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Sumario / Summary

Sweating, dehydration and prevention of heatstroke

Sudoración, deshidratación y prevención del golpe de calor

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In the thermoregulatory system, the sweat glands respond to a complex physiological relationship between the central nervous system, the cardiovascular system and the skin. At rest, 80% of heat is dissipated by conduction, convection and radiation. When ambient temperature exceeds the temperature of the skin, ~32ºC, these mechanisms are no longer effective and the body starts to secrete sweat, taking over the evaporation of 80% of the dissipated heat. It is necessary to maintain a balanced body temperature for the organism to work correctly and, increasing the internal temperature by more than a couple of degrees has significant physiological consequences that might even be life-threatening.

To maintain a normal internal temperature (36.8 ± 0.5°C), the maximum temperature of the skin is required to be 35ºC, to thereby produce an appropriate temperature gradient from the core to the skin. In this mechanism, an increase in relative air humidity will progressively and significantly reduce evaporation by sweating. These effects can be compensated by the wind that facilitates evaporation and its radiating effect. In any case, and without considering environmental conditions, there are very few types of exercise that produce enough wind speed itself for this, such as cycling.

In any of the conditions observed above, hydration is fundamental. Almost 80 years ago, the effects of physical performance in a hot atmosphere had already been observed, demonstrating the need to ingest liquids to replace losses due to sweat.[1] It should also be considered that there are considerable differences in daily hydration (0.74 L/day to 2.70 L/day) among healthy young adults.[2] Furthermore, it has been observed that in sport, continuous exercise and intermittent exercise do not have the same effect on hydration efficiency, and the latter is more efficient.[3] Scientific entities update this knowledge cyclically leading to a considerable number of recommendations on hydration, euhydration and hydration with supplementation, even in special environments.[4] There are specific recommendations to avoid pathologies associated with heat caused by effort.[5]

In situations of heat stress, increased activity in the vasodilation system is responsible for 80% to 90% of the increase in blood flow to the skin. During exercise, blood supply to the active muscles and blood flow to the skin to dissipate heat come into conflict, both are important in thermal regulation, regulation of arterial pressure, to cover metabolic needs, and in cardiovascular homoeostasis. These conditions seem to be associated with dehydration when the water loss is greater than 2%, 2-3% or 4% of body mass. Consequently, exercising when dehydrated, particularly in a hot atmosphere, can increase the risk of heat-related illnesses, including heat stroke. However, working from studies performed on more than 5,000 soldiers, only 17% of cases were associated with dehydration.[6] Heatstroke seems to be more associated with other factors such as acclimatising to the heat, medicines, genetic predisposition and injuries.[4,6] It has also been observed that incidence of heatstroke has increased greatly since the 1980s. In the USA alone, more than 3,300 deaths were attributed to this cause between 2006 and 2010.

At rest, urination is the best way of eliminating liquid, followed by the skin, respiration, faecal matter and sweat. However, when exercising, in a hot atmosphere, or a combination of the two, the situation is completely reversed. There is a great interest in finding out about and pinpointing biomarkers that represent both hydration and dehydration. These biomarkers can be found by collecting urine samples (osmolality, specific severity, colour, volume; considered to be non-invasive measurements)[4] or plasma/saline solution (osmolality, vasopressin, etc.). Biomarkers are considered to be just as important as the actual measurement of difference in body mass[3,4].

Dehydration induced by sweating not only causes changes in these markers but a loss of electrolytes that must be recovered, such as sodium.[4,5] Consequently, sweating during exercise also makes it possible

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to eliminate significant quantities of ammonia, urea and lactate, among other metabolic residue.

Dehydration can endanger life and affect not only athletes but also vulnerable populations. The situation is worsening for these populations due to climate change. There is a progressive spread of geographic areas that reach dry-bulb temperatures above 33ºC or 35ºC[7].

The stability point for our supposed heat-regulating centre, on the anterior hypothalamus, seems to change its control point in some conditions (fever or heatstroke). It is important to mention that it remains unclear that our hypothalamus is the only integrative centre or controller that determines our temperature stability. It has been suggested that other independent centres might exist, including the hypothalamus that, with their own afferent and efferent branches, manage to coordinate around a common variable that is body temperature[8,9]. It is possible that the classic heat-regulating model[10] might change considerably over time.

During prolonged exercise in a hot atmosphere over a long period of time, sweat production will drop and body temperature will rise, with cutaneous vasodilation, decrease in blood volume, renal flow and the antidiuretic hormone; a phenomenon that has been called "Sweating fatigue" that will reduce the capacity to respond to exercise. The low blood volume will cause inefficient muscular irrigation, intense fatigue, with an increase in the HR, less sweating and a high risk of hyperthermia, cardiac syncope and risk of death. Although temperature modifies the heart's vagal response, using heart rate as a control variable does not help us identify sweating fatigue.

Biosensor technology has been developed over the last 30 years. The use of non-invasive biosensors directly on the skin, making the most of the electric surface characteristics and/or the actual composition of sweat, is not a new idea. It is worth remembering that, although it seems mundane, a heart rate monitor is also a biosensor. Over the last few years, studies on biosensors have really taken off. An average of over 60 articles have been published every year. Since the 1990s, one of the first papers on biosensors began by testing an inefficient biosensor for amino acids and another for L-lactate[11].

Many of the biosensors being developed are intended for diagnosis or screening of pathologies, such as the case of glucose sensitive patches. These biosensors can be built into products or fabric clothing, they can also be designed as different models of patches or encapsulated systems that cover the skin. Some studies on biosensors associated with physical activity deserve a mention, such as the system to record bipolar ECG. This uses a system similar to headphones for ears, also making it possible to record sweat rate, pH and lactate[12]. In another study, nanoparticles have been used, built into a normal filter base, that was designed to measure sweat rate, and sweat loss[13].

When these contraptions are small enough with sufficient autonomy, they can be used to control athletes during sport. Of course, there are protocols for treatments against heatstroke, but the key to the problem revolves around seeking detection measures to stop it happening.

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Índice

Effect of strength training on people with HIV and immunometabolic disorders

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Summary

The introduction of highly active antiretroviral therapy (HAART) was able to help to control viral condition in patients living with HIV/AIDS, diminishing virus concentration and increasing T CD4 + cells. However, adverse effects follow the treatment, like lipodystrophy syndrome, characterized by morphological changes in body fat distribution and changes serum lipids and glycides levels, increasing the risk for chronical diseases with cardiovascular effects. Thus, complimentary non-drug practices, as strength training, are essential to treat these patients, helping to improve their immunometabolic condition, leading to a better coping with the disease. The aim of this study was to investigate the influence of a 12-week strength training protocol on immunometabolic system of people living with HIV/AIDS. It is a quasi-experimental study, conducted on 20 patients (16 men), all living with HIV/AIDS using HAART. T CD4 + cell numbers, serum triglycerides, cholesterol (total and fractions) and glycemia were measured before and after training. The data underwent to descriptive statistics using a paired T test, with the significance level set at p <0.05.There was a significant increase of 15.4% (p=0.009) on T CD4 + cells and, although not statistically significant, reduction on glycemia, total cholesterol and triglycerides and increase on HDL-cholesterol fraction. So, it is suggested that strength training may be effective on immunometabolic condition of people living with HIV / AIDS, increasing T CD4+ cells and controlling serum levels of lipids and glycides.

Key words:
Strength training. Human immunodeficiency virus. Acquired immunodeficiency syndrome. Highly active antiretroviral therapy. Lipodystrophy. CD4-Positive T-lymphocytes.

Efecto del entrenamiento de fuerza en personas con VIH y trastornos inmunometabólicos

Resumen

La introducción de la terapia antirretroviral altamente activa (HAART) ayudó a controlar la condición viral de los pacientes con HIV/AIDS, reduciendo la concentración del virus y aumentando las células T CD4 +. Sin embargo, los efectos adversos acompañan el tratamiento, como el síndrome de lipodistrofia, caracterizada por cambios morfológicos en la distribución de la grasa corporal y de los niveles metabólicos en los lípidos y glicidos séricos, creciendo el riesgo de enfermedades crónicas con impacto cardiovascular. Así, los tratamientos complementarios no medicados, como el entrenamiento de fuerza, son esenciales en el tratamiento de estos pacientes, lo que contribuye en las mejoras inmunometabólicas en esta población, lo que contribuye a hacer frente a la enfermedad. El propósito de esta investigación fue verificar la influencia de un protocolo de entrenamiento de fuerza con duración de 12 semanas en los sistemas inmunometabólicos de personas con HIV/SIDA. Este es un estudio cuasi-experimental, realizado con 20 pacientes (16 hombres), todos con HIV/SIDA usando la terapia HAART, sometidos a un protocolo de entrenamiento de fuerza de 12 semanas. Se tomaron medidas de las variables número de células T CD4 +, niveles séricos de triglicéridos, colesterol (total y fracciones) y glucosa en sangre, antes y después del entrenamiento. Los datos fueron analizados mediante estadística descriptiva, con prueba T pareada y nivel significativo establecido en p <0,05. El resultado mostró un aumento significativo en las células T CD4 + en un 15,4% (p=0,009), aunque no es estadísticamente significativo, tuve la glucosa en sangre reducida, así como el colesterol total y los triglicéridos, con respectivo aumento de la fracción de colesterol HDL. Por lo tanto, sugerimos que el entrenamiento de fuerza puede ser efectivo en las condiciones inmunológicas y metabólicas de las personas que viven con HIV/AIDS, aumentando las células T CD4 + y controlando los niveles de lípidos y glucosa en sangre.

Palabras clave:
Entrenamiento de fuerza. Virus de inmunodeficiencia humana. Síndrome de inmunodeficiencia adquirida. Terapia antirretroviral altamente active. Lipodistrofia. Linfocitos T CD4-positivos.

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Introduction

The Human Immunodeficiency Virus (HIV) is a human retrovirus that affects T-helper cells that have CD4 receptor, which are responsible for the immune response. Its infection causes an immunological impairment that leads to AIDS (Acquired Immunodeficiency Syndrome), which has the characteristics of multiple opportunistic infections and several rare diseases[1].

Several treatment improvements made possible the introduction of Highly Active Antiretroviral Therapy (HAART) that modifies the viral action on the body, changing the condition from lethal to chronic, helping to reduce viral load and to maintain CD4+ cells levels[2]. However, HAART has adverse effects, among them, the lipodystrophy syndrome, that is characterized by bad distribution of body fat and metabolic changes[3].

Changes in body fat are classified as lipohipertrophy, lipoatrophy and mixed lipodystrophy Lipohipetrophy is characterized as an increase in abdominal, thoracic and cervical fat, lipoatrophy as a decrease of fat in superior and inferior limbs as well as in face, while lipodystrophy is characterized by both manifestations[4-6]. Generally, these morphological changes do not affect health[5,6]. However, the metabolic changes caused by lipodystrophy start serum lipidic and glycidic variations, increasing the risk to chronic diseases with cardiovascular implications[6]. Lifestyle may influence lipodystrophy, and so, alimentary control and exercises may contribute positively on the manifestation and treatment of this syndrome.

HAART is aimed to control/increase the immunological system (CD4+ T-cells), since its deprivation key to the development of AIDS[1] and lifestyle changes are essential to diminish adverse effects as lipodystrophy syndrome[7].

So, complimentary non-drug practices that control T CD4 + cells are very important to help HAART to control the disease[8]. Among the complimentary therapies to HIV treatment, the regular exercise is one of the most important[9,10], since it may influence directly on the increase in T CD4 + cell numbers besides contributing to control serum lipids and glycemia.

Strength training has been widely used on people living with HIV/AIDS, because it has an important effect on lipodystrophy syndrome[11]. However, few studies demonstrated the effects of strength training on immunometabolic systems on this population. Thus, evidencing the effectiveness of therapeutic resources complementary to HAART are fundamental in coping with the disease, such as strength training in immunometabolic conditions, with a view to positively impacting the longevity and quality of life of these patients. Thus, in a short period (12 weeks), the study aimed to assess the effectiveness of strength training on changes in immunometabolism in people living with HIV / AIDS.

Material and method

It has been a quasi-experimental study, carried out in a continuous flow strength training program initiated in 2013, at the Clinics Hospital from Ribeirão Preto School of Medicine of University of São Paulo (HCFMRP-USP) and at the Guidance and Education Center for Adults and Elders from Nursery School of Ribeirão Preto of University of São Paulo (COEAI/EERP-USP), supported by São Paulo Research Aid Foundation (FAPESP), grants 2011/7300-4 and 2011/03136-5. The study was approved by the Ethics Research Committee from HCFMRP-USP (protocol - 6692/2010), and all subjects signed the free consent form to state the agreement to participate voluntarily on the study, and free to quit at any moment.

The sample was composed by 20 subjects, from both sexes, HIV-positive diagnostic, under HAART for at least 12 weeks. The subjects were between 35 and 70 years old, accompanied at HCFMRP-USP ambulatory and in a nutritional counseling program at the same institution. The subjects were not allowed to use nutritional supplements or other medication beyond HAART and antihypertensive and should not have practiced regular physical exercise for at least three months and should be able to do so, specifically strength training, with a written cardiologic allowance. All subjects not that not fit in the inclusion criteria, had any clinic changes during the training period or had more than 25% absences in the training sessions (9 of 36 sessions) were excluded from the study.

The subjects were recruited among 112 patients, from both sexes (86 males), that were clinically followed at HCFMRP-USP and were included on the nutritional program offered by the hospital. The subjects were invited during the medical advisement or by telephone. From the 112 patients, 97 were contacted and 48 agreed in participate of the training program. Among then, 13 were excluded because they did not fit in the inclusion criteria and three quitted before start training. Thus, 32 subjects begun the training program and, among them, 12 were excluded for absence criteria. The final sample were composed by 20 subjects (16 males), characterized at Table 1.

The strength training was composed of 36 sessions (12 weeks), during 40 minutes (between 2 pm and 5 pm) every Monday, Wednesday and Friday, allowing 48 to 72 hours intervals[12]. In all training sessions, the subjects were under supervision of three researchers involved in the study, all of them physical educators. The 36 sessions were divided in three consecutive phases: 1) preparation, six sessions with three series of 15 repetitions and a 60 seconds interval between exercises[12], with intensities determined according to Borg scale[13] ranging from 11 (fairly light) to 13 (somewhat hard); 2) adaptation, six sessions with three series of 15 repetitions and 60 seconds intervals between exercises, intensities ranging from 40 to 50% of the obtained at the maximum repetition test – 1MR[12]; 3) specific, 24 sessions with three series of with 8 repetitions and 90 seconds intervals, with intensities ranging from 70 to 80% of 1MR[12]. Based on the basic principles for periodization and physical exercise prescription[14] and due to the natural adaptation to physical exercise, at the end of the 12nd session of the specific period (total of 24 sessions), a new 1MR test was applied to readapt the training load intensity, still fixed at 70-80% of 1MR[12].

Strength training was composed by the following exercises (following the respective order): warm up (active stretching), supine, pull back, knee extension, knee flexion, elbow extension, abdominals, plantar flexion and relaxation (active stretching)[12].

Before each session, the subjects were questioned and evaluated for the general health status, vital signs measured (arterial pressure, heart rate, breath rate and oxygen saturation), repeated after the training. During training sessions, the subjects were oriented and monitored

to rehydration with water between the exercises series and had their clinical condition monitored. Any clinical instability before, during or after the training sessions were considered as an exclusion criteria and the subject were sent to medical care at HCFMRP-USP. The subjects were oriented about the importance of resting and sleeping between the training session.

Personal data as age, viral infection period, training time and medication used were collected using a questionnaire applied before the beginning of the training protocol, all data confirmed at their medical records. Body weight and height were measured using a scale (Welmy), intervals of 0.1 kilograms (kg) and 0.1 centimeters (cm).

Before and after the training program (36 sessions - 12 weeks) were measured the number of CD4+ T-cells, serum levels of triglycerides, total, HDL and LDL cholesterol (lipogram) and blood glucose. Lipogram analysis and blood glucose were made using the enzymatic method and the CD4+ T-cells count were obtained using Flux Cytometry (ACEA Biosciences).

Exams were collected during the routine examination at HCFMRP-USP. A maximum period of three months before the initial evaluation of this study was considered to accept the data from exams. If the patient did not have results in this period, a requisition for new exams were given to get them. After the training period, the patients received another requisition for post training exams.

The strength training protocol was conducted in equipment station (Athletic Way) with two independent 180 kg columns, allowing two patients to exercise at the same time. To determine the initial training intensity, the preparatory phase, the Borg scale were used[13]. This phase aimed to teach the correct movements, considering the efforts as fairly light and somewhat hard. The patients were oriented to point the physical effort at Borg scale, when the pointed value did not fit the expected interval, the training load were adjusted[12]. In all sessions of this phase, the patients were corrected to execute the right movements, at the right body position, movement amplitude and corrected breathing.

After learning the movement in the prior stage, the patients were submitted to 1MR test, to determine training intensity in the subsequent stages, this test was already used in people living with HIV[15-17]. This test was used in three moments: before the adaptation stage, in the middle of this specific stage (12 sessions, to readjust the intensity) and at the end of the training program. This test aims to register the maximum weight that the subject is able to execute a single repetition with the movement complete amplitude. The subjects were tested progressively, the load were increased until the subject were not able to complete the needed amplitude, then the previous load was registered as the maximum load[12,17]. However, only six attempts were made, in 80 seconds intervals between the attempts, if the 1MR were achieved, a new test were conducted after 72 hours[12]. Plantar flexion was conducted unilaterally on the floor and was not tested for 1MR.

A Shapiro-Wilks normality test was used to determine if the data were normally distributed. The sample was characterized by a descriptive analysis with the means, maximum and minimum values for age, body weight, height, infection time, HAART use, viral load and therapeutic regimen. Immunological and metabolic changes were measured pre and post training, then the data were analyzed through a paired T-test, using SPSS 13.00 software, with significant level set at $p < 0.05$. The calculation of the effect size was performed using the Cohen formula and the results were based on the following criteria: negligible effect (> = -0.15 and <.15), small effect (> =. 15 and <.40), medium effect (> =. 40 and <.75), large effect (> =. 75 and <1.10), very large effect (> = 1.10 and <1.45) and huge effect > 1.45.

Table 1. Sample characterization of trained group.

Variable (n=20)	Mean (min-max)	CI (95%)
Age (years old)	50.6 (38.0-67.0)	46.895 to 54.305
Weight (kg)	71.8 (51.1-111.2)	65.386 to 78.233
Height (cm)	169.3 (151.0-185.0)	165.352 to 173.198
HIV Infection Time (years)	11.3 (1.0-23.0)	8.147 to 14.453
HAART Use (years)	9.8 (1.0-23.0)	6.648 to 12.951
IP Use, n (%)	15/20 (75.0)	0.673 to 1.527
ITRAN Use, n (%)	19/20 (95.0)	1.336 to 1.964
ITRNN Use, n (%)	10/20 (50.0)	0.260 to 0.740
Training Frequency (%)	90 (81-100)	1.57 to 8.44

IP: Protease Inhibitors; ITRAN: Nucleoside Analogues Reverse Transcriptase Inhibitors; ITRNN: Nucleoside Non-Analogues Reverse Transcriptase Inhibitors.

Result

There were 20 subjects in this study (16 males) with the mean age of 50.6 years old, mean weight of 71.8 kg and mean height of 169.3 cm. As to infection time, the subjects were infected for 11.3 years (mean infection time), using HAART for 9.8 years, 15 individuals (75%) use protease inhibitors (IP), 19 (95%) use nucleoside analogues of reverse transcriptase inhibitors (ITRAN) and 10 (50%) nucleoside non-analogues of reverse transcriptase inhibitors (ITRNN; Table 1).

