (efecto mesociclo: $p = 0,003$) se encontraron diferencias significativas entre los mesociclos 2 y 3. En la interacción tiempo*mesociclo ($p = 0,002$), en la mayoría de las comparaciones, los valores post-sesión fueron menores de los valores pre-sesión, independientemente de mesociclo, excepto para el valor después de la sesión del mesociclo 3, que fue similar a los valores antes de la sesión de los mesociclos 2 y 4.

Conclusión: Doce semanas de entrenamiento aeróbico en aguas profundas con la periodización linear y creciente es capaz de reducir los niveles de glucosa en pacientes con diabetes tipo 2.

Palabras clave:

Ambiente acuático.
Ejercicio.
Diabetes mellitus.
Glucemia.

Correspondencia: Rodrigo Sudatti Delevatti
E-mail: rsdrodrigo@hotmail.com

Introduction

Type 2 diabetes mellitus (T2DM) is a worldwide public health problem predominantly resulting from obesity and a sedentary lifestyle. Interventions ensuring lifestyle changes have been effective both in the prevention and control of the disease, with exercise being one of the most effective nonpharmacological treatments for T2DM^{1,2}, through its beneficial effects on outcomes such as blood pressure, lipid profile and glucose levels³.

According to the American Diabetes Association (ADA), patients with T2DM should do 150 minutes or more of aerobic exercise at moderate intensity per week, and when without complications must combine this with two or three sessions per week of resistance training⁴. These guidelines demonstrate how important aerobic training is to this population, and it is generally recommended to all patients. However, despite a lot of evidence indicating the beneficial chronic effects, especially in glucose control in this population⁵⁻⁷, less is known about the acute glycemic effects of aerobic training during progressive training. Studies investigating this issue focused predominantly on the comparison between the effects of different exercise sessions in a specific training status⁸⁻¹⁰. To the best of the authors' knowledge, no study has investigated these effects at different times during a periodization, in which the intensity and/or duration increases along the training while the patients improve their physical fitness and metabolic status.

With regard to the periodization of aerobic training, it is worth noting that patients with a type 2 diabetes clinical profile, usually obese or overweight, can complicate increases in exercise dosage, especially in intensity, because in greater intensity for glucose control, such as those near of anaerobic threshold¹¹, patients are more susceptible to lower limb injury. An alternative to the necessary training progression is the training conducted in water, such as water aerobics, because the buoyancy provides attenuated impact forces, especially for the lower limbs¹². Moreover, deep-water running is another interesting modality for the progression of exercise training because the practitioners perform aerobic exercise at high loads with reduced risk of injury, since a float vest is used to keep the body in an upright position, preventing contact between the feet and the bottom of the pool¹³.

Because of its characteristics, deep-water running is favorable to progress in training without increasing the impact on joints, thereby enabling patients to exercise at high intensity or for long duration, optimizing glucose control. In addition, this modality has demonstrated a similar increase in strength to combined training in water¹⁴ and has glycemic metabolism benefits in glucose-intolerant women¹⁵. The fact that this modality allows progression in training intensity, including for patients with difficulties in supporting their own body mass¹⁶, indicates the need for knowledge about the acute glycemic effect in different stages of a linearly increasing periodization, because although it seems a great alternative, literature about "exercise and type 2 diabetes" is scarce on studies in water. Thus, the present study aimed to analyze acute glycemic responses in the first and last sessions in four mesocycles of a deep-water running program. Our hypothesis is that in mesocycles of three weeks, the acute glycemic effect not is attenuated, being similar in the first and last session of each mesocycle.

Materials and methods

Subjects

The sample consisted of 14 patients with T2DM (6 men and 8 women) who had not undertaken any physical exercise in the previous three months and were receiving their usual medical treatment. Patients with the following conditions were excluded from the sample: uncontrolled hypertension, autonomic neuropathy, severe peripheral neuropathy, proliferative diabetic retinopathy, severe nonproliferative diabetic retinopathy, decompensated heart failure, limb amputations, chronic renal failure (MDRD-GFR < 30 ml/min)¹⁷ or any muscle or joint impairments that prevented individuals from engaging in physical exercise. The presence of these conditions was confirmed by medical history as well as clinical and laboratory examinations. All patients had undergone effort electrocardiograms in the six months preceding the study.

Research design

Patients were identified from the records of the Endocrine Division of a tertiary hospital and were also recruited through advertisements in local newspapers between June and July 2012. All participants were fully informed of the procedures involved in the study, and provided written consent prior to participation. The study was approved by the Research Ethics Committees of the Universidade Federal do Rio Grande do Sul (protocol number 108.997) and of the Hospital de Clínicas de Porto Alegre (protocol number 54475). The research design, with intervention and evaluations performed are illustrated in the Figure 1.