As to immunological response, we found that, after the proposed protocol, the individuals showed a significant increase of 69.2 (15.4%; p=0.009) cell/µl in CD4+ T-cells. Regarding the metabolic conditions, we observed increase in HDL-cholesterol of 1.4 (3.9%) mg/dl and LDL-cholesterol of 1.5 (1.3%) mg/dl, decrease of serum triglycerides of 38.4 (16.9%) mg/dl, total cholesterol (14.7 mg/dl; 7.4%) and blood glucose of 4.8 (4.9%) mg/dl,

however, metabolic responses were not statistically significant. Regarding the size of the effect, a medium result (0.47) in the levels of trliglycerides was found significantly (Table 2).

Discussion

The control of the viral condition is very important to evaluate clinical appearance of HIV. HAART acts changing viral action on the body, helping to reduce viral count and maintaining CD4+ T-cells[2]. Nevertheless, HAART has adverse effects, as lipodystrophy syndrome, that leads to changes in metabolic lipids rate and insulin resistance, which may lead to chronical diseases with cardiovascular risks[3,6].

Since the longevity of people living with HIV/AIDS is increasing consistently, it became vital the development of therapies that help

Table 2. Immunological and metabolic responses after 12 weeks of training.

Parameter		Descriptive Mean (min-max)	Paired differences Diff mean (%) Effect size (result)	T	df	*p*
Trained group						
Lymphocytes T CD4+ (cell/µl)	Pre	449.8 (105.0-1073.0)	69.2 (15.4) 0.27 (small)	-2.8936	19	0.009*
	Post	519.0 (105.0-975.0)				
Triglycerides (mg/dl)	Pre	227.4 (95.0-521.0)	-38.4 (16.9) 0.47 (medium)	1.9192	19	0.070
	Post	189.0 (95.0-361.0)				
Total cholesterol (mg/dl)	Pre	197.2 (125.0-313.0)	-14.7 (7.4) 0.38 (small)	1.6363	19	0.118
	Post	182.5 (125.0-247.0)				
HDL Cholesterol (mg/dl)	Pre	35.74 (26.0-50.0)	1.4 (3.9) 0.21 (small)	-1.014	19	0.323
	Post	37.15 (26.0-54.0)				
LDL Cholesterol (mg/dl)	Pre	115.7 (75.0-221.0)	1.5 (1.3) 0.03 (negligible)	-0.1009	19	0.920
	Post	117.2 (72.0-266.0)				
Glycemia (mg/dl)	Pre	99.70 (79.0-165.0)	- 4.8 (4.9) 0.29 (small)	1.1231	19	0.275
	Post	94.85 (74.0-146.0)				

HAART on the control of CD4+ T-cells and, among the complementary therapies to the medication, the regular physical exercise is one of the most important[9,10], acting either in increasing CD4+ T-cells and controlling metabolic changes, those changes can increase the life spam for these individuals[18]. Strength training has been used as a complementary therapy in people living with HIV/AIDS[11]. However, few studies issue the effects of strength training on the viral condition of these population.

In the present study, the efficiency of strength training over the immunological and metabolic conditions in people living with HIV/AIDS. The proposed training protocol (12 weeks) were efficient in increasing the CD4+ T-cells by 15.4% (p=0.009). This increase can be influenced acute and chronically by exercise. The stimuli caused by the training recruits white cell subpopulations to the vascular lumen, as CD4+ T-cells, which remain slightly elevated after the exercise, increasing its concentration in result of chronic exercise[19].

Our results are in agreement to Zanetti *et al.*[20], who evaluated the efficiency of a 12 weeks strength training observing a significant increase in CD4+ T-cells (p=0.004), similar results were found by Anandh *et al.*[21] (p=0.041). On the other hand, in a case study with one man and one woman, Mesquita Soares *et al.*[22], found a decrease in the man and a increase in the woman on CD4+ T-cells, questioning the efficiency of the strength training on people living with HIV/AIDS. The number of subjects may be too small to observe the effect seen on this study, which presents the same results found in the systematic review conducted by Pedro *et al.*[23].

When we verified the metabolic responses to the strength training, we did not find any significant changes, however, the study showed strong evidence that strength training contributes to the metabolic changes seen in lipodystrophy syndrome, since the protocol adopted increased HDL-cholesterol (3.9%) and LDL-cholesterol (1.3%), reduced triglycerides (16.9%), total cholesterol (7.4%) and blood glucose (4.9%). Terry *et al.*[24] also showed no significant changes on metabolic parameters after strength training in people living with HIV/AIDS. However, Mendes *et al.*[25] demonstrated, in a 12 weeks duration strength training protocol, reduction of serum triglycerides (9.9%), total cholesterol (12.0%), LDL-cholesterol (8.6%) and an increase in HDL-cholesterol (16.7%). Robinson *et al.*[26] demonstrated that a 16 weeks strength training protocol reduced serum triglycerides (59 mg/dL; p=0.001) and insulin resistance (15.7%; p=0.001).

From the literature review carried out, we identified few studies that verified the effectiveness of strength training on immunometabolic variables in people living with HIV / AIDS. In this research, the authors understand as a limitation the fact that it was not possible to perform the sample calculation, due to the difficulty in recruiting patients with the profile necessary for the study, the sample being selected from 112 patients who were undergoing clinical and nutritional monitoring at HCFMRP-USP. Added to the fact that the nutritional monitoring carried out does not have a strict control in the domestic context, since the prescriptions made by the professionals were not controlled outside the hospital. In a complementary way, the findings of this study (except for the limitations of the study presented here) provided reflections on the disease and complementary non-drug therapeutic measures for the immunometabolic control of HIV / AIDS. However, the findings discussed here could only be generalized to other contexts based on strict dietary control (not addressed in the present study) and the faithful reproduction of the physical exercise protocol.

Thus, we observed that strength training can be effective on the immunological and metabolic conditions of people living with HIV/AIDS. It has an important role increasing CD4+ T cells, thus being a fundamental not-medicated treatment in this population. Strength training can also control serum levels of triglycerides, total and fractions cholesterol and the blood glucose, we propose that training protocols longer than 12 weeks can be effective to this effect. Thus, strength training may be a complementary resource to fight HIV/AIDS, however, it is suggested

that further studies may be needed to detect the most effective time and protocols of strength training.

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Conflict of interest

The authors do not declare a conflict of interest.

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Experimental pilot study after surgery on a food supplement for athletes to protect articular knee cartilage. A functional and biochemical study

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Summary

This double-blind experimental study evaluates the efficacy of chondroprotective supplementation (Carticure Plus®, 5000 mg Collagen – Bioactive Peptides, 1500 mg Glucosamine Hydrochloride, 1200 mg Chondroitin Sulfate, 1.1 mg Copper, 80 mg Vitamin C, 2 mg Manganese) in patients with meniscal and ligament pathology who have required arthroscopic surgery. 12 patients with ligamentous injury and 12 patients with meniscopathy were selected, who underwent the measurement of different inflammatory markers using ELISA, collagen 2A and hyaluronic acid, in addition to evaluating pain as well as functionality and quality of life through VAS (Visual Analogue Scale), WOMAC (Western Ontario McMaster Universities Osteoarthritis Index) and KOOS (Knee Injury and Osteoarthritis Outcome Score). Statistically significant differences of clinical improvement were observed in favor of Carticure Plus®, with an improvement in the functional capacity of the WOMAC scale, 76% Carticure Plus® vs 53% placebo, for all patients and with a clear improvement in the first month in meniscal injury, in improvement of the activities of daily life (KOOS), Carticure Plus® 31% vs placebo -1%, sports activity, (Carticure Plus® 41% vs placebo 13,2%) and sports and recreational activities (KOOS) (Carticure Plus® 128% vs Placebo 10,4%).
On the other hand, in ligamentous injury an improvement in quality of life (KOOS) Carticure Plus® 75% vs Placebo -8,8% and pain (KOOS) Carticure Plus® 49,6% vs Placebo 0,3% was observed in the first month compared to the baseline. In the patient group, pain (KOOS) Carticure Plus® 31,4% vs Placebo 1,3% and activities of daily living (KOOS) Carticure Plus® 43,9% vs Placebo 27,1% in the third month from baseline, are associated with an improvement due to Carticure Plus® when compared to the placebo group. Despite the small sample size, it is remarkable the fact that statistically significant differences have been found, the efficacy of Carticure Plus® could be assumed.

Key words:
Cruciate ligament. Meniscus. Carticure Plus®. Arthroscopy. Knee.

Estudio experimental piloto tras cirugía del uso de un complejo alimenticio en deportistas para la protección del cartílago articular de rodilla. Un estudio funcional y bioquímico

Resumen

En este estudio experimental doble ciego se evalúa la eficacia de la suplementación condroprotectora (Carticure Plus®, 5000 mg Colágeno (Péptidos Bioactivos) altamente asimilable, 1500 mg Glucosamina clorhidrato, 1200 mg Condroitín sulfato, 1,1 mg Cobre, 80 mg Vitamina C, 2 mg Manganeso) en pacientes con patología ligamentosa y meniscal que han requerido cirugía artroscópica. Se seleccionaron 12 pacientes con lesión ligamentosa y 12 pacientes con meniscopatía a los que se les procedió a la medición de distintos marcadores inflamatorios mediante ELISA, colágeno 2A y ácido hialurónico, además de a la evaluación del dolor así como la funcionalidad y calidad de vida a través de EVA (Escala Visual Analógica), WOMAC (Western Ontario McMaster Universities Osteoarthritis Index) y KOOS (Knee Injury and Osteoarthritis Outcome Score). Se observaron diferencias estadísticamente significativas de mejoría clínica a favor de Carticure Plus®, con una mejora de la capacidad funcional de la escala WOMAC del 76 % frente a un 53% del placebo para el conjunto de pacientes y con una clara mejoría en el primer mes en lesión meniscal, en mejora de las actividades de la vida diaria (KOOS), Carticure Plus® 31% frente a placebo -1%, actividad deportiva (Carticure Plus® 41% vs Placebo 13,2%), actividades deportivas y recreativas (Carticure Plus® 128% vs Placebo 10,4%). Por otro lado, en lesión ligamentosa se observa una mejoría en calidad de vida (KOOS) Carticure Plus® 75% vs Placebo -8,8% y dolor (KOOS) Carticure Plus® 49,6% vs Placebo 0,3% en el primer mes respecto al basal. En el conjunto de pacientes, el dolor (KOOS) Carticure Plus® 31,4% vs Placebo 1,3% y actividades de la vida diaria (KOOS) Carticure Plus® 43,9% vs Placebo 27,1% en el tercer mes respecto al basal se asocian a una mejora a Carticure Plus® en comparación al placebo. A pesar del pequeño tamaño muestral, es destacable el hecho de haber encontrado diferencias estadísticamente significativas que podría presuponer la eficacia de Carticure Plus®.

Palabras clave:
Ligamento cruzado. Menisco. Carticure Plus®. Artroscopia. Rodilla.

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Introduction

The Anterior Cruciate Ligament (ACL) injury is one of the most frequent ligament injuries among athletes, with an estimated incidence of 35/100,000 per year[1]. The standard treatment for these injuries is surgery as a general rule. The operation aims to stabilise the joint in an attempt to slow down the development of degenerative changes in it, in other words articular Osteoarthritis (OA). Despite this, the incidence of developing osteoarthritis after ACL reconstructions is high and furthermore, this risk increases if there is a meniscus injury involved[2,3].

Although incidence of meniscus repairs has been soaring over the last few years[4], for most patients who need operations on symptomatic meniscal injuries from the age of 30 onwards, a selective subtotal meniscectomy is usually still performed plus regularisation of the meniscal injury.

In other words, at least one third of these patients develop progressive OA in their knee in the first decade after the injury and the majority of them in the second decade[5].

Despite this, there is no effective treatment to halt this process. In one way or another, we might say that meniscal and ligament injuries of the knee lead the way to osteoarthritis[6,7]. In addition to classic functional scales, it might be interesting to evaluate biochemical markers that can indicate abnormal articular situations after surgery on this type of injury to understand and attempt to slow down this development[8].

Given that there is no scientific evidence of the impact of oral condroprotector supplements among patients with ligament and meniscal pathologies who require arthroscopic surgery, it is proposed to carry out an experimental, double-blind pilot study to evaluate the effectiveness of Carticure Plus®.

Material and method

Experimental, double-blind, pilot study, with two random treatment assignment branches (Carticure Plus® vs. placebo), analysing the effects on pain and different systemic markers among 24 amateur athletes aged between 30 and 50 years old. The indication for arthroscopy among patients with meniscal pathologies included in the study will be made by following usual clinical practice and good clinical practice guides. This excluded relevant interactions or known contraindications (hypersensitivity or allergies) with the excipients or the components of Carticure Plus® / placebo, patients who had received knee surgery on a previous occasion, diabetes *mellitus*, pregnancy or breast-feeding.

These patients were selected by ranking them into 12 patients with meniscopathy and 12 with an ACL ligament injury who received arthroscopy surgery and then took 1 sachet a day of Carticure Plus® (bioactive peptide made of 5,000 mg collagen, 1,200 mg chondroitin sulphate, 1,500 mg glucosamine hydrochloride, 80 mg ascorbic acid (Vitamin C), 2 mg manganese and 1.1 mg copper) compared to a placebo for three months.

The study variables were measurement of various blood markers using the ELISA test: pro-inflammatory/catabolism (PCR, IL-6, IL-1B, TNF-alfa), anabolism (TGF-beta and FGF-21), collagen 2A and hyaluronic acid. Various scales and questionnaires were also used to evaluate pain, functionality and quality of life. Pain was assessed using the Visual Analogue Scale (VAS) which represents intensity along a 10 cm line numbered from 0 to 10, where 0 represents "no pain" and the other end is "the worst pain imaginable"[9]; *Western Ontario McMaster Universities Osteoarthritis Index* (WOMAC) questionnaire: this is one of the best questionnaires from the point of view of its psychometric properties. This questionnaire contains three subscales that measure pain, rigidity and functional capacity[10]; KOOS Scale *(Knee Injury and Osteoarthritis Outcome Score)*: questionnaire validated in the Spanish population. It evaluates several aspects: symptoms, rigidity, pain, daily activities, sports and recreational activities and quality of life[11].

Given the sample size, a non-parametric, U by Mann-Whitney, test compares independent data on the mean difference in the quantitative variables from the first, second and third month compared to the baseline value, for each pathological group and in total. Consequently, this compares improvements in pain (EVA), WOMAC questionnaire and KOOS questionnaire between the baseline visit and the rest of the monitoring (Table 1) among the patients who took Carticure Plus® and the placebo, both in the meniscus and ligament pathologies as a whole and separately.

The study took place at the Arthroscopy and Sports Orthopaedic Unit, Clínica San Miguel in Pamplona (Navarre) and it was approved by the Ethics Committee. All the patients gave their informed consent voluntarily after receiving information on the study.

The data obtained from the pilot study were used to evaluate whether to carry out a study with greater statistical power and select the main variable for the study.

The promoter asked the ARAFARMA GROUP S.A. laboratory to donate the food and fund the monitoring in the study. There are no conflicts of interest for the authors.

Table 1. Time frame for collecting variables.

		Visit			
		Baseline	1 month	2 months	3 months
Carticure Plus	EVA	X	X	X	X
	WOMAC	X			X
	KOOS	X	X	X	X
	Inflammatory markers	X			X
Placebo	EVA	X	X	X	X
	WOMAC	X			X
	KOOS	X	X	X	X
	Inflammatory markers	X			X

Results

Patients with a meniscus injury not associated with a ligament injury or a deficit of rough tissue were 83.3% men who played various sports (running, football, crossfit, etc.). Similarly, 83.3% of patients with an anterior cruciate ligament pathology were male, 58.3% played football and the rest did a variety of sports (rugby, skiing, running, etc.). The patients' descriptive data are given in Table 2.

When analysing the different articular inflammatory, anabolism and catabolism markers in the two pathologies, together (Table 3) or separately, we did not notice statistically significant differences between the patients taking Carticure Plus® compared to the placebo regarding the difference in the value obtained at the baseline moment, after three months or in the difference between the basal moment and after three months.

Tables 4, 5 and 6 show the evolving results of the EVA scales and the WOMAC and KOOS questionnaires for the patients.

In meniscal pathologies there are no statistically significant differences regarding the decrease in pain measured by the EVA scale in the first month compared to the baseline (p=0.24), where the average drop of pain between Carticure Plus® and the control group is 2.83 (CPmEVA) and 1.6 (CtrlmEVA) respectively, with results from the second month (p=0.48, CPmEVA=3.33, CtrlmEVA=3) and the third month (p=0.84, CPmEVA=2.8, CtrlmEVA=3). Similarly, in ligament pathologies, no statistically significant differences were obtained regarding the reduction of pain measured by the EVA scale when we compare the improvement in pain with the baseline moment after one month (p=0.48, CPmEVA=1.83, CtrlmEVA=0.83). After two months (p=0.54, CPmEVA=1.83, CtrlmEVA=1.8) and after three months (p=1, CPmEVA=2.83, CtrlmEVA=2.4).

When considering the whole set of patients, an improvement is obtained in the functional capacity of the WOMAC scale among patients taking Carticure Plus® compared to the placebo (p=0.04, CP average

Table 2. Description of the patients with a meniscus injury not associated with a ligament injury or a deficit of rough tissue and patients with an anterior cruciate ligament pathology.

	Meniscus		Ligament	
	Mean	Std. dev.	Mean	Std. dev.
Age	36.99	4.9	37.65	6.30
Weight	79.92	10.12	76.38	6.70
Height	178	7.01	172.42	7.79
BMI	25.24	3.02	25.72	1.91

Std. Dev.: Standard deviation; BMI: Body mass index.

Table 3. Inflammatory indicators of articular anabolism and catabolism.

		CP	CTRL
PCR (mean)	Baseline	306.15	398.05
	3 months	655.17	610.10
	differential	394.09	270.86
FGF (mean)	Baseline	8.64	7.80
	3 months	8.56	3.12
	differential	-0.08	-4.67
TGF (mean)	Baseline	634.20	642.73
	3 months	685.47	788.74
	differential	68.78	49.43
TNFa (mean)	Baseline	22.57	24.68
	3 months	24.93	33.34
	differential	2.36	11.48
IL1b (mean)	Baseline	27.17	28.29
	3 months	29.53	16.60
	differential	0.60	-11.00
IL6 (mean)	Baseline	3.33	4.62
	3 months	3.35	2.79
	differential	0.02	-1.37
HA (mean)	Baseline	38.98	48.36
	3 months	35.96	50.03
	differential	-3.03	1.67
Col2a (mean)	Baseline	25.01	24.79
	3 months	24.54	23.33
	differential	0.67	-0.35

CP: CarticurePlus; CTRL: control; PCR: Protein C reactive; FGF: fibroblast growth factor; TGF: transforming growth factor; TNFa: tumour necrosis factor α; IL1b: Interleukin 1 β; IL6: Interleukin 6; HA: hyaluronic acid; Col2a: collagen 2a.

Table 4. Pain evaluation on the EVA scale.

	Meniscus			Ligament		
	Month	Mean	Std. dev.	Month	Mean	Std. dev.
Carticure Plus	0	4.83	1.47	0	4.33	1.97
	1	2.00	1.10	1	2.50	0.84
	2	1.50	2.35	2	2.50	1.52
	3	1.60	2.07	3	1.50	1.98
Control	0	3.83	0.75	0	3.50	1.64
	1	2.17	0.98	1	2.67	1.37
	2	0.83	0.41	2	2.20	0.84
	3	0.83	0.45	3	1.60	1.14

Std. Dev.: Standard deviation.

Table 5. WOMAC Questionnaire.

		Pain		Rigidity		Functional capacity	
	Month	Mean	Std. dev.	Mean	Std. dev.	Mean	Std. dev.
Meniscus							
Carticure Plus	0	6.33	3.83	2.50	1.64	19.83	12.70
	3	1.00	1.73	1.80	3.49	4.40	7.80
Control	0	2.83	1.72	1.33	1.03	8.83	6.49
	3	1.00	0.71	0.40	0.55	2.40	2.70
Ligament							
Carticure Plus	0	6.17	6.21	3.17	2.40	24.83	21.19
	3	1.67	3.61	1.67	1.51	6.33	10.37
Control	0	4.33	4.63	2.50	2.35	17.83	16.62
	3	2.40	2.30	1.80	1.79	10.20	10.87

Std. Dev.: Standard deviation.

Table 6. KOOS Questionnaire.

		Month									
		0		1			2			3	
		CP	CTRL	CP	CTRL	*p*	CP	CTRL	*p*	CP	CTRL	*p*
Meniscus												
Number of patients		6	6	6	6		6	6		5	5	
Symptoms	Mean	62.50	77.50	82.50	75.00		90.83	91.67		94.00	86.00	
	Std. Dev.	23.61	10.84	17.54	15.49		8.61	7.53		8.22	11.94	
Rigidity	Mean	72.92	75.00	91.67	75.00		91.67	9.75		95.00	97.50	
	Std. Dev.	21.53	17.68	20.41	25.00		10.21	10.46		11.18	5.59	
Pain	Mean	63.89	75.46	78.89	80.09		88.43	93.98		94.44	95.56	
	Std. Dev.	16.29	10.46	19.10	13.77		15.26	4.09		9.62	5.76	
AVD	Mean	66.42	85.29	87.01	84.56	**0.002**	93.63	96.57	**0.041**	94.12	96.47	
	Std. Dev.	18.16	14.11	15.35	15.19		9.87	3.56		9.36	4.94	
ADyR	Mean	26.67	40.00	60.83	44.17	**0.04**	75.00	78.33		80.00	79.00	
	Std. Dev.	12.52	24.29	27.10	16.56		18.17	8.16		20.00	14.75	
Quality of life	Mean	36.46	45.83	50.00	55.21		79.17	77.08		77.50	72.50	
	Std. Dev.	17.42	14.61	28.78	22.51		20.79	14.61		28.84	23.63	
Ligament												
Number of patients		6	6	6	6		6	5		6	5	
Symptoms	Mean	53.33	61.67	55.83	54.17		67.50	61.00		76.67	68.00	
	Std. Dev.	26.39	12.11	11.58	16.56		21.85	23.82		20.66	8.89	
Rigidity	Mean	45.83	62.50	62.50	56.25		77.08	72.50		79.17	70.00	
	Std. Dev.	39.26	30.62	29.58	15.31		22.94	18.54		18.82	31.37	
Pain	Mean	53.24	67.59	75.00	64.81		79.63	67.78	**0.03**	78.70	75.00	
	Std. Dev.	28.40	19.77	26.00	16.36		25.01	17.41		22.13	21.06	
AVD	Mean	62.50	73.04	73.97	69.61		83.82	77.65		91.42	75.29	
	Std. Dev.	33.32	27.97	31.86	15.72		23.66	14.42		17.51	29.42	
ADyR	Mean	27.50	34.17	17.50	13.33		22.50	29.00		46.67	46.00	
	Std. Dev.	30.29	24.98	29.79	13.29		32.98	24.85		40.21	37.82	
Quality of life	Mean	20.83	35.42	36.46	32.29	**0.04**	47.92	33.75		54.17	51.25	
	Std. Dev.	11.64	17.08	10.01	15.52		24.90	16.89		25.82	28.09	

CP: Carticure plus; CTRL: control; AVD: daily activities; ADyR: sport and recreational activities; Std. Dev.: standard deviation.

increment of 16.97 points, 76% compared to Ctrl of 7.03 points, 53%) between the final and baseline visit. The pain dimension for the same scale is close to a statistically significant difference (p=0.055, CP average increment of 4.92 points, 79% compared to the Ctrl of 1.86, 53%), with no differences seen in the rigidity subscale.

Statistically significant differences can be observed in the improvement of the Carticure Plus® group compared to the placebo for the subscale of daily life activity (KOOS) between the basal visit and the first visit (one month from the initial visit) in the meniscal pathology (p=0.002, CP average increment of 20.59 points, 31% compared to Ctrl of -0.74 points, -1%). This difference is maintained between the baseline visit and the second visit (two months) in the meniscal pathology (p=0.041, CP average increment of 27.21 points, 41% compared to Ctrl of 11.27 points, 13.2%). Statistically significant differences were also observed in favour of Carticure Plus® on the subscale of sports and recreational activities (KOOS) in the meniscal pathology between the baseline visit and the visit the following month (p=0.04, CP average increment of 34.17 points, 128% compared to Ctrl of 4.17 points, 10.4%). We also detect statistically significant differences in the Carticure Plus® group compared to the placebo for the subscale of daily life activity (KOOS) between the basal visit and the visit carried out the following month (p=0.04, CP average increment of 15.63 points, 75% compared to Ctrl of -3.13 points, -8.8%) in the ligament pathology. In the latter pathology, we also observed improvements in pain among the Carticure Plus® group compared to the placebo (p=0.03, CP average increment of 26.39 points, 49.6% compared to Ctrl of 0.19 points, 0.3%) between the second and the baseline month. If we consider all the patients, irrespective of the type of pathology, we see an improvement in pain (KOOS subscale) between the baseline and first visit in favour of Carticure Plus® compared to the placebo (p=0.007, CP average increase of 18.38 points, 31.4% compared to Ctrl of 0.93 points, 1.3%) and an improvement in daily life activities between the baseline visit and the visit after one month (p=0.007, CP average increase of 16.03 points, 24.9% compared to Ctrl of -2.08 points, -2.6%), after two months (p=0.027, CP average increase of 24.26 points, 37.6% compared to Ctrl of 7.94 points, 10%) and after three months (p=0.024, CP average increase of 28.31 points, 43.9% compared to Ctrl of 21.42 points, 27.1%). In no case are statistically significant differences seen (p<0.05) between the two groups at the baseline visit.

Discussion

In the clinical data, despite the small sample size, statistically significant differences in clinical improvement are seen in favour of Carticure Plus® compared to the placebo. During the first month, the KOOS scale showed an improvement in pain, activities in daily life, sports and recreational activities and quality of life (Figures 1 and 2).

This makes it possible to detect a faster improvement, that equals out over the three months in the case of the ligament injury (Figures 3 and 4) but in the case of the meniscal injury a clinical improvement is maintained in the Carticure Plus® group. Despite the small number of patients, statistically significant differences were observed in the daily activities, sport and recreational activities in meniscal injuries between the baseline visit and the first month, and in quality of life in ligament pathologies between the baseline visit and the first month. It should be highlighted that statistically significant differences were found in very few cases (12 patients in each pathological group), which favours the clinical evaluation of improvement in the first month of Carticure Plus®. In the set of 24 patients, the improvement in pain after one month and the improvement of daily life after one, two and three months leads us

Figure 1. KOOS scale, baseline moment, after one month and after 3 months, in patients with meniscus injury not associated with ligament injury or deficit of rough tissue. (CP: Carticure Plus®).

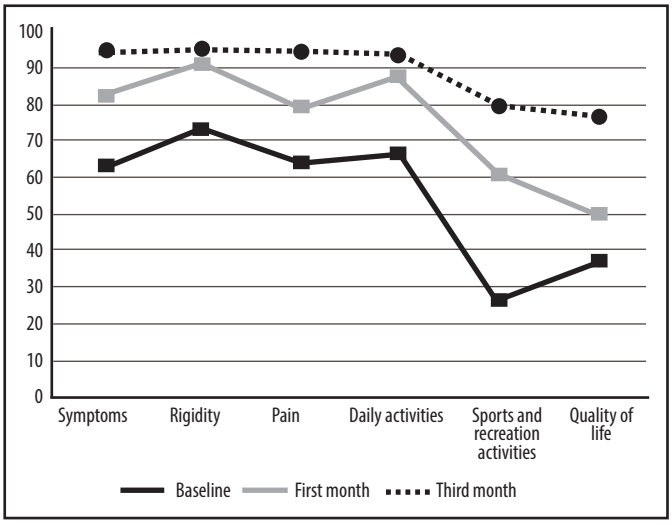


Figure 2. KOOS scale, baseline moment, after one month and after 3 months, in patients with meniscus injury not associated with ligament injury or deficit of rough tissue. (CTRL: Control).

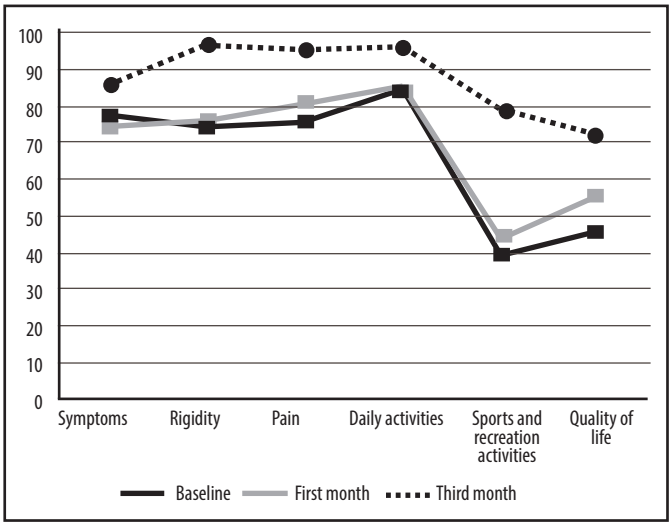


Figure 3. KOOS scale, baseline moment, after one month and after 3 months, in patients with anterior cruciate ligament pathology. (CP: Carticure Plus®).

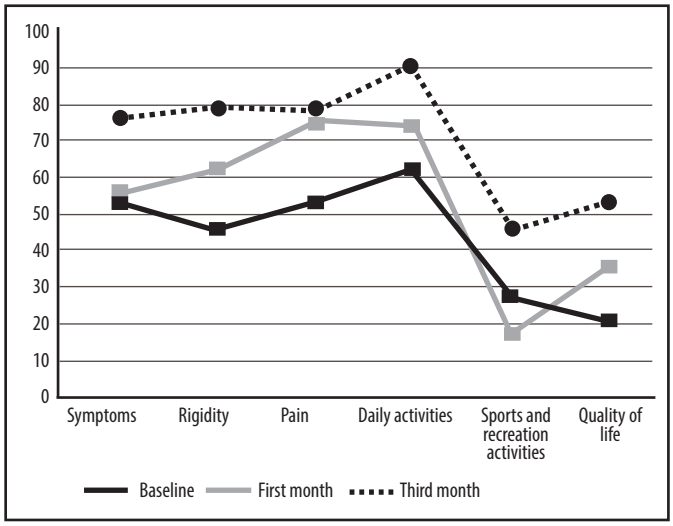
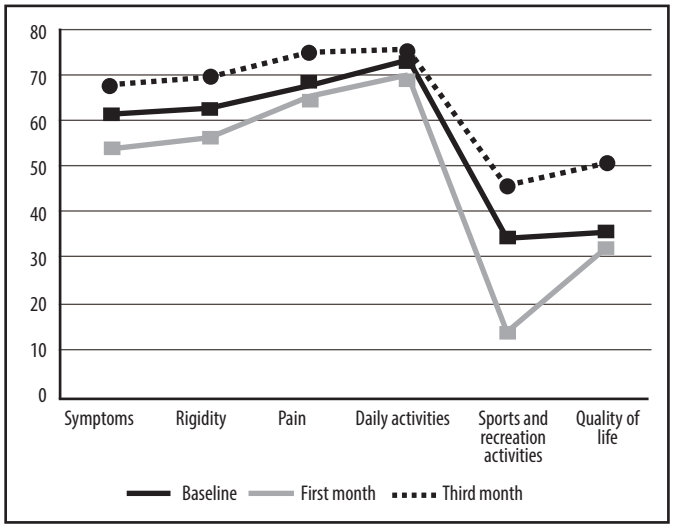


Figure 4. KOOS scale, baseline moment, after one month and after 3 months, in patients with anterior cruciate ligament pathology. (CTRL: Control).



to believe that the faster improvement associated with Carticure Plus® produces a sustained recovery that lasts for all three months compared to the absence of food supplement, that might be explained by the characteristics of the product. Detecting differences, the three-month improvement on the WOMAC scale regarding functional capacity and only just missing out on this improvement in pain on the same scale in this reduced set of 24 patients demonstrate a measurement of the high impact of Carticure Plus® in improving pathologies.

The sample size has not made it possible to discriminate statistically significant differences for the markers analysed between the patients treated with Carticure Plus® and placebo. It remains to be determined which blood biomarkers might offer a better approximation to the diagnosis and prognosis of developing early onset OA after this type of surgery. It is undeniable that we need to design new studies on this line. In the same way, it could be particularly useful to associate concentrations of these biomarkers with other new magnetic resonance diagnostic tests.

Therefore, we can conclude that incorporating Carticure Plus® for three months, after the surgical intervention on the meniscal or ligament pathology will improve the clinical response quickly in the first month and this will give better values in terms of daily activities in all patients after three months.

Conflict of interests

The authors do not declare any conflict of interests.

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Systematic review of the effects of physical activity during pregnancy

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Summary

There are many queries regarding about the effects of physical activity during the gestation period. The aim of this study is to conduct a systematic review in order to find out the effectiveness of physical activity during pregnancy, as well as to determine which are the most beneficial. For this purpose, several databases have been used, such as Scopus, Scielo, Elsevier, ScienceDirect, ResearchGate, Springer Link, World Wide Science, MedlinePlus, Dialnet and Google Scholar using the keywords "physical activity" and "pregnancy". The documents selected were 79, including articles and theses in Spanish and English published between 2004 and 2020. To carry out the descriptive analysis, eight variables have been extracted: research objectives, mean age of pregnant women, data collection tools, planning of physical activities performed, gestational period in which physical activities begin, the most frequent mode of delivery, intensity of activities and results of the study. After that, they have combined with each other, in order to obtain outcomes. The outcomes indicate that the main objective of the studies is to evaluate the effect of physical activity on the health of the mother over thirty years of age and that the period in which it is most commonly put into practice is from the first and second trimesters onwards. In conclusion, physical activity has very positive effects on pregnant women, as it does not alter the health of either the mother or the child. Likewise, the most beneficial are activities programs with moderate intensity.

Key words:
Exercise. Health. Pregnancy. Systematic review.

Revisión sistemática sobre los efectos de la actividad física durante el embarazo

Resumen

Existen dudas sobre los efectos de la actividad física durante el periodo de gestación. El objetivo del presente estudio es realizar una revisión sistemática para conocer la efectividad de la actividad física durante el embarazo, así como para determinar cuáles son las más beneficiosas. Para ello, se han empleado diversas bases de datos, como son Scopus, Scielo, Elsevier, ScienceDirect, ResearchGate, Springer Link, World Wide Science, MedlinePlus, Dialnet y Google Scholar, utilizando las palabras claves "actividad física" y "embarazo". Los documentos seleccionados han sido 79, entre los cuales destacan artículos y tesis en español e inglés publicadas entre 2004 y 2020. Para llevar a cabo el análisis descriptivo, se han extraído ocho variables: objetivos de la investigación, edad media de las embarazadas, instrumentos de recogida de datos, planificación de las actividades físicas realizadas, periodo gestacional en el que comienzan las actividades físicas, parto más frecuente producido, intensidad de las actividades y resultados del estudio. Tras ello, se han combinado entre sí, con la finalidad de obtener unos resultados. Estos indican que los estudios tienen como principal objetivo evaluar el efecto de la actividad física sobre la salud de la madre en mujeres mayores de 30 años y que el periodo en el que más se pone en práctica es del primer y segundo trimestre en adelante. Se puede concluir que la actividad física tiene efectos muy positivos en las gestantes, no alterando la salud de la madre y del bebé. Del mismo modo, las más beneficiosas son la realización de actividades físicas programadas con una intensidad moderada.

Palabras clave:
Ejercicio. Embarazo. Revisión sistemática. Salud.

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Introduction

The World Health Organisation defines physical activity as "any bodily movement produced by skeletal muscles that requires energy expenditure[1]." Sport provides many health benefits, preventing the appearance of disease such as cancer, high blood pressure, diabetes or strokes[1].

Over history, it has been determined that exercise during pregnancy can lead to a simpler delivery[2]. Even so, there are some aspects yet to be resolved by science[2]. This explains why many doctors and Sports Science graduates continue researching the effects of physical activity during pregnancy[2].

During pregnancy, women try to follow advice from a range of experts, such as doctors or philosophers, in an attempt to bear the nine months as best they can[2]. This includes physical activity during pregnancy and all the points to consider on this matter: time, intensity and type[2].

Doing physical activity during pregnancy helps reduce weight gain over the 9 months, even among women with obesity[3]. In addition, it can be useful to strengthen muscles to avoid back pain, increase agility and achieve better adaptation to the woman's weight gain[3].

A doctor must determine whether some physical activity can be done during pregnancy, as this requires no pathology that might affect the life of the mother or the baby[4]. These sports include any intended to strengthen the musculoskeletal system and improve two fundamental systems: cardiovascular and respiratory[4]. Therefore, it is advisable for pregnant women to do aerobic activities which are recommended by specialists. Static bikes and treadmills are also recommended[4]. Finally, running is also possible although this is only advised for women who already ran before their pregnancy, and a doctor should monitor them continuously[4]. In addition to the above, it has been demonstrated that physical activity in water has many benefits for pregnant women, aided by their floatability. Consequently, swimming is recommended for them[5].

Only a very low percentage of women do physical activity during their pregnancy: 15.1%[6]. The reasons for this include the perception of physical activity as a risk for both the mother and the baby[6]. However, women who want to exercise for the nine months of their pregnancy enjoy better health than those who do not[5]. Consequently, pregnant women should do some physical exercise and thereby prepare for the delivery, as long as there are no contraindications for this[7].

Exercising during pregnancy might incur risks such as low birth weight for the baby[8]. This might be due to the low quantities of glucose reaching the foetus as the mother is consuming a considerable amount during exercise[8]. In addition, when doing physical activity, the blood flow between the uterus and the placenta drops, so the foetus receives less oxygen and nutrients from the mother[9]. Even so, most research determines that this does not represent a risk for the baby[9].

Physical activity has very positive effects when it comes to giving birth, as it reduces the probability of surgery. Furthermore, it helps mothers control their pain and breathing during delivery, which is very important if the birth lasts for several hours[10]. In the same way, women who are in good physical condition or who do some exercise during pregnancy feel less pain when it comes to giving birth[10]. In addition, they benefit from recovering sooner from the delivery, suffer less incontinence and their circulation becomes more efficient[10]. In the same way, physical activity produces stronger musculature, and better pelvic mobility, creating greater flexibility. This helps when opening the uterus, favouring a natural delivery[10].

The general aim of this study is to systematically review physical activity and pregnancy. Specifically, it aims to find out how effective physical activity is in pregnancy and determine which type is most beneficial.

Material and method

Design

Documents were selected for the systematic review from the following databases: Scopus, Scielo, Elsevier, ScienceDirect, ResearchGate, Springer Link, World Wide Science, MedlinePlus, Dialnet and Google Scholar. The review took place in March and April 2020.

Identification and selection of studies

Articles and dissertations were selected for this study. The latter were divided into two types: Master's and doctoral dissertation. In terms of language, documents were selected in both Spanish and English.

The keywords were *actividad física* and *embarazo*. And the terms in English are *physical activity* and *pregnancy*. Boolean operators *and/y* were used to combine them. Finally, a total of 79 documents were selected from the different databases, published between 2004 and 2020.

Inclusion and exclusion criteria

A series of inclusion and exclusion criteria were considered to perform the systematic review. The inclusion criteria were as follows:

- Articles or dissertations published between 2004 and 2020.
- Articles or dissertations written in Spanish or English.
- The articles or dissertations should contain a methodology section.
- The main topic of the documents should be physical activity and pregnancy.