Anthropometric measurements

Prior to the intervention, patients underwent anthropometric measurements. Body mass and height were assessed using a digital scale and a stadiometer (FILIZOLA; Sao Paulo, Brazil). These values were used to calculate patient body mass index (BMI) using the following formula: mass (kg)/height² (m). Waist circumference was measured at the mid-point between the iliac crest and the last rib. Additionally, skinfolds were measured at the following eight sites: tricipital, subscapular, suprailiac, abdominal, chest, midaxillary, thigh and leg. The equations proposed by Petroski¹⁸ were used to estimate the body density of men and women, while body fat percentages were estimated using the Siri formula¹⁹.

Blood analysis

Blood samples (4ml) were obtained from an antecubital vein after fasting for 12 to 14 h. The samples were collected in tubes with EDTA and kept frozen at -80 °C as total blood (without centrifugation). After blood data collection, the levels of HbA1c were determined through high-performance liquid chromatography (HPLC) to characterize the glycemic control of the patients.

Capillary glycemia

Capillary glycemia was assessed before and immediately after the first and last sessions of each training mesocycle using a clinical

glucometer (Accu-Check Performa, Roche, São Paulo, Brazil), which assesses glycemic levels in approximately 5 seconds, and a lancet device (Accu-ChekMulticlix, Sao Paulo, Brazil).

Intervention

Patients underwent 12-week training program involving deep-water running with a life vest. The interval-training program consisted of four mesocycles of three weeks each. Training was conducted three times per week (Monday, Wednesday and Friday), and each 45-minute session was divided into a warm-up period (5 min), followed by the main training program (35 min) and a cool-down section (5 min). The intensity of the physical exercise prescribed was adjusted according to each subject's heart rate deflection point (HRDP), which was determined by a progressive maximal test conducted in the water environment. This method was chosen due to its ease of application and association with the second ventilatory threshold, a precise indicator of the relative stress caused by exercise²⁰. Participants were asked to wear HR monitors (RSX 300, Polar) during the exercise sessions to control training intensity. Each individual was asked to read and report their heart rates to one of the three instruc-

tors who supervised the exercise sessions. Each instructor then used a table containing subjects' training heart rate ranges to provide feedback on the recommended exercise intensity for each patient. The 12-week training program prescribed to each participant is described in Table 1.

Statistical analysis

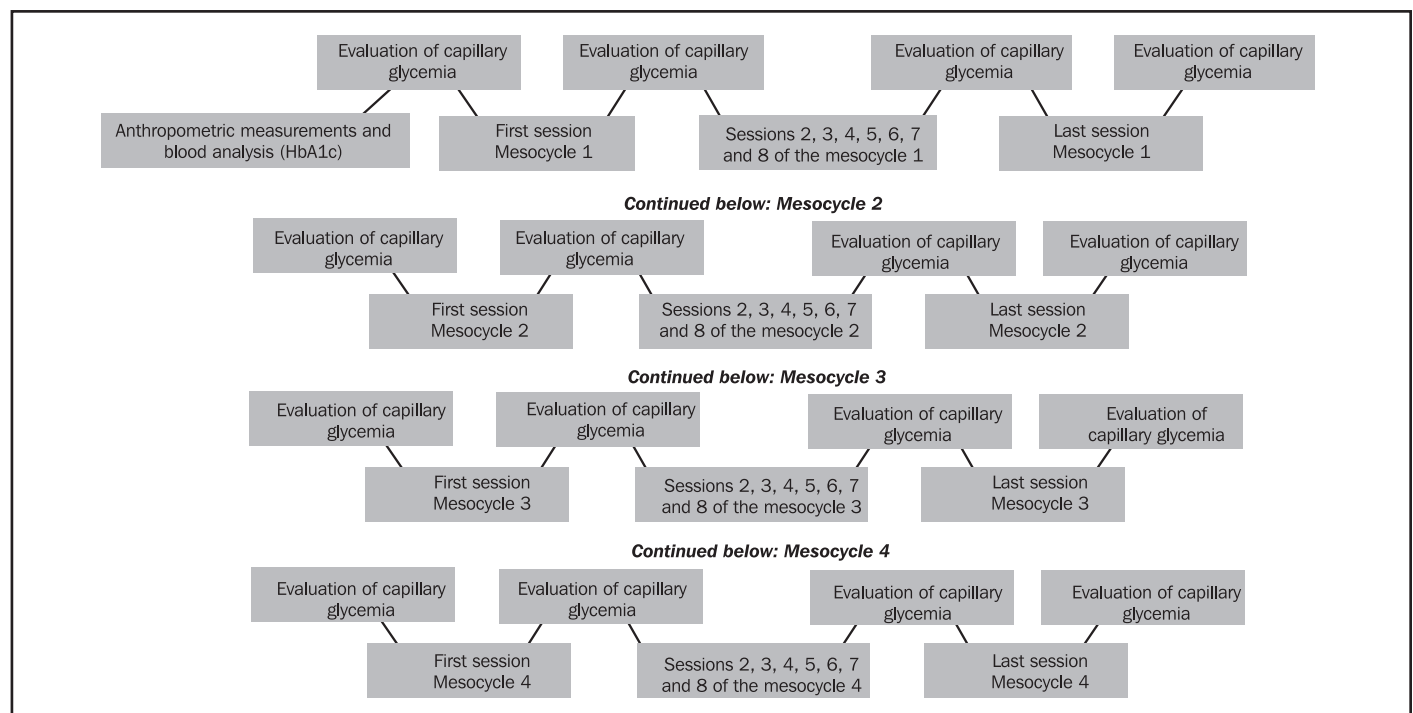
Descriptive data of the subject characteristics are presented as mean and standard deviation for continuous variables and as n for categorical variables. Glycemic levels are presented as mean and standard error. A generalized estimation equation (GEE) was used to assess alterations in glucose levels (pre versus post) in different sessions (first and last) in each mesocycle of training, taking into consideration the three factors involved in the analysis (time, session and mesocycle). Given that exogenous insulin use could potentiate an exercise glucose-lowering effect, we performed the analyses for all patients, and excluding those patients using insulin. Multiple comparisons were performed with Bonferroni correction. The level of significance was set at $\alpha= 0.05$. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 19.0.