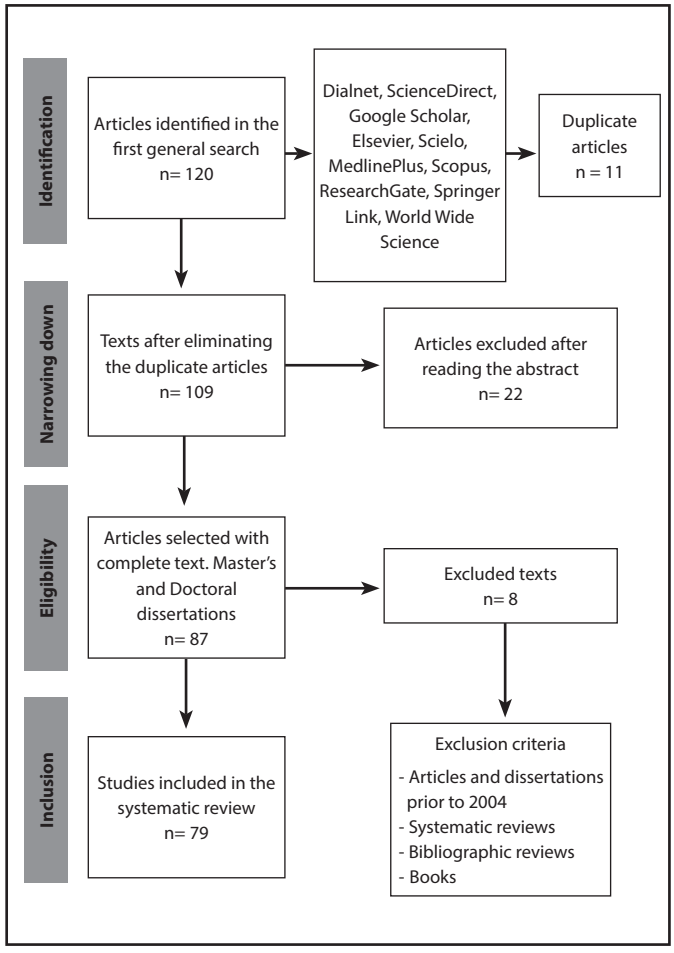
Furthermore, books, reports, systematic reviews and biographical reviews were excluded.

Figure 1 shows a flow chart with the selection process for the documents for systematic review.

Variables

The following variables have been extracted from the various documents being analysed: research objectives, average age of the pregnant women, data collection instruments, planning for the physical activity performed, gestational period when the physical activity began, most

Figure 1. Flow chart.



Source: Compiled by author.

frequent type of delivery, activity intensity and results of the study. They were all analysed using a database created in Microsoft Excel.

The variables analysed and the categorisation system used to organise each of them properly are explained below:

- Research objectives: this determines what the study is pursuing. Considering objectives that are proposed in the different research projects, the following categorisation has been determined:
  - Evaluate the effect of PA on the mother's health.
  - Evaluate the effect of PA on the health of the mother and the baby.
  - Evaluate the effect of PA on the baby's health.
- Average age of the pregnant women: given that the average age of the pregnant women was around 30 years old, the categorisation system is as follows:
  - Under 30 years old.
  - Over 30 years old.
- Data collection instruments: the following categorisation system was specified to analyse this variable:
  - Observation: when the instrument used was observation.
  - Questionnaire: when the data collection instrument was a questionnaire.
  - Interview: when the data collection instrument was an interview.
  - Medical review: when the data collection instrument was a medical review.
  - Questionnaire and medical review: when the data collection instrument was a questionnaire and a medical review.
  - Interview and questionnaire: when the data collection instruments were a questionnaire and an interview.
- Planning the physical activities: the following categorisation has been used to classify the different activities performed in the different studies:
  - Programmed: the subjects carry out a programme with varied or specific physical activity that was designed for the actual study.
  - Semi-programmed: the subjects perform varied or specific activities that have been recommended by professionals or specialists, such as walking, running or swimming, although without following a programme of physical activity imposed by the study.
  - Not programmed: the subjects perform varied or specific physical activities autonomously.
- Intensity of the physical activity: the following categorisation system was specified to analyse this variable:
  - Light: subjects carry out low intensity daily activities, such as walking to the shops, housework, walking to work, etc.
  - Moderate: subjects carry out medium intensity activities, such as aerobics, swimming, static bike, fast walking, etc.
- Gestational period when the physical activity began: the following categorisation system was specified to analyse this variable:
  - First trimester onwards: the physical activity began in the first trimester.
  - Second trimester onwards: the physical activity began in the second trimester.
  - Third trimester onwards: the physical activity began in the third trimester.
  - First trimester: the physical activity was specifically done in the first trimester.
  - Second trimester: the physical activity was specifically done in the second trimester.
- Most frequent type of delivery: considering the most frequent delivery in each of the studies, the categories for this variable were determined as follows:
  - Vaginal: the baby comes out of the maternal uterus through the vagina.
  - Undetermined: when the study does not indicate the type of delivery.

– Study results: to classify the contents of this variable, due to the high number of documents analysed, the following categorisation was considered:
  - Physical activity reduces the duration of delivery.
  - Physical activity improves the mother's health during pregnancy and/or the postpartum period.
  - Physical activity does not affect the mother and/or the baby's health during pregnancy and/or the delivery.

Objectives

The objectives proposed in relation to the variables are as follows:

– Determine the purpose of the various investigations (research objectives).
– Find out the average age when the research was carried out (average age of the pregnant women).
– Indicate the most-used instruments to perform the studies (data collection instruments).
– Determine the gestational period when physical activity is most often implemented and the most frequent planning (gestational period and planning of the physical activity).
– Determine which intensity of physical activity most favours a vaginal delivery (most frequent delivery and intensity of physical activity).
– Determine which intensity of physical activity favours the best results (intensity of the physical activity and results obtained).

Results

The results obtained after analysing the different variables presented in the previous section are shown below.

Descriptive analysis of the objectives

Regarding the 65 documents analysed, it was observed that the research projects mainly focus on evaluating the effects caused by physical activity during pregnancy on the health of the mother given that more than 75% of the studies analysed set this as their main objective.

Descriptive analysis of the average age of pregnant women

The average age of the pregnant women in over half of the 63 documents examined is over 30 years old. The results concur with the latest data from 2018 from the National Statistics Institute (INE)[11], in which the pregnant women presented an average age of 31 years old (Table 1).

Descriptive analysis of the instruments used

Regarding the 79 documents analysed, it is observed that in more than 60% of the studies, the information compilation instrument used is the questionnaire or a combination of interview and questionnaire (Table 2).

Table 1. Analysis of the average age of pregnant women.

Average age of pregnant women	
Over 30 years old	55.6%
Under 30 years old	44.4%
General total	100.0%

Source: Compiled by author.

Table 2. Analysis of data collection instruments.

Data collection instruments	
Questionnaire	31.6%
Questionnaire and medical review	3.8%
Interview	17.7%
Interview and questionnaire	29.1%
Observation	10.1%
Medical review	7.6%
General Total	100.0%

Source: Compiled by author.

Descriptive analysis of the gestational period when the physical activity took place and planning of the physical activity

Considering the 70 documents analysed, a considerable increase can be appreciated among any that focus their attention on the activities carried out in the first and second trimester onwards with more than 90%. However, studies that focus on the activities developed during just one trimester and from the third onwards are less frequent. In addition, programmed activities stand out, with more than 70% (Table 3).

Descriptive analysis of the most frequent type of delivery and the intensity of physical activity

After analysing these variables, depending on the 21 documents analysed, it might be concluded that there is a major link between carrying out moderate intensity activities and a subsequent vaginal delivery. This determines that women who perform activities at this intensity demonstrate more physical capacity when it comes to giving birth, thereby leading to a much more natural, simpler delivery.

Descriptive analysis of the intensity of the physical activity and the study results

It has been demonstrated by almost 90% of the 63 studies analysed that it is moderate physical activity that gets the best results, benefiting and not affecting the health of the mother and/or baby during the pregnancy and/or the postpartum period. Therefore, it is determined that light physical activity does not obtain such positive results as for moderate activity (Table 4).

Table 3. Analysis of the gestational period and planning of the physical activity.

Gestational period when PA begins	Programmed	Semi-programmed	Not programmed	General total
First trimester	0.0%	0.0%	1.4%	1.4%
First trimester onwards	31.4%	1.4%	8.6%	41.4%
Second trimester	2.9%	0.0%	0.0%	2.9%
Second trimester onwards	35.7%	2.9%	12.9%	51.4%
Third trimester onwards	1.4%	1.4%	0.0%	2.9%
General total	71.4%	5.7%	22.9%	100.0%

Source: Compiled by author.

Table 4. Analysis of the physical activity intensity and the study results.

Study results	Light	Moderate	General total
Physical activity drops during the delivery	0.0%	3.2%	3.2%
Physical activity improves the mother's health during pregnancy and/or the postpartum period	6.3%	46.0%	52.4%
Physical activity does not affect the mother and/or baby's health during pregnancy and/or delivery	1.6%	42.9%	44.4%
General total	7.9%	92.1%	100.0%

Fuente: Elaboración propia.

Discussion

The two specific objectives proposed at the start of this study were to find out about how effective physical activity is in pregnancy and determine which type is most beneficial.

The average age of the pregnant women in the various documents analysed is over 30 years old, matching INE[11] data over the last decade.

On the other hand, the data suggest that performing moderate intensity physical exercise favours a natural delivery and reduces the probability of surgical intervention. The results of this systematic review match the study by Miranda and Navio[12], whose conclusions determine that physical activity reduces the chances of a C-section.

The physical activity in the various types of planning is not focussed on just one physical quality, many of the investigations under review indicate that they combine stamina, strength and flexibility exercises, given that they all generate different types of health benefits among pregnant women, both during pregnancy and during delivery.

The results attained in this research indicate that the greatest number of physical activities are implemented from the first and second trimester onwards. They follow the line of research carried out by Moreno[13], where the conclusions determine that most of the published studies focus on pregnant women in the second trimester onwards.

In the same way, in relation to what is obtained in this study, where more than half the research projects carry out programmed physical activity, Barakat *et al.*[3] advocate for a supervised and planned physical exercise programme during pregnancy.

On the other hand, conclusions drawn by Sánchez-García *et al.*[14], demonstrate that moderate physical activity obtains very positive benefits among pregnant women, coinciding with the results of this systematic review, where moderate intensity activities (aerobics, swimming, static bike, fast walking, etc.) stand out as opposed to light exercise, causing more positive effects. Furthermore, Perales *et al.*[15] determine that aerobic physical activity during pregnancy improves some parameters of the cardiovascular system. In turn, Vázquez[10] determines that a physical activity programme in water produces benefits in hemodynamic parameters and improves quality of life for pregnant women (body pain, general health and mental health).

Analysis of the documents included in this study determines that physical activity is beneficial for the mother's health during pregnancy and/or the postpartum period. This data does not differ from the conclusions obtained by Aguilar *et al.*[16] and Puente *et al.*[17], who show that women who set out to do physical exercise during the 9 months of pregnancy enjoy better health than women who do not.

Conclusions

Working from the study, it is possible to determine a series of conclusions according to the objectives proposed throughout it.

Firstly, it can be understood that most of the studies analysed have the main purpose of evaluating the effect of physical activity on the mother's health in women aged over 30 years old, where the questionnaire and the interview are the most frequently used information collection instruments.

It can be stated that, after having analysed the different documents, the gestational period where physical activity is most frequently implemented is the first and second trimester onwards, where programmed activities are particularly relevant. Furthermore, it is determined that there is a major link between carrying out moderate intensity activities and subsequently having a vaginal delivery.

Before drawing to a close, it should be highlighted that this systematic review contributes to the field of research, as it questions the current belief on the effects of performing physical activity during pregnancy.

Consequently, it would be interesting if future lines of research might focus on checking the type of planning for physical activity (programmed, semi-programmed or not programmed) that might obtain the most health benefits for pregnant women.

Regarding the limitations of this research, three can be mentioned: the limited size of the studies that meet the set inclusion criteria, the difficulty to extract common variables in the different documents, and the lack of specification on the type of physical activity performed.

Finally, based on the two specific objectives, it can be concluded that physical activity has very positive effects in pregnant women, not affecting the health of the mother and the baby. In the same way, the most beneficial is moderate intensity, programmed physical activity.

Conflict of interests

The authors do not declare any conflict of interests.

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Evaluation methods and objectives for neuromuscular and hemodynamic responses subsequent to different rest intervals in resistance training: a systematic review

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Summary

Introduction: The training routine planned, and performed correctly results in exercises that, systematically organized, influence the levels of strength, and muscle hypertrophy. However, the magnitudes of these gains vary considerably. To optimize these gains, it is important to underst, and the interaction between training variables such as external load, volume, number of exercises, number of repetitions, duration of repetitions, the order of exercises, number of series, recovery interval between series, and the exercises, as well as the time under tension. The influence of the recovery interval on the response following exercise on neuromuscular components is very important. However, different objectives, and instruments are used to evaluate these responses.
Objective: The purpose of this study is to conduct a systematic review of the assessment methods, and objectives for responses after different recovery intervals in strength training. METHODS: The present study is characterized by a systematic review study. Articles found in the following databases were considered for the systematic review: Scopus, PubMed / MEDLINE, Web of Science, Cochrane Library. The following descriptors, and their respective synonyms according to the terms MeSH were used in the databases, both singular, and plural: "Resistance Training", "Rest Interval", and "Bech Press". As filters were used: a) species (humans), and type of study (original).
Results: Seven studies were analyzed that met the established criteria.
Conclusion: The studies presented have verified the influence of different recovery intervals on muscle, and hemodynamic responses. Evaluating image measurements such as ultrasound, and resonance, blood measurements such as GH, Testosterone, IGF-1, and Lactate, number of repetitions for performance, and fatigue, as well as heart rate, and blood pressure.

Key words:
Resistance training. Muscle stress. Rest. Recovery.

Métodos de evaluación y objetivos para las respuestas neuromusculares y hemodinámicas posteriores a diferentes intervalos de descanso en el entrenamiento de resistencia: una revisión sistemática

Resumen

Introducción: La rutina de entrenamiento planificada y realizada correctamente da como resultado ejercicios que, organizados sistemáticamente, influyen en los niveles de fuerza e hipertrofia muscular. Sin embargo, las magnitudes de estas ganancias varían considerablemente. Para optimizar estas ganancias, es importante comprender la interacción entre las variables de entrenamiento como la carga externa, el volumen, el número de ejercicios, el número de repeticiones, la duración de las repeticiones, el orden de los ejercicios, el número de series, el intervalo de recuperación entre series y los ejercicios, así como el tiempo bajo tensión. La influencia del intervalo de recuperación en la respuesta después del ejercicio en los componentes neuromusculares es muy importante. Sin embargo, se utilizan diferentes objetivos e instrumentos para evaluar estas respuestas.
Objetivo: El propósito de este estudio es realizar una revisión sistemática de los métodos y objetivos de evaluación para las respuestas posteriores a los diferentes intervalos de recuperación en el entrenamiento de fuerza. MÉTODOS: El presente estudio se caracteriza por un estudio de revisión sistemática. Los artículos encontrados en las siguientes bases de datos se consideraron para la revisión sistemática: Scopus, PubMed / MEDLINE, Web of Science, Cochrane Library. Los siguientes descriptores y sus respectivos sinónimos según los términos MeSH se utilizaron en las bases de datos, tanto en singular como en plural: "Entrenamiento de resistencia", "Intervalo de descanso" y "Bench Press". Como filtros se utilizaron: a) especies (humanos) y tipo de estudio (original).
Resultados: Se analizaron siete estudios que cumplieron con los criterios establecidos.
Conclusión: Los estudios presentados han verificado la influencia de diferentes intervalos de recuperación en las respuestas musculares y hemodinámicas. Evaluación de mediciones de imagen como ultrasonido y resonancia, mediciones de sangre como GH, testosterona, IGF-1 y lactato, número de repeticiones para el rendimiento y la fatiga, así como la frecuencia cardíaca y la presión arterial.

Palabras clave:
Entrenamiento de resistencia. Estrés muscular. Descanso. Recuperación.

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Introduction

Resistance training has usually applied to overload the musculoskeletal system[1]. This type of training is established as an effective method for the development of musculoskeletal fitness, and is recommended to improve health, and performance[2]. The planned, and properly executed training routine results in exercises that, systematically organized, influence muscle strength, and hypertrophy levels[3]. However, the magnitudes of these gains vary considerably[4].

To improve these gains, it is important to underst, and the interaction between training variables such as external load, volume, number of exercises, number of repetitions, repetition duration, exercise order, number of series, the interval of recovery between series, and exercises, as well as tense time[5]. Thus, the understanding, anding of definitions, principles, and methods for the prescription of a strength training routine is necessary for a safe, and efficient prescription[6].

An important variable explored during training is the rest interval time (RI) between the series. The RI can be defined as the recovery period between exercise series during a training session. Intervals can be set in short (up to 1 minute), medium (1 to 3 minutes), and long (more than 3 minutes)[7]. Through it, one can manipulate the stress exerted in the musculature by the adequacy or maintenance of the intensity, and volume of training.

According to the data included in a recent systematic review[8], when the goal of training is strength gains, long RI should be prioritized thus allowing the maintenance of the number of repetitions. However, to optimize muscle hypertrophy gains, short RI is suggested to promote increased metabolic stress, and possible anabolism[9].

In addition to the muscle system, the prescription of strength training exercises also influences the responses of other systems of the human body[10]. Different RI between series promotes different influences on cardiovascular, endocrine, and neural systems[11]. The variation in heart rate, blood pressure, the varying curves of specific hormone, and enzyme levels, and the behavior of the spread of action potential are some examples.

Some instruments, and methods are used to evaluate these parameters. Blood collections, imaging tests such as thermography, and ultrasound, electromyography, dual Energy radiological absorptiometry (DXA) are examples of specific evaluations on biological response. Moreover, the maintenance of the number of repetitions performed also represents an important response to the exercises[12].

The influence of these RI on the response following the exercise of neuromuscular, hemodynamic, and biochemical components is very important. However, as exposed, different objectives, and instrumentations are used to evaluate these responses. Thus, the present study aims to conduct a literature review aimed at identifying, and analyzing the objectives, and evaluation methods for the responses after different recovery intervals in resistance training.

Material and method

This study is in line with the American College of Sports Medicine policies regarding animal, and human experimentation.

The present study is characterized by a systematic review study, being carried out according to the instructions of the Preferred Reporting Items for Systematic Reviews, and Meta-Analysis (PRISMA) statement[13]. Thus, this systematic review adopted the following inclusion criteria: a) studies that investigated the influence of rest intervals in muscle performance; b) studies that presented detailed methodology, sufficient for full understanding of the experimental design; c) Studies that used some instrumentation for muscle performance analysis; (d) articles using the bench press exercise; f) Articles published in English. Articles dated before 2014 were deleted.

Articles found in the following databases were considered for the systematic review: Scopus, PubMed/MEDLINE, Web of Science, Cochrane Library. The following descriptors, and their respective synonyms under the terms MeSH: "Resistance Training", "Rest Interval", and "Bech Press) were used in the databases." As filters were used: a) species (humans), and type of study (original).

These terms have been adjusted for search in each database. The complete search strategy was carried out in four phases. In phase 1 (Identification), publications potentially eligible for review were verified. This phase was from 03 to 7 of September in 2019. In the 2nd phase (Screening) two experient PhD researchers with expertise in systematic review performed the reading of the titles to verify the adequacy to the purpose of this review, and the duplicity of the articles derived from the databases. When a decision could not be made from the readings of the titles, the abstract was used, and, remaining doubt, the reading of the article in full was made. In the 3rd phase of the selection of articles (eligibility) the inclusion, and exclusion criteria established according to the objective proposed in the systematic review, and the verification of the risk of bias were applied to attest to the methodological quality of each study also by experienced researchers in the area of the study. After this phase, the publications that filled out these assumptions moved to the 4th phase (inclusion), thus being included in this review. If necessary, in the items where there was no consensus, the third researcher did the final analysis. All data were entered, and quantified in a data sheet.

Results

Of the 79 studies found through the search strategy, 72 were excluded, and 7 studies met the inclusion criteria proposed, and were included in the present study. The following flowchart presents the process of selecting articles (Figure 1).

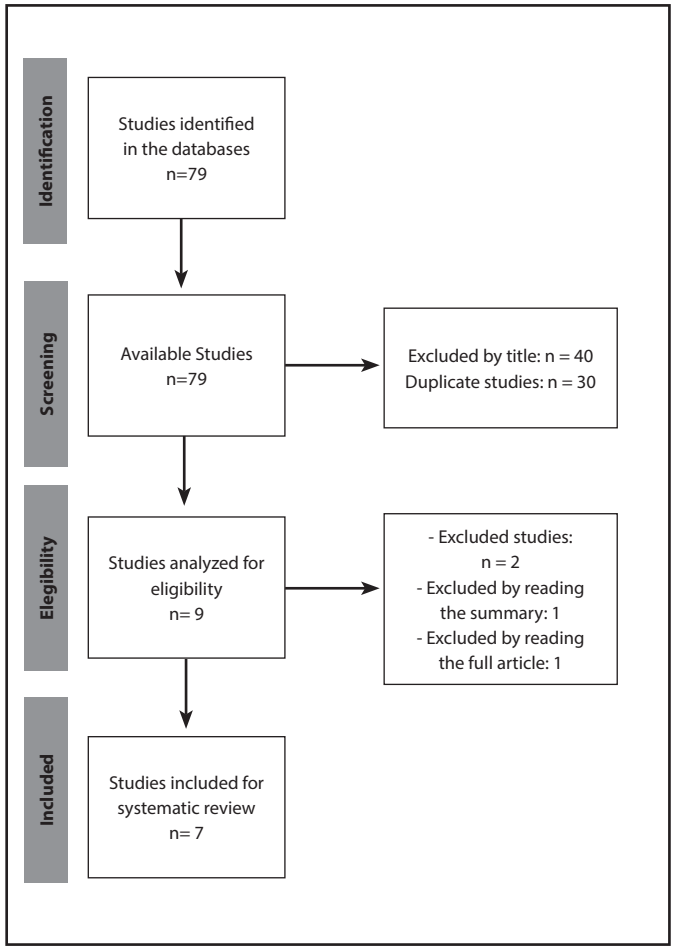
The Table 1 describes the sample participants, and the protocols used in each reviewed study.

The Table 2 presents the objective results, measured variables, and methods used to contemplate the objectives.

Discussion

After the selection process of articles, seven studies were included, and analyzed in full by this systematic review. These showed comparisons between different times of recovery intervals, and used the straight supine exercise. Of these, four studies included only men, two included men, and women, and one of them did not present this

Figure 1. Flowchart of selection of articles.



information. Thus, no studies were observed, and there were no women exclusively in their samples. Considering that this population has specific characteristics, such as hormonal ones, for example[21], the information on the influence of the recovery interval on bodybuilding exercises on biological responses is an important gap in the literature.

In addition, only one investigation observed the influence of different recovery intervals on strength in the elderly. In his study, Villanueva *et al.*[14] verified the effect of 1, and 4 minutes of recovery intervals on body composition, and muscle, and functional performance in 22 elderly men. A 12-week intervention was performed with a program that contained seven strength training exercises, including exercises for upper, and lower limbs. X-ray absorptiometry (DXA) was used to assess body composition. The Star excursion balance, and Margarida power tests checked the performance of the functional control variables of the movement in addition to the 1RM Test to assess muscle strength. The results for this population differ from those performed in young people, when they found that 8 weeks of high-intensity strength TR periodized with short IR induces significantly greater improvements in body composition, muscle performance, and functional performance, compared to the same prescription of RT with higher IR.

From the above, it is understood that for the elderly, a short IR may be sufficient for muscle strength gains. However, for trained young people, most studies have concluded that individuals need a longer-term IR to maximize gains in muscle strength[9]. However, these results are still controversial, as considerable gains in muscle strength can be achieved with a short-term interval. A great example is the study by Bottaro *et al.*[22] that verified similar muscle strength gains when comparing short intervals with longer intervals.

To make up the protocols of the studies evaluated in this review, the researchers chose to use percentages of the maximum load, thus making the execution of the exercises at submaximal intensities. Of the

Table 1. Authors, sample, and protocols used.

Author	Sample	Protocol
Villanueva *et al.*[14]	22 men	2/4 sets/exercise, 8-15 repetitions of 7 exercises for 3 days/week for 12 weeks 2 RI protocols: 1 and 4 minutes
Fink *et al.*[15]	14 men	4 sets of bench press followed by 4 sets of 40% 1RM squats with 1 sec in concentric phases, and 2 sec in eccentric phases for 8 weeks 2 RI protocols: 30s (n=7), and 150s (n=7)
Davó *et al.*[16]	31 students (18 men, and 13 women)	5 sets of 8 repetitions on bench press straight with 40% of 1RM 3 RI protocols: 1, 2, and 3 minutes
De Salles *et al.*[17]	27 people divided into 2 groups: G1 - exercises for lower limbs, and G2 - exercises for upper limbs.	3 sets with 75% of 1RM 2 RI protocols: 2 min, and self-suggested
Schoenfeld *et al.*[18]	21 men	3 sets of 8 to 12 RM of 7 different exercises per session, 3 times/week for 8 weeks 2 RI protocols: 1 and 3 minutes.
Figueiredo *et al.*[19]	11 prehypertensive men	3 sets of 8 to 10 repetitions with 70% of 1RM 2 RI protocols: 1 and 2 minutes
Monteiro *et al.*[20]	28 participants: 12 women, and 16 men	4 sets with 100% 10RM 4 RI protocols: 1) Bench press followed by Leg Press with 3 minutes of RI; 2) Leg Press followed by a bench press with 3 minutes of RI; 3) Straight bench press followed by leg press without RI; 4) Leg Press followed by Straight Bench Press without RI

Table 2. Objectives, variables, and methods used.

Author	Objective	Measured variables	Methods
Villanueva *et al*.[14]	Check the effects of RI on body composition, and muscle performance	1. Body composition 2. Functional Performance 3. Muscle Performance	1. X-ray absorptiometry (DXA) 2. Star excursion balance test, Margaria power test, 400-m walk
Fink *et al*.[15]	Check different RI in acute, and chronic hormonal responses in hypertrophy, and strength gains.	1. GH, T, IGF-1 were verified before (B), immediately after (P0), 15 min after (P15), 30 min after (P30), and 60 min after (P60) TF sessions. 2. Total volume of training performed in the 4 sets 3. Muscle cross-sectional area before the start of the TF program, and in the last week after the last training session (week 9) 4. Muscle strength tests were performed during the week, before, and after the training period.	1. Precubital Blood Samples 2. Total number of repetitions 3. Magnetic resonance 4. 1RM Test
Davó *et al.*[16]	To verify the influence of different RI between the series on the output power performance, and the physiological, and perceptual variables.	1. Average power, and peak power 2. Lactate concentration was co-llected 1 minute before, and after each protocol. 3. Perceived effort after training session 4. Late muscle pain was reported 24, and 48 hours after the training session.	1. T-Force System 2. Ear lobe blood samples 3. Borg Scale (CR-10) 4. The subjects were asked: "How painful are the muscles?". Subjective feeling on a scale of 0 to 10 (0 = no pain; 10 = much pain)
De Salles *et al.*[17]	Check the effects of fixed RI compared to self-suggested	Exercise Performance	Number of repetitions
Schoenfeld *et al.*[18]	Check the effects of different RI	1. Muscle strength 2. Muscle endurance 3. Muscle thickness	1. 1RM test 2. 50% from 1RM to failure 3. Ultrasonography
Figueiredo *et al.*[19]	To compare the effects of different RI between sets, and exercises on hemodynamic variables.	1. Systolic Blood Pressure 2. Heart Rate	1. Automatic oscillometric device 2. Heart Rate Monitor
Monteiro *et al*.[20]	Check the influence of exercise order, and RI for an alternating TF sequence of bench press (BP), and leg press (LP) exercises.	Neuromuscular Fatigue Resistance - Fatigue Index (FI)	Number of repetitions completed using the equation proposed by Dipla *et al*. (2009)

seven studies analyzed, two used in their protocols the maximum value of overload verified in the preliminary tests also in their experimental protocols. Just like Villanueva *et al.*[14], Fink *et al.*[15] also used the 1RM test to assess strength gains. However, Fink *et al.*[15] also used blood measurements collected in the antecubital fossa to analyze GH, Testosterone, and IGF-1 levels. Magnetic resonance imaging to evaluate the cross-section area completed the measurements applied by Fink *et al*.[15] to compare the effects of 30, and 150s of recovery interval between 4 sets to 40% of 1RM in 14 men. Load intensity is an important variable for strength training because it influences muscle responses[10]. However, in conclusion, the results of Fink *et al*.[15] suggest that acute hormonal responses, as well as chronic changes in hypertrophy, and muscle strength in low load training to failure, are independent of the duration of the rest interval.

Fink *et al.*[15], blood measurements also served as a parameter for Davó *et al*.[16] evaluate the influence of different recovery intervals in the performance of 5 sets of the supine exercise straight to 40% of 1RM in 31 participants. However, unlike Fink *et al*.[15], the authors verified lactate levels, coming from blood collections in the earlobe. The T-Force dynamic strength measurement system was used to evaluate muscle strength. The perception of subjective exertion, and late muscle pain were also verified, respectively, through the Borg scale (CR-10), and the specific question "How sore are your muscles". The results suggest that an IR of 2 or 3 minutes is required for mechanical, and physiological recovery, however, there may be little difference between the rest intervals of 2, and 3 minutes.

Schoenfeld *et al.*[18] then used 1, and 3 minutes of recovery interval for 3 sets of 8-12RM to verify muscle parameters in 21 men. However, the authors differed when using ultrasonography as an instrument. Muscle resistance was also verified through the number of repetitions performed with 50% of 1RM up to concentric failure. Schoenfeld *et al*.[18] applied the 1RM test to verify muscle strength approaching this time to the study by Fink *et al.*[15], and that conducted by Villanueva *et al*.[14]. Thus, the 1 RM test is widely used in the studies, although in practice it is ineffective because it does not represent the reality of the prescription of ST exercises[23].

An alternative to check the accumulated volume of the training is the count of the number of repetitions. This method was used by De Salles *et al.*[17] who observed the influence of the recovery interval in 27 men. The study by De Salles *et al.*[17] unlike demias, used a different strategy for the recovery interval. It compared the set interval of 2 minutes with the self suggested by the participants. The results showed no significant differences in the number of repetitions between 2 min, and with the self-suggested interval, and that the self-suggested IR group spent on average less time recovering than the group with IR fixed in 2 min. The authors suggest that for trained individuals, the self-suggested method may be an effective option. In addition, the suggested auto IR can reduce the total duration of the training session, which can be an interesting strategy.

Monteiro *et al*.[20] also used the number of repetitions to calculate the muscle fatigue index in 28 participants divided into 4 recovery protocols. However, this was the only study verified in this review that aimed to evaluate the influence of different recovery intervals that included both sexes. Twelve women, and 16 men, both trained, performed four sets with 100% load of 10RM until the concentric failure in order to complete the maximum number of repetitions with different recovery intervals between the straight supine, and squat exercises.

Figueiredo *et al*.[19] were the only researchers found in the present review, who verified the influence of different recovery intervals on hemodynamic variables. 1, and 2 minutes of interval were applied to 3 sets of 8-10 repetitions with 70% of 1RM. Through an automatic oscillometric device, and a monitor of its own, and specific measurements of heart rate, and blood pressure were obtained. The authors found that 1 or 2 minutes of rest between sets, and exercises can reduce blood pressure after training sessions. However, resting 1 minute between sets, and exercises were associated with increased cardiac stress, and, therefore, this may require the prescription of longer rest intervals between sets, and exercises when working with individuals who have been diagnosed with cardiovascular dysfunction.

Conclusion

The studies presented verified the effect of different rest intervals on muscle, and hemodynamic responses. Imaging measurements such as ultrasound, and resonance, blood measurements such as GH, Testosterone, IGF-1, and Lactate, repetition numbers for performance, and fatigue, as well as heart rate, and blood pressure were observed.

However, according to this systematic review, articles in the literature need to analyze the association of these measures, demonstrating how these variables behave together. Moreover, neuromuscular behavior is a variable that includes muscle, and neural parameters, reflecting both muscle activation, and the fatigue process, and electromyography is an appropriate instrumentation for this purpose. In addition, time under tension (TUT) is an important variable for the evaluation of the volume, and intensity of the training, which is not verified in any study of the present systematic review.

Given the above, studies that associate muscle, blood, and hemodynamic measurements, as well as those using electromyography as instrumentation, and TUT as a variable, are suggested.

Conflict of interest

The authors do not declare a conflict of interest.

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Does isolated and combined acute supplementation of caffeine and carbohydrate feeding strategies modify 10-km running performance and pacing strategy? A randomized, crossover, double-blind, and placebo-controlled study

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Summary

Background: Long distance practice running are growing and nutritional ergogenic are commonly used as a potential aid in final training and competition performance. Caffeine (CAF) and carbohydrates (CHO) are among the most commonly used supplements due to their expected ergogenic properties that can optimize energetic systems. The objective of this study was to examine potential changes in 10-km running performance with acute isolated and combined CAF and CHO supplementation.
Material and method: Fifteen recreational endurance-trained runners performed four 10-km running performance on an official athletic track (400 m) under four supplementation conditions: placebo and placebo (PLA+PLA), placebo and caffeine (PLA+CAF), placebo and carbohydrates (PLA+CHO), caffeine and carbohydrates (CAF+CHO). CAF and CHO supplementation consisted of capsules of 6 mg·kg^{-1} and 8% CHO solution (1 g·kg^{-1}) respectively, ingested 60 and 30 minutes before the performance tests. Placebo was obtained through empty capsules for CAF and juice for CHO without sugar (Clight®). During each trial running speed to calculate 10-km mean velocity (MV) and maximum heart rate (HR_{max}) were analyzed.
Results: There was a difference in the pacing strategy adopted by the runners with higher MV during the initial phase for PLA+CAF and CAF+CHO groups and in the final phase for PLA+ CHO. However, there was no statistically significant difference in 10-km running performance between the conditions, as well as for HR_{max}.
Conclusions: The use of acute, isolated and combined CAF+CHO supplementation had influence in the pacing strategy, but no in 10- km final performance, of recreational runners.

Key words:
Ergogenic aid. Endurance. Runners. Physical endurance.

La suplementación aguda, aislada y combinada de cafeína y carbohidratos como estrategias de alimentación cambia el rendimiento y un ritmo de carrera de 10-km? Un estudio aleatorizado, cruzado, doble ciego, controlado con placebo

Resumen

Introducción: Las carreras de larga distancia están creciendo y los ergógenos nutricionales se usan comúnmente como una ayuda potencial en el entrenamiento final y el rendimiento en competición. La cafeína (CAF) y los carbohidratos (CHO) se encuentran entre los suplementos más utilizados debido a sus propiedades ergogénicas que pueden optimizar los sistemas energéticos. El objetivo de este estudio fue examinar posibles cambios en el rendimiento de carrera de 10-km con suplementación aislada aguda y combinada de CAF y CHO.
Material y método: Quince corredores recreativos realizaron cuatro carreras de 10-km en una pista deportiva oficial (400 m) bajo cuatro condiciones de suplementación: placebo y placebo (PLA + PLA), placebo y cafeína (PLA + CAF), placebo y carbohidratos (PLA + CHO), cafeína y carbohidratos (CAF + CHO). La suplementación con CAF y CHO consistió en cápsulas de 6 mg·kg^{-1} y solución de CHO al 8% (1 g·kg^{-1}) respectivamente, ingeridas 60 y 30 minutos antes de las carreras. El placebo se obtuvo usando cápsulas de CAF vacías y jugo sin azúcar para CHO (Clight®). Durante cada carrera, se analizó la velocidad de carrera para calcular la velocidad promedio de 10-km (VP) y la frecuencia cardíaca máxima ($FC_{máx}$).
Resultados: Hubo una diferencia en la estrategia de carrera adoptada por los corredores con la VP más alta durante la fase inicial para los grupos PLA + CAF y CAF + CHO y en la fase final para PLA + CHO. No hubo diferencias estadísticamente significativas en el rendimiento de carrera de 10-km entre las condiciones, así como en la $FC_{máx}$.
Conclusiones: El uso de suplementos agudos, aislados y combinados de CAF + CHO influyó en la estrategia de carrera, pero no en el rendimiento final de 10-km en corredores recreativos

Palabras clave:
Ayuda ergogénica. Resistencia. Corredores. Desempeño atlético.

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Introduction

Scientific research's designed to assess physiological and performance parameters responses with the aim of improve professional and recreational running performance are growing due to the increase in long distance running practices[1,2]. In this context, nutritional ergogenic are commonly used as potential aid in final training and competition performance. Among the possible nutritional supplements that are commonly used, the isolated and combined caffeine (CAF) and carbohydrates (CHO) feeding strategies are the most ergogenic resources used in endurance exercise[2-4]. Previous studies have indicated that CHO ingestion has a positive effect on endurance performance[5,6]. This effect have been attributed to the maintenance of plasma glucose concentrations and, high rates of CHO oxidation late in exercise when muscle and, liver glycogen level are low[5].

Additionally, CAF has been widely used as an ergogenic aid to increase physical performance[7,8], and is the most frequently aid used by athletes for it influence in the central nervous system (CNS)[9], optimize skeletal muscle function and reduce the perception of pain[10]. Cox *et al.*[7] demonstrated an increased endurance performance (~ 3.1% in time trial) in twelve highly trained cyclists after the ingestion of 6 mg·kg^{-1} of CAF, independent of the time it was ingested (i.e., pre-exercise, each 20 minutes during exercise and, between 100 and 120 minutes during exercise), which the authors hypothesized to be related to an increase in plasma free fat acids (FFA) concentration and to an increase in fat oxidation, both from blood-borne and intramuscular stores during the exercise. However, few studies have investigated the effects of CAF ingestion prior to exercise performance in runners, which still is restrict to shorter running distances[11,12].

Previous studies have also investigated the potential effect of the combination of these two supplements, which has demonstrated greater improvements in endurance performance when they are co-ingested than either independently[13], possibly due to CAF increasing the rate at which CHO can be absorbed[14]. The absorption of glucose in the intestine regulates the amount that it is delivered into circulation, becoming saturated at higher glucose ingestion rates, which may further prevent absorption limiting CHO availability to circulation[14]. CAF consumption could then significantly increase intestinal glucose absorption increasing CHO availability and increase exogenous CHO oxidation during exercise[14]. However, some studies that have evaluated the potential effect of the ingestion of CAF combined with CHO on endurance performance than that of CHO alone have been equivocal[7].

Nonetheless it is not well established whether their combination can produce different results from isolated use during physical exercise due to contradictory results reported by studies using different doses, types and time management in addition to exercise protocols with different energy requirements[3,15]. Moreover, few studies have found isolated and combined effect of CAF and CHO in running[16], however the researchers investigated the independent and synergistic ability of CHO and CAF mouth rinsing to improve intermittent running performance. However, it is currently unknown whether the acute isolated and combined supplementation of caffeine and carbohydrate feeding strategies influences endurance performance during running.

Therefore, the aim of this study was to verify potential changes in 10-km running performance with acute isolated and combined CAF and CHO supplementation, and in addition, to verify the effects of both supplementations on the pacing strategy and other associated physiological variables. Our hypothesis is that the combined and isolated use of these two supplements modifies 10-km running performance as well as the pacing strategy, but with larger changes observed when these supplementations are combined.