Table 1. 12-week aerobic training program.

Mesocycle	Week	Training sessions	Duration (main part)
1	1 - 3	7x (3 min 85-90% ATHR with 2min <85% ATHR)	35 min
2	4 - 6	7x (4 min 85-90% ATHR with 1min <85% ATHR)	35 min
3	7 - 9	7x (4 min 90-95% ATHR with 1min <85% ATHR)	35 min
4	10 - 12	7x (4 min 95-100% ATHR with 1min <85% ATHR)	35 min

Note: ATHR: Anaerobic threshold heart rate.

Figure 1. Study design (evaluations and intervention).



Results

Sample data regarding disease duration, age, anthropometric measurements and medication use are shown in Table 2.

Table 2. Subject characteristics.

Age (years)	54.3 ± 2.4
Duration of DM2 (years)	5.4 ± 1.0
HbA1c (%)	7.9 ± 0.7
Body mass (kg)	93.1 ± 3.6
Body mass index (kg.m ⁻²)	34.5 ± 1.0
Waist circumference (cm)	111.7 ± 2.9
WHR	0.68 ± 0.02
Fat mass (%)	37.5 ± 1.1
Sex (male/female)	6/8
Medical treatment	
Metformin (n)	12
Sulphonylurea (n)	6
DPP-4-inhibitors (n)	1
Pioglitazone (n)	1
Diuretics (n)	4
Beta blockers (n)	4
ARAs II (n)	4
Acetyl-acetylsalicylic (n)	5
Statins (n)	7
Insulin (n)	3

DPP-4: dipeptidyl peptidase-4; ARAs: Angiotensin receptors antagonists; WHR: waist/height ratio; Values of age, duration of DM2 and anthropometric measures are expressed as the mean ± SE; Values of sex and medication are expressed by n.

All training sessions determined a reduction in glucose levels (time effect: $p < 0.001$). In all mesocycles, the first session values did not differ from the values found in the last session (session 1 = session 9, session 10 = session 18, session 19 = session 27, session 28 = session 36; session effect: $p = 0.738$). Between the mesocycles (mesocycle effect: $p = 0.003$), significant differences were found only between the pre-session values of mesocycles 2 and 3 (Table 3). In time*mesocycle interaction ($p = 0.002$), significant differences were found between pre-session and post-session values in most comparisons, except for the post-session value of mesocycle 3, which was similar to the pre-values of mesocycles 2 and 4.

Given that exogenous insulin use could potentiate an exercise glucose-lowering effect, we performed an analysis excluding those patients using insulin. The results, however, were very similar: Exercise sessions determined reductions in glucose levels (time effect: $p < 0.001$), without differences between the first and last session of each mesocycle (session effect: $p = 0.889$). Between the mesocycles (mesocycle effect: $p = 0.018$), significant differences were found only between the pre-session values of mesocycles 2 and 3 (Table 4). In time*mesocycle interaction ($p = 0.012$), significant differences were found between pre-session and post-session values in most comparisons, except for the post-session value of mesocycle 1, which was similar to the pre-value of mesocycle 2.