Material and method

The sample size was calculated with the software G*Power version 3.1.9.2 (Düsseldorf, Germany), considering an effect size of 0.25, power of 80% and alpha of 0.05 for the primary outcome performance. The *priori* power analysis revealed a minimal sample of 15 participants. Fifteen male, recreational, endurance-trained runners (age 25.2 ± 2.8 years old, height 180.0 ± 6.0 cm, body mass 79.9 ± 7.7 kg, body mass index (BMI) 24.6 ± 1.9 kg·m^{-2}, body fat 14.2 ± 2.9 % and basal metabolic rate (BMR) 2185.7 ± 232.0 kcal·day^{-1}) from regional and local standard level with a minimum of 2 years of training experience and a training volume of at least 20 km·wk^{-1} (training experience 4.1 ± 3.5 years, frequency 2.7 ± 1.4 days·wk^{-1} and distance between 60 and 70 km·wk^{-1}) volunteered to take part in this study. The 10-km running times of the participants were between 35 and 60 min, with a pace between 10 and 17 km h^{-1} (≈ 44 and 75% of the World record). Prior to testing, all participants provided a proper written informed consent and The University Ethics Committee approved the experimental protocol (#41915/2012).

Experimental overview

In a randomized, crossover, double-blinded and placebo-controlled design, each participant performed four 10-km running performance under four supplementation conditions in alternate order: placebo and placebo (PLA+PLA), placebo and caffeine (PLA+CAF), placebo and carbohydrate (PLA+CHO), caffeine and carbohydrate (CAF+CHO). The interval between each performance was at least 72 to 96 h; participants were instructed to avoid eating 3 h before the tests, to abstain from CAF and alcohol, and to refrain from strenuous exercise also for 24 h before. All tests were performed on a 400 m official outdoor track at the same time of the day to minimize the influence of circadian variance. Participants received a dietary control that was made during all protocol for CAF and blood glucose levels control.

10-km performance

Participants undertook four 10-km running performance on the track field (400 m) outdoor without the presence of opponents or another competitor on the track being all preceded by a self-determined warm-up of 10 min. To determine 10-km running performance, participants were asked to complete the distance as quickly as possible on the track field. Participants freely choose their pacing strategy during the performance being then blinded for pacing through the test and the time was hand-timed every 400 m to the nearest second. The overall mean velocity (MV) for each trial was calculated by dividing the total

distance covered by the trial duration. Additionally, partial MV were calculated in three phases: (1) start (first 400 m), (2) middle (400-9.600 m) and (3) end (last 400 m), as previously reported[1,17]. Mineral water was provided *ad libitum* in cups throughout performances, so that runners could hydrate themselves as they were used to do in long-distance races. Heart rate was recorded each trial (Polar® RS800sd, Kempele, Finland) to calculate submaximal heart hate (HR_{submax}) and maximal heart hate (HR_{max}) was defined as the highest HR value recorded during the test.

Supplementation protocol

The CAF capsules doses were administrated for each participant in the amount of 6 mg·kg^{-1}, 60 minutes before the test[18]. The 8% CHO solution was offered in maltodextrin powder form with 1 g·kg^{-1}, 30 minutes before the test. The PLA effect was obtained through empty capsules with the same characteristics of form, weight and color as CAF. The PLA for maltodextrin was juice by Clight® without sugar (0 g carbohydrates) and with the same flavor[6].

Statistical analyses

The data were analyzed using the Statistical Package for the Social Sciences 13.0 software (SPSS® Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to verify the data distribution normality and the data are presented as mean ± standard deviation (SD). The variables were compared using a two-way analysis of variance (Anova) with repeated measures, with condition (PLA+PLA, PLA+CAF, PLA+CHO and CAF+CHO) and distance (0 – 0.4 km, 0.4 – 9.6 km and 9.6 – 10-km) for MV and HR, as factors followed by the Bonferroni *post hoc* test. The sphericity assumption was verified through the Mauchly's test and, where violations occurred, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. Statistical significance was set at $P<0.05$. Comparisons were confirmed through graphical error to avoid type I error. In addition, a Bayesian Anova was used to determine changes in MV and HR as dependent variables, condition and distance as fixed factors., using the software JASP® (University of Amsterdam, Department of Psychology & Psychological Methods unit), considering BF10 as Bayes Factor and Bayes Factor inclusion (BF_{incl}) to analyze the effects for it model.

Results

The variables time 10-km, MV 10-km and HRmax obtained during 10-km running performance in PLA +PLA, PLA+CAF, PLA+CHO and CAF+CHO supplement conditions are presented in Table 1. These variables did not differ between supplement conditions.

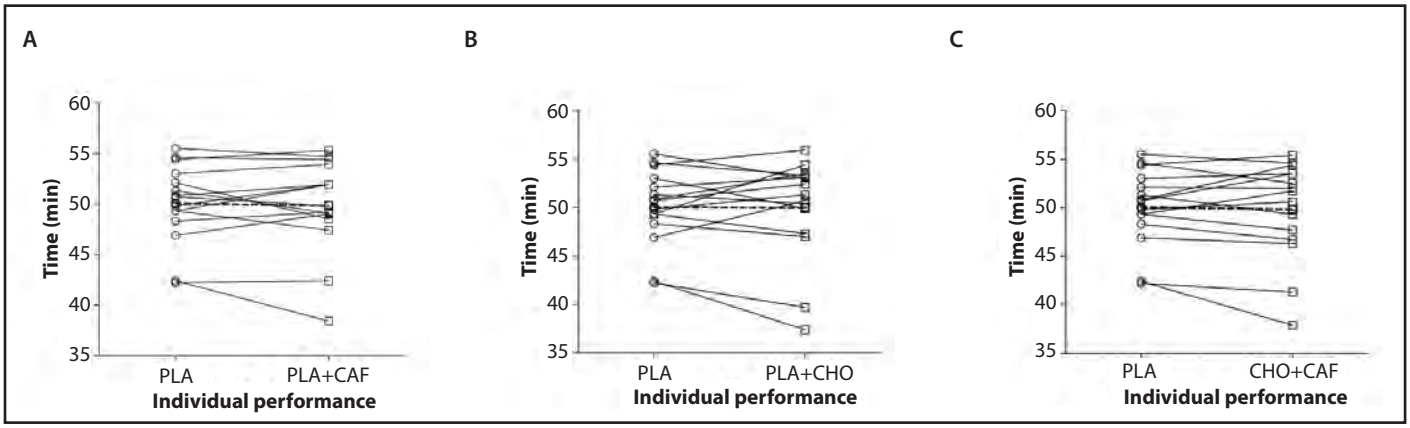
The individual results of the 10-km running performance in each of the conditions are presented in Figure 1. Although there was no statistical difference in 10-km performance between conditions ($P = 0.981$), individual analysis shown that of the 15 participants who completed the experimental protocol, 7 presented a shorter time in PLA+CAF condition (Figure 1 A); 8 in the PLA+CHO condition (Figure 1 B) and 9 in the CHO+CAF condition than in the PLA condition (Figure 1 C).

Table 1. Comparison of 10 km final time, MV and HR_{max} obtained in 10-km running performance between PLA, PLA+CAF, PLA+CHO and CAF+ CHO (n = 15).

Variables	PLA	PLA+CAF	PLA+CHO	CAF+CHO	*F*	*P*
Time 10 km (min)	50.0 ± 3.9	50.0 ± 4.7	50.0 ± 5.2	49.9 ± 5.0	0.05	0.981
MV 10 km (km·h^{-1})	12.1 ± 1.0	12.1 ± 1.3	12.2 ± 1.5	12.2 ± 1.4	0.21	0.882
HR_{max} (bpm)	186 ± 8.1	186 ± 8.8	185 ± 8.0	189 ± 9.4	1.27	0.297

Note: PLA placebo and placebo, PLA+CAF placebo and caffeine, PLA+CHO placebo and carbohydrate, CAF+CHO caffeine and carbohydrate, MV mean velocity, HR_{max} maximum heart rate. $P < 0.05$

Figure 1. Mean and individual results of the 10-km running performance in each of the conditions. PLA vs PLA+CAF (A), PLA *vs* PLA + CHO (B), PLA *vs* CHO + CAF (C). Dash line represents the mean values.



*$P < 0.05$ in relation placebo condition.

Figure 2. Running pacing strategy adopted by the participants of the present study for the PLA, PLA+CAF, PLA+CHO and CAF+CHO condition, during 10 km running performance.

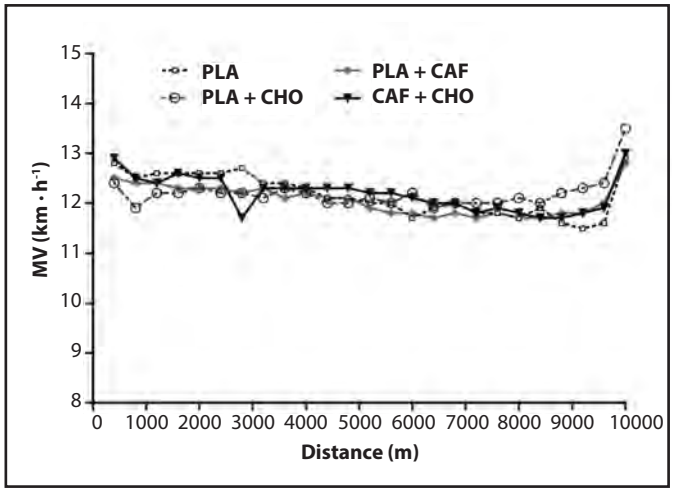


Figure 2 shows the variation of MV according to distance, which demonstrate that the participants used the "constant" running pace as a test strategy in PLA condition. In the conditions PLA+CAF and CAF+CHO a "negative" strategy was observed, and in PLA+CHO condition a "J" strategy was observed.

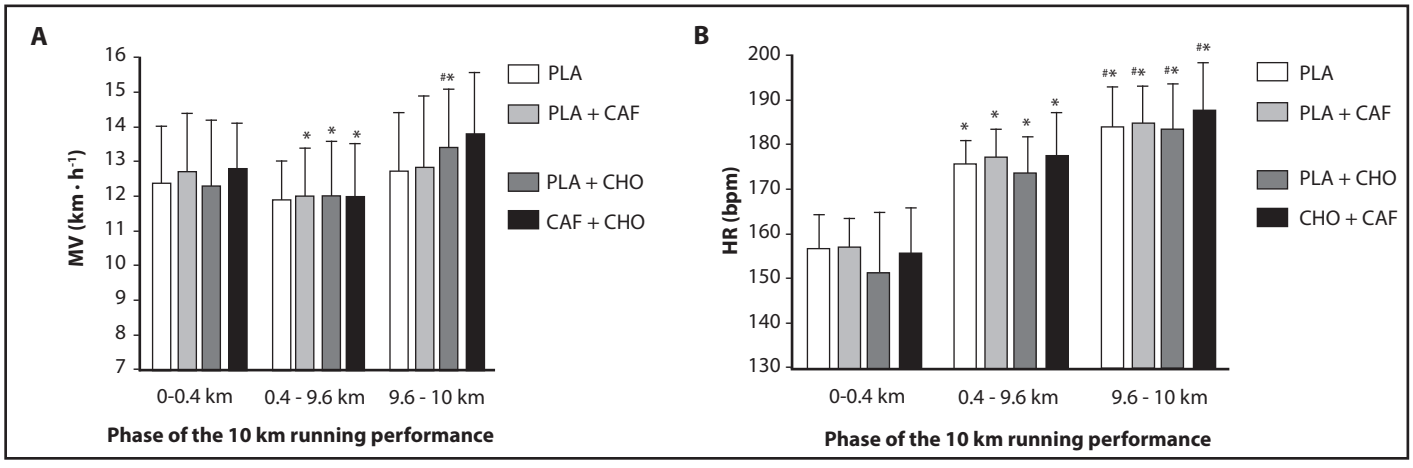
Figure 3A shows the MV in each phase (start, middle and end phase) of the 10-km running performance. There was no significant difference between conditions for MV during each phase of the 10-km running performance. In addition, there was a significant main effect for MV during each phase within group for the 10-km running performance. *Post-hoc* analysis showed that there was a significant difference between the start phase than that in the middle phase for the PLA-CAF group (12.8 ± 1.6 km·h^{-1} *vs.* 12.1 ± 1.2 km·h^{-1}; P = 0.017). For the CAF+CHO group, the MV in the middle phase were lower than the initial phase (12.8 ± 1.6 km·h^{-1} *vs.* 12.1 ± 1.2 km·h^{-1}; P = 0.017), with no significant difference between the end phase (13.0 ± 1.6 km·h^{-1}) when compared to the middle (12.1 ± 1.2 km·h^{-1}) and start phase (12.8 ± 1.6 km·h^{-1}). For the PLA-CHO group, the MV in the start phase were lower than that in the end phase (12.4 ± 1.7 km·h^{-1} *vs.* 13.5 ± 1.6 km·h^{-1}; P = 0.03), and the middle phase were lower than the end phase (12.1 ± 1.4 km·h^{-1} *vs.* 13.5 ± 1.6 km·h^{-1}; P = 0.001). In addition, for the CAF-CHO group there was a significant difference for MV during the start phase compared to the middle phase (12.9 ± 1.2 km·h^{-1} *vs.* 12.1 ± 1.4 km·h^{-1}; P = 0,019). Nonetheless, there was no difference for MV during each phase of the 10-km running performance for PLA group. In addition, the Bayesian analysis demonstrated that when compared to the Null model, phase is a better model (BF_{10}= 12.769; BF_{incl}= 8.531), but when the condition and the interaction between condition and phases are analyzed the Null model was considered better (BF_{10}= 0.010; BF_{incl}= 0.025 for condition; BF_{10}= 0.463; BF_{incl}= 0.006 for interaction).

Figure 3B shows the HR_{submax} during each phase of the 10-km running performance. There were no statistical differences between groups for each phase of the 10-km running performance. Within group analyses demonstrated that there were statistical differences between HR during each phase (P < 0.001). *Post hoc* analyses demonstrated that there was an increase in HR during each phase of the 10-km running performance for all groups (P < 0.001). The Bayesian analysis demonstrated that when compared to the Null model, phase (BF_{10} < 0.001; BF_{incl} < 0.001), condition (BF_{10} < 0.001; B_{Fincl} = 0.208), and the interaction (BF_{10} < 0.001; BF_{incl} = 0.034) were not considered better models.

Discussion

The aim of this study was to verify potential changes in 10-km running performance with acute isolated and combined CAF and CHO supplementation, and in addition, to verify the effects of both supplementations on the pacing strategy and other associated physiological variables. The main finding was that acute isolated and combined CAF and CHO supplementation did not modify the final 10-km running performance, with differences only in pacing strategy, partially confirming our initial hypothesis.

Figure 3. Mean velocity (A), Heart rate (B) during the different phases adopted by the participants of the present study for the PLA, PLA+CAF, PLA+CHO and CAF+CHO condition.



* P < 0.001 in relation to initial phase (0-0.4 km); # * P < 0.001 in relation to middle phase (0.4-9.6 km).

The CAF is an ergogenic aid, widely used mainly in endurance events, which has demonstrated positive effects in the performance of most of the studies[19,20], however in the present study no difference was observed in performance of 10-km after ingestion of CAF. Similar results were found by Bell, McLellan, & Sabiston[21] who evaluated CAF intake in 10- km on a treadmill showing that 4 mg·kg^{-1} dosage did not affect performance (CAF: 46.0 ± 2.8 minutes; PLA: 46.8 ± 3.2 minutes). Although there was no statistical difference between PLA + CAF compared to PLA, 7 participants had a small improvement in performance (Figure 1A). This difference between the participants can be explained by individual factors, such as genetic factors that could explain this individual variability. Previous studies have suggested that inter-individual variations in polymorphisms of CYP1A2 and ADORA2A lead to different responses on running performance[12,19]. The first gene is responsible for metabolizing the caffeine in paraxanthine, theobromine, and theophylline; the second gene regulates the adenosine receptors[12,19].

In addition, this small effect of supplementation on endurance performance is in agreement with the literature. In a recent systematic review and meta-analysis that verified the effect of acute caffeine ingestion on endurance performance, Southward *et al.*[20] concluded that caffeine can be used as an effective ergogenic on environment like sport settings, where small increases in performance could lead to greater results.

Nonetheless, the role of CHO feeding as an ergogenic strategy to increase endurance capacity were consistently demonstrated in previous studies[22,23]. It has been demonstrated that during prolonged exercise the induced fatigue is often associated with muscle glycogen depletion and reduced blood glucose concentrations[24] and, therefore, an increased pre-exercise muscle and liver glycogen concentrations are believed to be essential for optimal endurance performance. Previous studies have shown that the improvements in performance during prolonged (*e.g.* > 2 h) and short (*e.g.* < 60 minutes) exercise durations cannot be explained by the same mechanisms[22,25].

However, during short exercise durations these ergogenic effect of CHO as a substrate point of view is unlikely to be influenced by the exogenous CHO, since muscle glycogen stores is generally not limiting to performance[22], when exercise durations are less than ≈ 60 minutes[25]. The finding of the present investigation further supports the notion that for exercises ranging for up to ≈ 60 minutes, the demands are adequately met by the endogenous CHO stores and rather than providing addition benefits, exogenous CHO intake may have any further effect on endurance performance, as no statistical difference was observed for the group after supplementation and a slight improvement in 8 of the 15 participants after supplementation (Figure 1B), which could perhaps be more pronounced if the activity had a longer duration.

Studies that have verified the effect of CAF and CHO combined supplementation yield controversial results[2,26,27]. It is believed that one of the advantages of this combination would be the fact that during prolonged exercise, CAF could contribute to the final part of the performance due to its potential ergogenic effect of the stimulation of the central nervous system (CNS), reducing perceived exertion[28], as demonstrated in previous studies that found improvement in performance after evaluating the combination of CAF and CHO[26,27].

Despite the positive effects of the combination of CHO and CAF on performance, in the present study no improvement in 10-km performance was observed after the combined intake of CHO and CAF, a similar result of literature studies[2,26]. The results of the present study reinforce the growing number of studies which found that combining multiple ingredient supplementation may not confer exactly greater benefit than isolated supplementation[26,29].

The ingestion of the supplement on this present study in the form of capsules may also have inhibited its potential ergogenic effect, as studies show benefits in performance only with the mouthwash of CHO and CAF due to initial activation of the mouth receptors that later activate the nervous system and the central nervous system (CNS)[30,31]. Perhaps the most efficient way of supplementing these substances for performance improvement would be in liquid form or in gums[31].

The pacing strategy can be influenced by several factors, among them are the inventories of intramuscular energy substrates and metabolic alterations[32]. In the present study, a difference between the conditions for the pacing strategy was observed (Figure 2). For the PLA condition the participants of the present study adopted a more conservative strategy during the performance of 10-km. Such a strategy is called "constant" and is characterized by the maintenance or by a small change of velocity during the test[33-35]. This strategy seems to be more common for athletes with this profile (recreational). Previous studies that compared the race strategy adopted during a 10-km race between runners of different levels[1,36], identified that lower-level athletes usually chosen the same "constant" strategy as observed in the present investigation for the PLA condition. The choice of this more conservative strategy can be explained by the fact that if the initial velocities are very high they can induce a large imbalance at the beginning of the exercise, which would harm the athlete for the rest of the race, which may induce a premature fatigue, making it impossible to maintain speed impairing the performance[34].

For the conditions of caffeine supplementation (PLA+CAF, CAF+CHO), a "negative" strategy was observed during the 10-km running performance. This strategy is characterized by a fast start and with a later reduction in speed until the end of the performance[33-35]. Caffeine appears to stimulate a faster onset of performance, which may be related to its potential ergogenic effects, mainly the effect of the stimulant on the central nervous system (CNS), thus increasing alertness and reducing perceived exertion[31]. Bertuzzi *et al.*[17], concluded after evaluating the contribution of some physiological and muscular variables for the pacing strategy adopted during 10-km running performance running, that the rating of perceived exertion is the variables that best explain the performance in the start phase (0.4 km) of the 10-km running performance, and its reduction may have been responsible for making runners perceive a slower speed or effort than they actually are performing.

Different from caffeine, the carbohydrate appears to have an effect on the final outcome of the performance, since the pacing strategy adopted by participants in the PLA + CHO condition was a "J" strategy, characterized by a faster onset, then a reduction in the intermediate phase and with a greater increase of velocity at the end phase, being this one higher than the start phase[33-35]. This high increase in speed at the end of the performance for this condition could be related to the greater availability of CHO, which is the main energy substrate for high

intensity exercise[5,37]. However future studies are needed to identify the associations of pacing strategy adopted and the availability of CHO during prolonged exercise durations like the 10-km running performance.

Although different running strategies were observed for each supplementation condition, at the end of the performance it was possible to observe an increase in velocity, a phenomenon known as "end spurt" or "final sprint"[37]. In the present study, it was found that all the conditions were more pronounced in the PLA + CHO condition.

Regarding the HR no difference was observed between the conditions (Figure 3B), there was only difference between the three phases of the performance for the same condition. This increase in HR over the course of performance, even with no statistical difference in velocity in some conditions, can be attributed to the increased metabolic demand imposed by the intensity of the activity[38], as well as by extrinsic factors such as environmental temperature and hydration status of the participants[39]. In the end phase, an increase in HR was observed in both conditions, reaching the maximum values. This increase is related to sprint performed by runners to obtain a better result at the end of the race[33,35,40].

Conclusion

In conclusion, the use of acute, isolated and combined CAF+CHO supplementation had no influence in the final 10-km running performance, HRmax, for the group. However, performance improvement was observed in most participants when analyzing the results individually. In addition, supplementation was responsible for causing changes in the pacing strategy for recreational runners. These findings provide important insight into the specific conditions in which the CAF and CHO condition supplementation could be used as an ergogenic substance for some individuals. Thus, isolated and combined CAF+CHO supplementation strategies can be used as an important tactical advantage (i.e. pacing strategy) in 10-km running performance depending on the strategy previously chosen by the athletes.

Conflict of interest

The authors do not declare a conflict of interest.

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Postactivation potentiation improves jumps performance in children ages 6 to 8 years old

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Summary

Introduction: The aim of the present study was to investigate the effects of postactivation potentiation (PAP) in vertical and horizontal jump performance in pre-pubertal children.
Material and method: One hundred and nineteen children (65 girls and 54 boys; 6.8 ± 0.7 years old; 124.5 ± 6.4 cm; 25.2 ± 5.1 kg) participated in this study. This was a transversal cross-sectional study which incorporated a within-subjects repeated-measures design, where participants completed all protocols. The experimental procedure required four total testing, separated by one week, using a counterbalanced. This study investigated jumping performance associated with weighted jumps, low-load vertical jumps, and horizontal jumps. During two sessions the participants performed vertical jumps with and without PAP, the other two sessions the same procedures were performed for horizontal jumps. The PAP protocol consisted of one set of five weighted countermovement jumps with low-load (10% of body mass) and a rest interval of four minutes prior to the jump tests. Paired t-tests were used between conditions (PAP and control) in the vertical jump and horizontal jump test. In addition, Cohen's d effect size and 95% confidence interval was used.
Results: Significant jump height was observed in the vertical jump in the PAP condition compared to the control condition ($p = 0.007$). Similar results were observed for the horizontal jump tests, with significant longer distance observed in the PAP condition ($p = 0.036$).
Conclusions: Pre-pubertal children can benefit from the effects of PAP in vertical and horizontal jumping performance when preceded by low-load ballistic movements. A protocol implementing low-loads, determined by a relative percentage of body mass is effective to promote PAP for young children.

Key words:
Post-activation Potentiation. Youth. Jumps. Neuromuscular.

La potenciación postactivación mejora el rendimiento de saltos en niños de 6 a 8 años

Resumen

Introducción: El objetivo del presente artículo fue investigar los efectos de la potenciación postactivación (PAP) en el rendimiento del salto vertical y horizontal en niños prepuberal.
Material y método: Ciento diecinueve niños (65 niñas y 54 niños; 6,8 ± 0,7 años; 124,5 ± 6,4 cm; 25,2 ± 5,1 kg) participaron en este artículo. Este fue un estudio transversal que incorporó un diseño de medidas repetidas dentro de los sujetos, donde los participantes completaron todos los protocolos. El procedimiento experimental requirió cuatro pruebas totales, separadas por una semana, utilizando orden aleatorio. Este estudio analizó el rendimiento de salto asociado con saltos ponderados, saltos verticales de baja carga y saltos horizontales. Durante dos sesiones, los participantes realizaron saltos verticales con y sin PAP, en las otras dos sesiones se realizaron los mismos procedimientos para saltos horizontales. El protocolo PAP consistió en un conjunto de cinco saltos de contra movimiento ponderados con baja carga (10% de la masa corporal) y un intervalo de descanso de cuatro minutos antes de las pruebas de salto. Se utilizaron pruebas t pareadas entre condiciones (PAP y control) en la prueba de salto vertical y salto horizontal. Además, se utilizó el tamaño del efecto de Cohen y el intervalo de confianza del 95%.
Resultados: Se observó una altura de salto significativa en el salto vertical en la condición PAP en comparación con la condición de control ($p = 0,007$). Se observaron resultados similares para las pruebas de salto horizontal, con una distancia significativamente mayor observada en la condición PAP ($p = 0,036$).
Conclusiones: Los niños prepuberales pueden beneficiarse de los efectos de la PAP en el rendimiento de salto vertical y horizontal cuando están precedidos por movimientos balísticos de baja carga. Un protocolo que implementa cargas bajas, determinado por un porcentaje relativo de la masa corporal, es efectivo para promover la PAP en niños pequeños.

Palabras clave:
Potenciación Postactivación. Juventud. Saltos. Neuromuscular.

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Introduction

Postactivation potentiation (PAP) is an acute phenomenon of enhanced force output and power development following a maximal or near maximal muscle contraction[1]. One factor that contributes to the effects of PAP is attributed to neural activation in which the prior muscle contraction stimulus increases the capacity to recruitment higher threshold motor units during subsequent activity[2,3]. Another factor is attributed to skeletal muscle alterations, regulated by the release of Ca^{2+} molecules during contraction and phosphorylation of myosin regulatory light chains, which alter the myosin structure and increase the rate of cross bridge cycling[4]. Additionally, alterations in muscle architecture may occur, with a decrease in pennation angle and enhancements in force transmission to the tendon, which may increase the effects of PAP, although these mechanisms have yet to be fully elucidated[2,5].

PAP has been studied extensively with various protocols, exercises implemented and different populations but less is known about these effects in children[1]. Previous studies with youth subjects reported that both pre-pubertal and post-pubertal subjects can benefit from the effects PAP on performance[6,7]. Paasuke *et al.*[7] showed that although post-pubertal boys (16-years-old) showed higher maximal voluntary contraction (MVC) than pre-pubertal boys (11-years-old), both improved plantar flexor muscle twitch peak force during a PAP complex. However, PAP protocols generally use heavy loads, ≥ 80% of [1] repetition maximum (RM), but when prescribing resistance exercise for children, it is not recommended to use heavy loading with this population[1,8].

Strategies to promote PAP in very young children are scarce and published meta-analyses have no specific suggestions to improve PAP effects for this population[1,8]. Investigating PAP in young children can contribute to understanding the physiological mechanisms and which populations can successfully implement this type of training. Additionally, resistance training to improve strength and power is an increasingly popular training modality with children since several guidelines have been published over the years citing its efficacy[9-11] and additional methods to optimize prescription is necessary for strength and conditioning. The addition of a stimulus of conditioning activity (CA) and subsequent power activity can contribute to neural development and basic motor skills for children. Therefore, based on this previous information, the purpose of this study was to investigate the effects of a PAP protocol on vertical and horizontal jumps in pre-pubertal children.

Material and method

Experimental approach to the problem

This was a transversal cross-sectional study which incorporated a within-subjects repeated-measures design, where participants completed all protocols in random order. The experimental procedure required a total of four visits, each separated by one week. All subjects performed the visits during afternoon, at the same time, between midday to 4:00 pm. During two visits, participants performed a vertical jump test and a horizontal jump test. The other two visits the same tests were used, however, a PAP protocol was performed before them. Before each protocol, a dynamic warm-up was used, consisting of one minute of slow running, 30 seconds high knees, 30 seconds raising heels, 30 seconds with low jumps, and 30 seconds of jumping jacks. Two minutes of passive rest was provided before PAP protocol or jump tests. At the day without PAP, children performed jump tests following the same warm-up procedure and rest interval. Detail of the methods is displayed in Figure 1.

Subjects

One hundred and nineteen children (65 girls and 54 boys) aged between 6 to 8 years old participated in this study. Sample characteristics can be found in Table 1. A priori sample size was estimated by the software G*Power (version 3.1.9.2. Dusseldorf, DEU) previously recommended by Beck[12]. Considering an effect size of 0.5, an α error of 0.01 and the power (1 - β) of 0.99, the total sample calculation was 100 subjects. A larger sample was recruited to account for subject dropout which could

Figure 1. Study design and experimental protocols.

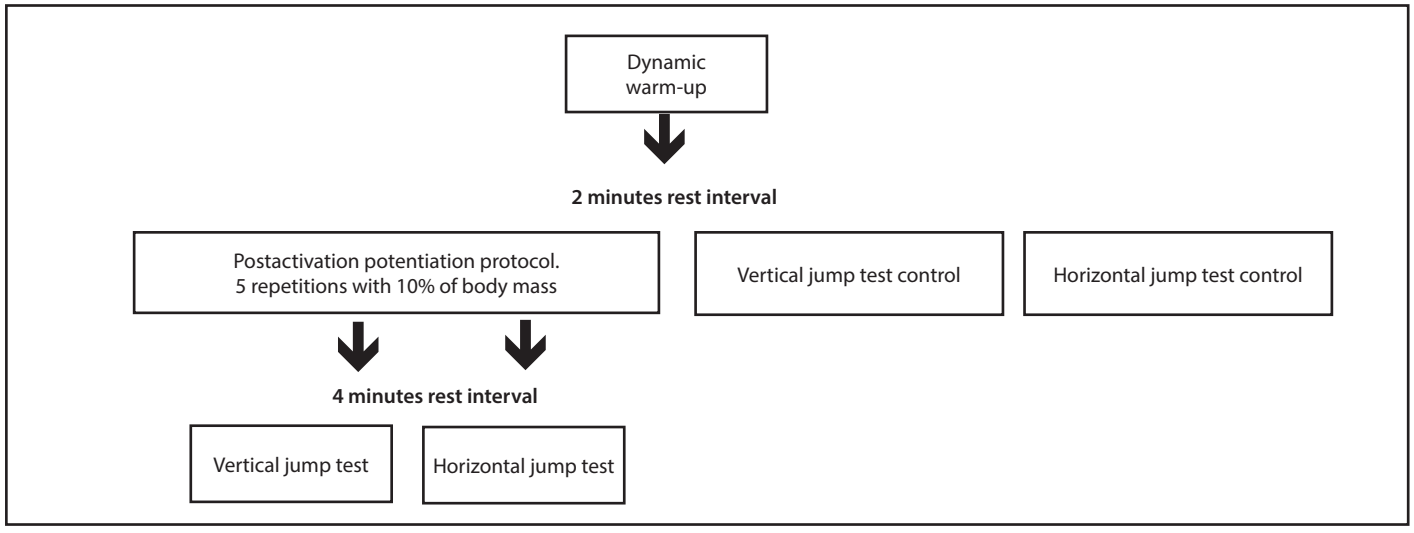


Table 1. Sample characterization (mean and standard deviation).

	Group (n = 119)	Girls (n = 65)	Boys (n = 54)
Age (years)	6.8 ± 0.7	6.8 ± 0.7	6.9 ± 0.7
Height (cm)	124.5 ± 6.4	124.4 ± 6.3	125.3 ± 6.5
Weight (kg)	25.2 ± 5.1	24.4 ± 4.6	26.2 ± 5.7
BMI	16.17 ± 2.34	15.76 ± 2.48	16.66 ± 3.46

BMI: body mass index.

confound the results. Participants were healthy and not engaged in any kind of high-performance sports or strength and conditioning training. All subjects were considered in the infancy phase, without complete maturation[10]. On the first visit to the laboratory, participants had height and body mass measured using a measuring tape attached on the wall and a digital scale (Worker, São Paulo, Brazil) and were familiarized with the jump tests. Body mass were measured in kilograms and height were determined with 0.5 cm intervals. In the familiarization session, subjects were instructed of the procedures of the jump tests, position of the arms and the exercise that was used. During experimental sessions, the researchers observed carefully all procedures. Subjects were excluded for any injuries on knee, ankle and foot the that would compromise the jumping exercise execution and/or jump tests. This study followed the ethical procedures for experimental research with humans, according to the resolution 466/2012 of National Health Council and was approved by the ethics committee in research at University under the number: 68385017.8.0000.5257. An informed parental consent which all procedures adopted in this study were read and signed by parents prior to the participation of the children in this study.

Postactivation potentiation protocol

On the day of vertical jump test, vertical countermovement jumps were used. On the day of horizontal jump test, horizontal countermovement jumps were performed. Two minutes after the dynamic warm-up, participants performed a PAP protocol, previously reported by Burkett *et al.*[13] that compared four warm-up protocols consisting of: weighted jumps with 10% of body mass; submaximal jump warm-up with 75% of the participants' maximum vertical jump; stretching protocol with 14 position; and a no warm-up control protocol. Significantly higher vertical jump performance was observed in the protocol of five repetitions with 10% of body mass. Based on it, the PAP protocol consisted of one set of five jumps with the load corresponding to 10% of body mass. However, in the study of Burkett *et al.*[13], young adults jumped over a box with the height of 63.5 centimeters. In this study, participants performed free jumps on the floor, with instructions to jump as high as possible, since these children were not able to jump over the previously mentioned box height. During the PAP jumps, subjects held weight plates in their hands and the values were rounded when necessary. Four minutes of passive was provided between the PAP protocol and jump tests. Generally, greater rest interval is used between CA and jump test, however, this recommendation is made for high-load protocols[1].

Jump tests

In the vertical jump test, initial measurement of standing reach height was obtained. Then, the participants were positioned near the tape measure and instructed to jump as high as possible and touch the tape measure with the fingertips which were marked with chalk. During all testing, strong verbal encouragement was provided for each subject. Subjects were allowed to use arm swing and self-selected depth in the countermovement jump. Three maximal attempts were provided and the best of these jumps was used for analysis. Jump height was determined as the distance between the outstretched standing reach and the mark made at the apex of the vertical jump.

For the horizontal jump test, the participants were positioned on the 0-cm marked point, with feet shoulder width apart. During test, the subjects were instructed to jump as far as possible. Verbal encouragement was provided during each jump and subjects were allowed to arm swing and self-selected countermovement depth. Three maximal attempts were given and the best of theses jumps was used for analysis. Jump distance was determined as the distance from the starting line to the back of the heel upon landing marked with a tape measure[14]. During landing, subjects should not move the foot due to unbalance. When this happened, an additional attempt was made.

Statistical analyses

The statistical analyses were initially performed using the Shapiro-Wilk normality test and homoscedasticity test (Bartlett's criterion). Descriptive and parametric statistics were used for all analyses, with the results presented as means and standard deviations. Paired t-tests were used between conditions (PAP and control) in the vertical jump and horizontal jump test. Statistical analyses were performed using the software SPSS (version 20, Chicago, IL, USA), using $p \leq 0.05$ as a standard of statistical significance. In addition, Cohen's d effect size (ES) and 95% confidence interval (CI) was used, consisted of the difference between two means divided by pooled standard deviation, and rated according to the magnitude of < 0.20 trivial; 0.20-0.49 small; 0.50-0.79 moderate; and > 0.80 large[15].

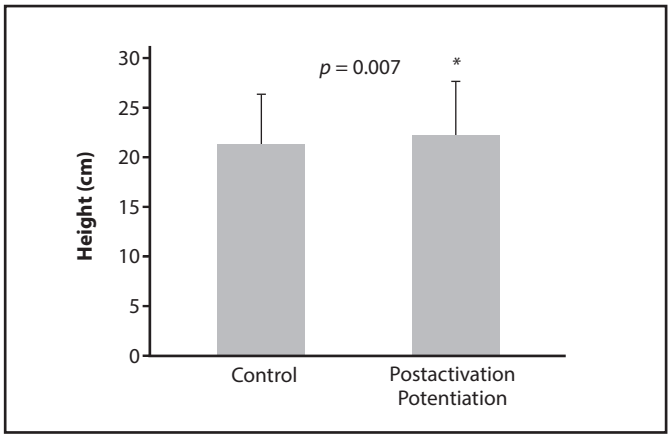
Results

Significant differences were observed between conditions for both tests ($p < 0.05$). The PAP improved the vertical jump test when compared to control (Figure 2; 22.29 ± 5.13 *vs.* 21.57 ± 4.68 cm, respectively; $p = 0.007$). Cohen's d revealed a trivial magnitude of the difference of 0.15 (95% CI = 0.13-0.16). Similar results were observed for the horizontal jump test, with significantly longer distances in the PAP protocol when compared to control (Figure 3; 107.05 ± 17.35 *vs.* 104.97 ± 18.76 cm, respectively; $p = 0.036$). Cohen's d revealed a trivial magnitude of the difference of 0.11 (95% CI = 0.10-0.13).

Discussion

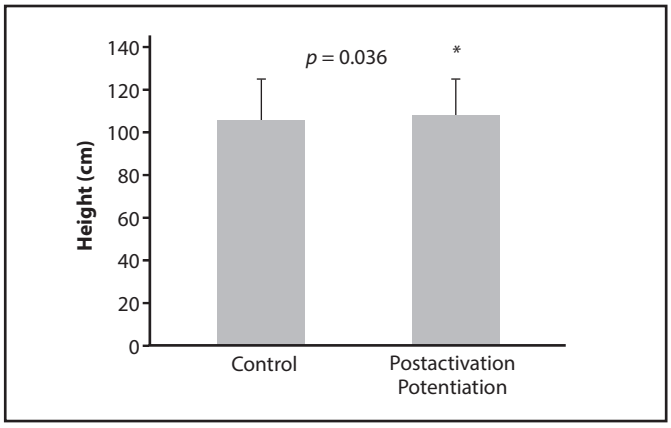
The present study revealed that children ages 6 to 8 years old can improve performance of vertical and horizontal jumps following a PAP

Figure 2. Vertical jump test comparing the postactivation potentiation (PAP) protocol and control condition.



*Significant higher jump height for PAP.

Figure 3. Horizontal jump test comparing the postactivation potentiation (PAP) protocol and control condition.



*Significant greater jump distance for PAP.

protocol. However, this improvement is clinically relevant, based on a trivial magnitude of this difference. Pre-pubertal children generally have lower twitch force production when compared to post-pubertal and young adults[7]. An incomplete maturation process, with lower muscle activation and reduced intra- and intermuscular coordination may compromise the force production and motors skills in young children[9]. Seitz *et al*.[16] found a large correlation between PAP responses during an isokinetic protocol related to maximal knee extensor torque ($r = 0.62$), quadriceps cross sectional area ($r = 0.68$) and muscle volume ($r = 0.63$). This finding suggests that training status, with greater strength and muscle volume, will influence the PAP response. The participants of the present study were very young, without previous experience in resistance training to improve power and strength and still achieved a positive PAP effect with low-load jumping movements.