No hypoglycemic episodes or other adverse effects were reported over the course of the study.

Discussion

This study showed that acute exercise sessions performed in an aquatic environment are effective in reducing glycemia. The mesocycle composition of three weeks was enough to maintain the glucose mag-

Table 3. Glucose levels pre and post exercise sessions along the four mesocycles during a deep-water running periodization in all patients (n=14).

	First session			Last session		
	Pre session	Post session	Mean difference	Pre session	Post session	Mean difference
Mesocycle 1	171.3 ± 20.5	138.7 ± 11.8*	-32.6	174.0 ± 22.5	137.9 ± 17.2*	-36.1
Mesocycle 2	163.2 ± 19.6 ^a	131.2 ± 16.2*	-32.0	164.7 ± 22.0 ^a	144.6 ± 19.7*	-20.1
Mesocycle 3	208.6 ± 28.1 ^b	140.7 ± 18.5* ^a	-67.9	192.4 ± 27.4 ^b	150.7 ± 24.3* ^a	-41.7
Mesocycle 4	168.8 ± 18.6 ^a	130.2 ± 16.3*	-38.6	169.8 ± 19.3 ^a	141.0 ± 15.3*	-28.8

Data are reported as mean and standard error; *indicates significant difference between pre vs. post session values; Different letters indicate significant difference between pre values of mesocycles 2 and 3; Same letters indicate that pre-session values of mesocycle 2 are similar to post-session values of mesocycle 3; Generalized estimated equation; Bonferroni correction.

Table 4. Glucose levels before and after the exercise sessions in the four mesocycles of deep-water running in patients excluding those using insulin (n=11).

	First session			Last session		
	Before session	After session	Mean difference	Before session	After session	Mean difference
Mesocycle 1	146.8 ± 19.2	118.0 ± 5.7* ^a	-28.8	135.2 ± 10.8	106.2 ± 7.4* ^a	-29.0
Mesocycle 2	128.8 ± 8.5 ^a	102.3 ± 5.2*	-26.5	131.6 ± 12.1 ^a	115.7 ± 7.5*	-15.9
Mesocycle 3	165.0 ± 21.9 ^b	109.10 ± 11.0*	-55.9	145.0 ± 14.4 ^b	112.8 ± 12.4*	-32.2
Mesocycle 4	134.9 ± 7.5	100.1 ± 6.6*	-34.8	135.5 ± 10.0	117.0 ± 8.2*	-18.5

Data are reported as mean and standard error. *indicates significant difference between pre vs. post session values; Different letters indicate significant difference between pre values of mesocycles 2 and 3; Same letters indicate that post-session values of mesocycle 1 are similar to pre-session values of mesocycle 2; Generalized estimated equation; Bonferroni correction.

nitude reduction during the mesocycles, without deteriorating effects as the patients adapted to the session model. The increasing intensity between the four different mesocycles was able to continue to impact glucose levels beneficially during the 12 weeks, underlining the similarity of post-exercise values in the third mesocycle to pre-exercise values in the fourth mesocycle, indicating a possible training adaptation.

Glucose reduction after training sessions has been the target of many investigations⁸⁻¹⁰. However, the aim of these studies is usually to compare the acute glycemic effects of different modalities. In this context, aerobic training has shown a greater glucose reduction than resistance training¹⁰ and a similar glucose reduction to combined training with a similar duration (40 min)⁹. Bachi *et al.*¹⁰ reported an area under the curve of glucose during 60 min of aerobic exercise lower than that observed during 60 min with no exercise. Figueira *et al.*⁹ found a glucose reduction of approximately 16% after sessions in both aerobic and combined training, a reduction that was sustained for only three hours after the end of the sessions. However, these investigations are restricted to land, which creates difficulties in performing exercise for some patients, because the disease is usually associated with obesity^{21,22}, sarcopenia²³, muscle weakness²⁴ and chronic complications characteristic of the disease, such as peripheral neuropathy²⁵ which end up limiting this population's adherence to exercise programs. These patients' clinical profile emphasizes the importance of our findings, because we found an expressive glucose reduction (average of the eight evaluated sessions: 34 ± 14 mg/dl; $19 \pm 6\%$) without joint impact, something that is extremely important, especially because in addition to glycemic disorder, patients were obese and many had pain and a history of musculoskeletal injury.

One thing in common among studies analyzing glucose reduction with exercise is that they compared the effect of different training modalities or different manipulations of the same modality in a given state of trainability (sedentary or trained). However, it is necessary to elucidate possible physiological adaptations caused by aerobic training, which can attenuate glucose reduction in a given dosage of exercise, needing an adequate progression in the variables of the training for continuity of this desirable effect. Among aerobic training adaptations, we find the improvement in muscle oxidative capacity, the increase in fatty acid oxidation²⁶, and in the expression and activity of signaling enzymes and proteins, important for glucose metabolism, like glycogen synthase and GLUT 4²⁷. This leads to a greater use of lipid pathways at the same relative intensity and a greater storage of muscle glycogen, which sometimes is 50% smaller in patients with T2DM than in nondiabetic ones²⁸. Thus, trained patients will be able to have a greater glucose supply derived from muscle storage during exercise, because skeletal muscle is the major site of available glucose in human²⁹, with the same input of blood glucose not being necessary for a given activity compared to a sedentary situation, with low muscle glycogen storage. Because of these alterations, we believe that, in order for an expressive acute effect on glucose levels to continue to exist, it is necessary to have periodic increases in the dosage of the exercise (i.e. intensity). Although the adaptations to training referred to have been well demonstrated, the glucose effects of a same session model in different stages of a periodization have not been compared. With this proposal, we didn't find differences between the first and the last sessions of each mesocycle, which demonstrated

that up to three weeks, the adopted prescription in the present study enables acute glucose reduction through all mesocycles.

When comparing the different mesocycles, the importance of progression, either by changes in relationship stimulus: recovery (mesocycle 1 for mesocycle 2), or in stimulus of intensity (mesocycle 2 for mesocycle 3; mesocycle 3 for mesocycle 4) was also evidenced by the present findings. When analyzing the differences we found, it is noticeable that there was no attenuation in glycemic responses, something expected if the exercise dosage is not increased adequately. The fact that all sessions resulted in glucose reductions showed that the increases were efficient in terms of progression during the mesocycles. It is possibly for the fixed duration (35 min) and increases in intensity, which leads to increased volume and intensity, the main components of physical training. The association between training progression and reduced capillary glucose has not been sufficiently studied in patients with type 2 diabetes, which prevents comparisons between the present findings and those of other studies. Calculating an mean of the eight deltas in the present study, the reduction found (34 ± 14 mg/dl) was similar to the findings of Terada *et al.*⁸, in which a similar sample underwent a 12-week land-based aerobic training program, and it was found that participant glucose levels decreased by a mean of 34.2 ± 30.6 mg/dl. In the study in question, however, only exercise volume was increased, by increasing the duration over the course of the intervention, maintaining a mean intensity of 40% of oxygen uptake reserve over the mesocycles. Analyzing simultaneously this progression of training and the one used in the present study, we have two models that focus on different variables, but with a similar magnitude of glycemic reduction. While Terada *et al.*⁸ adopted a progression focused on the duration of the training sessions, the present study adopted a progression based especially on intensity. Both strategies of periodization seem appropriate, and can be used as needed. The different progressions can be adapted to the profile of patients: While subjects with limitations for training at high intensity (i.e. land-based exercise, leading to higher joint impact) can progress in training duration, subjects with little available time for training may fix the duration of sessions and increase the intensity.

Another important issue to discuss is the effect of using or not exogenous insulin on glycemic responses and the possibility of exercise causing hypoglycemia. In a study³⁰ analyzing the effect of a single session of aerobic exercise performed on a cycle ergometer, with moderate intensity (35-50% of maximal power), a similar glycemic reduction effect was shown between insulin users and nonusers, differing only with respect to glycemic variability and the prevalence of hypoglycemia, which was higher in the insulin users. In the present study, an analysis without exogenous insulin users showed minimal differences in relation to the overall analysis, these being the differences between the post-exercise values of the third mesocycle and the pre-exercise values of the fourth mesocycle, besides the similarity between the post-exercise values of the first mesocycle and the pre-exercise values of the second mesocycle, which was not demonstrated in the overall analysis. These small differences do not modify the posterior analysis, because the training periodization adopted allowed glucose reductions throughout its course (all patients or without insulin users).

In conclusion, deep-water aerobic training with an increasing linear periodization, especially progressive in intensity every three weeks, is

able to reduce glucose levels in patients with type 2 diabetes over 12 weeks – important information for structuring training aimed at controlling the glucose levels in this population. These findings suggest the need for further studies investigating glycemic behavior at the beginning and end of training cycles with different durations (>3 weeks), aimed at widening knowledge of the influence of different training adaptations on the effects of acute exercise on blood glucose levels.

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