The findings of this study are different from Arabatzi *et al*.[6] that did not observe PAP benefit for both pre-pubertal boys when during squat jump (SJ) test. This is probably attributed to CA applied in the children previous SJ, which consisted of an isometric stimulus. The present study used a protocol based on an earlier study[13] that showed higher vertical jump performance following the protocol of five repetitions with 10% of body mass in the collegiate football players, suggesting a specific low-load warm-up before jump training may be beneficial. These findings suggest that the CA should simulate the movement specificity that will be performed in the main activity. Another important consideration is that not only higher loads should be used in a PAP protocols, but further studies should consider low-load protocols combined with explosive movements, especially for those who are untrained and pre-pubertal.

Considering the rest interval between the PAP protocol and the jump testing, this study corroborates with the previous meta-analyses of Dobbs *et al*.[17] which concluded that three to seven minutes are appropriate to recover from acute fatigue generated during the preceding movement and the main activity. This study used a four minutes passive rest interval, although the recommendation for longer rest intervals generally are made for higher loads PAP protocols[18]. The rest interval is an important consideration since an optimal time between conditioning activity and main activity should be used to overcome the acute fatigue while still maintaining the potentiation effect, thus, improving performance[18]. Previous studies indicate that a short-rest interval can be detrimental to performance due to excessive fatigue, and longer-rest periods may dissipate the potentiation effect[19,20]. However, these recommendations are generally made when high-load PAP protocols are used in adults, differing from this study. Hatzikotoulas *et al*.[21] showed that pre-pubertal boys are more fatigue resistant than men after a protocol performed to exhaustion. This suggest that the rest interval between CA and main activity for children may be shorter than adults, especially when low-loads are used during the CA.

The major limitation in this study was the inclusion of untrained subjects without previous experience in resistance training. However, due to the age of the children, it is difficult to recruit trained young athletes. Additionally, this study provides evidence of the effects of PAP in young children, independent of training status. It is important to highlight that the development of the maturation process is more important than sports performance for very young children recruited in this study. However, this study brings novel for literature of PAP that can be used and even prior a RT session as warm-up or in physical education classes for motor development. Future studies should consider investigating potential mechanisms of PAP in very young children, which may differ from adolescents and adults.

In conclusion, this study demonstrated that PAP can improve vertical and horizontal jumps performance in very young children, between the ages of 6 to 8 years old. As practical application of the results of this study, strength and conditioning coaches should consider incorporating this specific low-load training strategy as warm-up to acutely improve power in youth athletes. A protocol implementing low-loads, determined by a relative percentage of body mass is effective to promote PAP for young children, thus being an efficient and safe strategy.

Conflict of interest

The authors do not declare a conflict of interest.

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Therapeutic effects of hippotherapy in the elderly: a review of the literature

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Summary

The present work aims to carry out a structured and bibliographic review based on the results found regarding the terms Hippotherapy and Elderly people. For the reference search, the following keywords in English, Hippotherapy and Elderly, were used as descriptors, these keywords being always entered in databases of the same language. The computerized databases *SCOPUS, WOS, SPORTDiscus were used. PubMed* and *Cochrane*. To limit the search for documents, four inclusion criteria were introduced: i) Mention at least some of the characteristics of Hippotherapy for the elderly (minimum 20 words that mention the subject), ii) Select only scientific documents (journal articles) These articles may have an experimental design or be review articles, iii) Be accessible and be available in full text or with access to the abstract, and iiii) Be written in Spanish, English or Portuguese. The results show that the papers on Hippotherapy in the elderly address different research topics and show that equestrian therapies have beneficial therapeutic effects in the elderly population. Hippotherapy interventions improve static balance and dynamic balance, postural balance, functional mobility, flexibility, muscular strength, gait and cadence of steps. They reduce spasticity, causing a decrease in the risk of falls and an improvement in the quality of life of the elderly. In addition, they cause benefits on a psychological level, reducing levels of stress and depression, which produces an improvement in the quality of sleep and positively influences mood.

Key words:
Hippotherapy. Elderly people. Benefits.

Efectos terapéuticos de la hipoterapia para personas mayores: revisión de la literatura

Resumen

El presente trabajo tiene por objetivo realizar una revisión bibliográfica y estructurada basada en los resultados encontrados en torno a los términos *Hipoterapia* y *Personas mayores*. Para la búsqueda de referencias, se utilizó como descriptores las siguientes palabras clave en inglés, *Hippotherapy* y *Elderly*, siendo estas palabras clave siempre introducidas en las bases de datos del mismo idioma. Se utilizaron las bases de datos informatizadas *SCOPUS, WOS, SPORTDiscus. PubMed* y *Cochrane*. Para limitar la búsqueda de documentos, se introdujeron cuatro criterios de inclusión: i) Mencionar al menos alguna de las características de la Hipoterapia para personas mayores (mínimo 20 palabras que mencionen la temática), ii) Seleccionar solamente documentos científicos (Artículos de revistas), pudiendo tener estos manuscritos un diseño experimental o ser estudio de revisión, iii) Ser accesible y estar disponible a texto completo o con acceso al resumen, y iiii) Estar escrito en el idioma español, inglés o portugués. Los resultados muestran que los documentos sobre Hipoterapia en personas mayores abordan tópicos de investigación diferentes, y muestran que las terapias ecuestres tienen efectos terapéuticos beneficiosos en la población de edad avanzada. Las intervenciones con Hipoterapia mejoran el equilibrio estático y el equilibrio dinámico, el equilibrio postural, la movilidad funcional, la flexibilidad, la fuerza muscular, el modo de andar y la cadencia de pasos. Disminuyen la espasticidad, provocando una disminución del riesgo de caída y una mejora de la calidad de vida de las personas de edad avanzada. Además, provocan beneficios a nivel psicológico, reduciendo los niveles de estrés y depresión, lo que produce una mejora en la calidad del sueño e influye positivamente en el estado de ánimo.

Palabras clave:
Hipoterapia. Personas mayores. Beneficios.

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Introduction

Animal-assisted therapies, specifically with horses, are officially practised almost everywhere in the world[1], as a therapeutic alternative within the areas of rehabilitation and re-education. This is a specialised work methodology[2], that has shown improvements in the quality of life and general state of health of individuals[3], by providing psychological, social and educational benefits that improve the performance of daily activities[4,5]. To conduct this technique, the horse first needs to be trained and must also have a docile nature so that it can be approached by, and come into contact with people who may have behavioural disorders, involuntary movements or who use some kind of device (walking stick or wheelchair), conditions which could scare an untrained horse[6]. It is therefore a direct intervention with some pre-designed goals, for the purpose of achieving physical, social, emotional and cognitive benefits, individually or in a group of persons with different abilities, taking advantage of the characteristics of the animals.

Furthermore, studies have also reported evidence of the effectiveness and benefits of Hippotherapy in different groups of disabled persons, such as with cerebral palsy[7,8], psychomotor retardation[9], multiple sclerosis[10], Down syndrome[11], or the elderly[4,12,13], among others. Hippotherapy is a comprehensive, neurologically based, multidisciplinary treatment that uses the horse as its main element, taking advantage of its qualities (movement, rhythm and heat) to stimulate multiple psychomotor and sensory areas[9,14]. It has therefore become an effective intervention, and there is increasing scientific evidence of its benefits, acting across the board in the social, physical and intellectual sphere of participants[15].

On the other hand, ageing is a natural, inevitable process[16]. Population growth together with increased life expectancy is leading to a considerable increase in the number of elderly persons in developing countries[17], causing an increase in chronic ageing-related diseases[18]. As a result, the ageing process entails biological, cognitive and social changes, with the progressive presence of molecular and cellular damage[19], as well as a loss of muscle power and strength[20]. These factors can cause an alteration of physical functions that have a negative impact on the functional daily life skills, and usually accompanied by a concern for the cognitive change occurring[21], as well as frame of mind[22].

Given the scarcity of review documents on this subject, and analysing the different databases, a new review of the literature to complete the state-of-the-art with regard to investigations into the use of Hippotherapy in the elderly and to provide conclusions on the benefits of equine therapies for this group, was considered to be of interest.

Material and method

Design

This investigation comes within theoretical studies. For this purpose, a search and compilation process was made of scientific documents using the *"Data accumulation and study selection"* model"[23], in order to analyse the articles published in relation to the benefits of Hippotherapy in the elderly.

Sample

The sample consisted in articles from scientific journals. From a total of 1292 articles in the initial phase of the search, conducted in October 2020 among the three databases, using *Hippotherapy* as the first term selected, 1243 articles were subsequently rejected after including the second term Elderly. 15 documents were then selected, which met the inclusion criteria pre-established by the investigators.

Criteria for the selection of studies

For the document search and selection, the following key words were used: *Hippotherapy* and *Elderly*. Furthermore, the documents selected to be part of the sample had to meet a series of inclusion criteria (Table 1). The following computerized databases were used, which store the main scientific publications on any field of knowledge: *SCOPUS, WOS, SPORTDiscus, PubMed* and *Cochrane*.

Coding of the variables

The documents selected were classified, based on the following criteria: *Title, Author(s), Year, Keywords, Database, Abstract, Type of study, Sample, Benefits and Quality* of the documents selected (Table 2).

Study recording procedure and data analysis

The procedure used for this study is similar to those found in the scientific literature[4,24,25]. Good planning of the literature search is key to success[26], making it possible to draw relevant conclusions[24]. All the documents selected for the study met the inclusion criteria established.

Table 1 Document inclusion and exclusion criteria.

No.	Inclusion criteria
1	Mention at least some of the characteristics of Hippotherapy for the elderly (minimum 20 words).
2	Select only scientific documents (articles from journals).
3	Full text or abstract available.
4	Written in Spanish, English or Portuguese.
	Exclusion criteria
5	Exclude those documents in which only the keywords entered in the databases are mentioned.
6	Exclude those articles based solely on mechanical horse-riding simulators.
7	Leave out documents that cannot be referenced.
8	Exclude articles that only refer to the elderly.

Table 2. Characteristics of the literature review study variables.

Variable	Description
Title	Title in English of selected article.
Author(s)	Scientific name of each author of selected document.
Year	Year of official publication of selected article.
Keywords	Keywords used in article.
Database	Data platform providing access to selected article.
Summary	Brief indication of the principal ideas and objective(s) of selected document.
Type of study	Classification of selected articles based on study type according to Montero & Leon (2007): Theoretical studies, Empirical studies with quantitative methodology & Qualitative empirical studies.
Sample	Set of individuals or data randomly chosen, which are considered to be representative of the group to hich they belong and which are taken to study.
Benefits	Indication of the beneficial effects of Hippotherapy in the elderly.
Quality of the	Percentage relating to the quality of the documents documents selected by observers external to the investigation.

Figure 1. Flow diagram of the bibliographic search process.

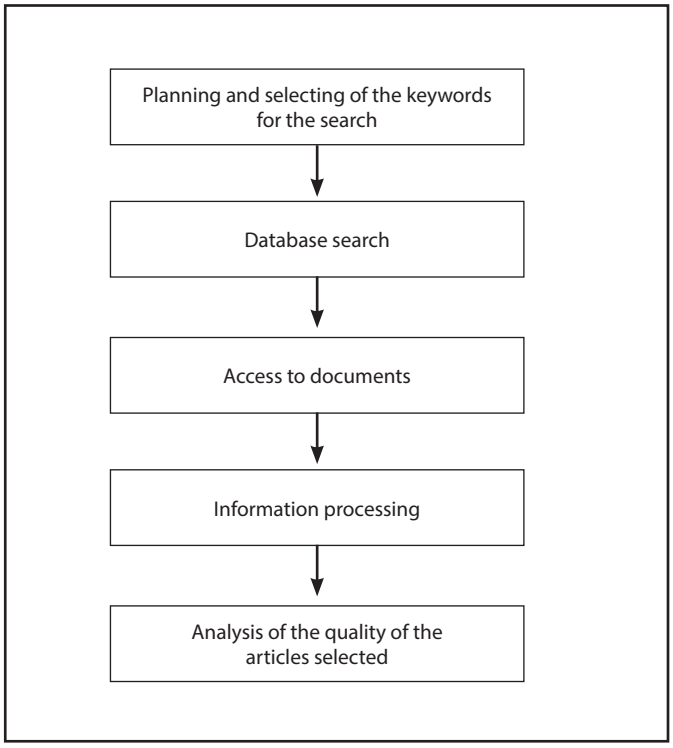
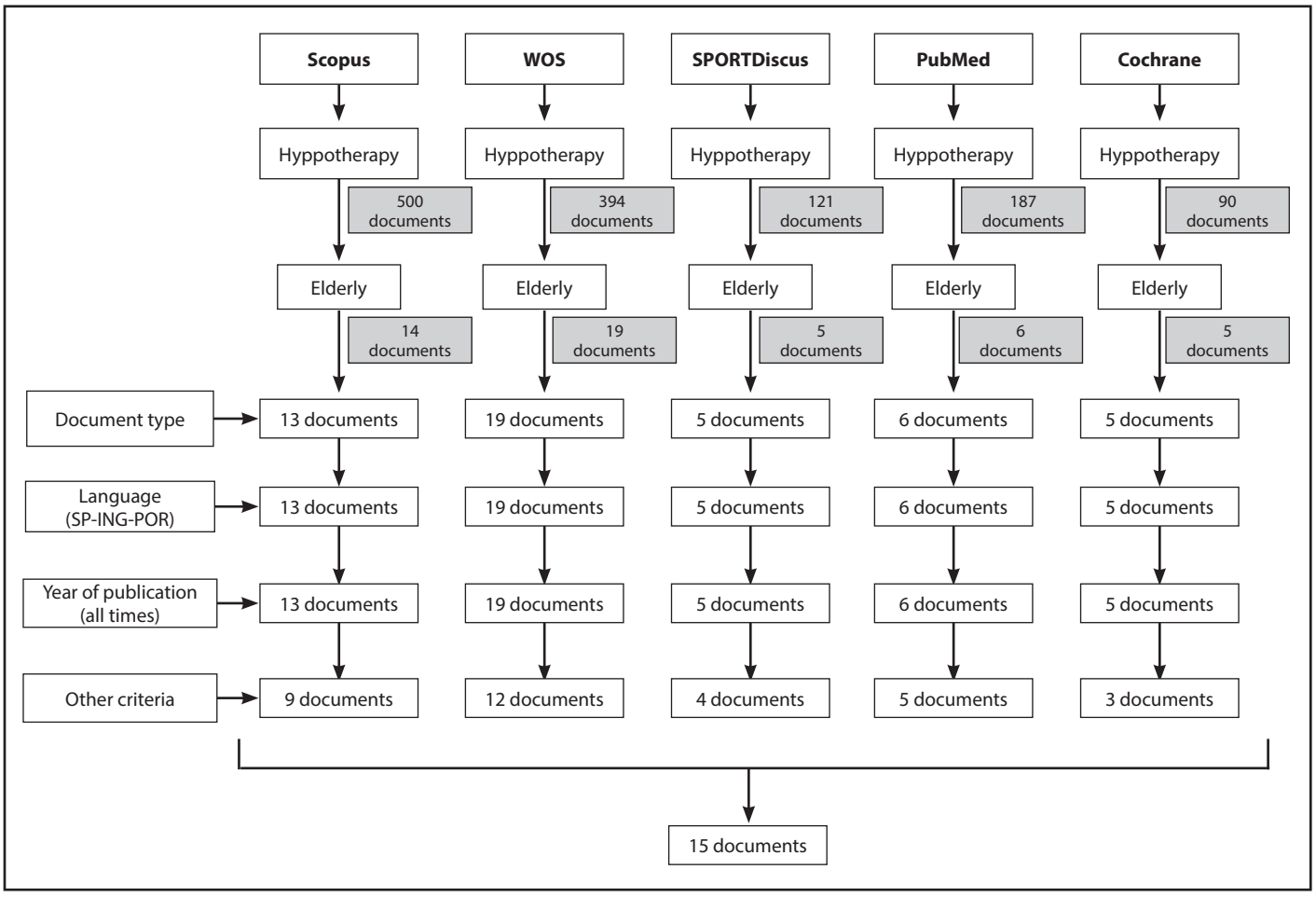


Figure 1 sets out the search process conducted for this work.

- *Phase 1 Planning and selecting of the keywords for the search.* For the selection of the key words, account was taken of the objectives of the literature review relating to the benefits of Hippotherapy for the elderly. In order to locate the highest number of related scientific documents (journal articles), a search was made using the keywords in English *"Hippotherapy"* and "*Elderly".* The aforementioned inclusion criteria were established (Table 1). The same keywords, and the same order were used in all the databases consulted.
- *Phase 2 Database search.* Five bibliographic searches were made in the following computerized databases: *SCOPUS, WOS, SPORTDiscus, PubMed* and *Cochrane.* To do so, the same Boolean search procedure (And) was used in each database for the purpose of finding the greatest possible number of related documents. The final search phrase was: *Hippotherapy* - And - *Elderly.* The documents selected for the study met the inclusion criteria established. The document search structure in the different databases is shown in Figure 2. As keywords were progressively added in the search engine, the results decreased considerably. The document inclusion and exclusion criteria were subsequently applied.
- *Phase 3 Access to documents.* Some of the databases used for the search for references do not allow access to full-text documents. Therefore, in order to consult the greatest number of original full-text articles, the web portal of the electronic library of the University of Extremadura was used, as well as different platforms and web search engines to contact the authors[7,25]. The sample was reduced to 15 articles, which were reviewed in depth. The number of documents selected must not be too large given that the processing of the information could be contaminated by the researcher[27].
- *Phase 4 Processing of information.* For each article, an analysis was made of the *Title, Author(s), Year, Keywords, Database, Abstract, Study type, Sample, Benefits and Quality.* For this purpose, it is important to organise and categorize all the information obtained[7]. Furthermore, a summary of each document was made, by preparing a table with all the information that would allow for an optimal and efficient review. Likewise, a descriptive analysis was made of the following variables: *Year, Keywords* and *Databases* in the various articles in order to identify their relationship with the study topic, as conducted by the authors[5]. For those articles with no keywords, the investigators themselves determined a series of terms, based on the subject of the study. Finally, the main benefits of Hippotherapy for the elderly were drawn from the selected articles. Figure 3 shows the main keywords used in the selected journal articles. Furthermore, Figure 4 shows the number of articles selected based on the *Year of publication*, and Figure 5 shows the number of articles selected based on the *Database*. These statistical analyses provide the link with the objective of this study, and also make it possible to identify a larger amount of relevant information related to the documents selected.

Figure 2. Schematic of the documents found in the different databases.



– *Phase 5 Analysis of the quality of the articles selected.* For the analysis of the quality of each study, a quality questionnaire was prepared, similar to the one proposed by the authors[28]. This questionnaire comprised 16 questions with either a Yes or No answer (Table 3). Furthermore, the evaluation process was conducted by 3 outside observers (holding a Degree in Physical Activity and Sport Sciences) and with a deep knowledge of the study subject (Table 4). The studies analysed were assessed according to purpose (Q1), bibliographical data/background (Q2), design (Q3), sample (Q4 and Q5), the use of informed consent (Q6), measurements and result (Q7 and Q8), method and description (Q9), the importance of the results (Q10), the methods of analysis (Q11), information on the practical importance (Q12), subject drop-outs (Q13), conclusions (Q14), practical implications (Q15) and the study limitations (Q16). The 16 document quality criteria were given a score on a binary scale (Yes=1/No=0). Each article was classified as (A) *Excellent methodological quality*, with a score > 75% (B) *Good methodological quality*, with a score from 51% to 75%, and (C) *Poor methodological quality*, with a score < 50%. For the review articles, those questions that could not be answered by the methodology used, were assumed to be 1=Yes.

Results

The results are shown in the same order in which the bibliographic review was conducted. Table 5 shows the different articles and their main characteristics regarding the benefits of Hippotherapy in the elderly, based on the criteria defined in the method. Moreover, they are shown in chronological order, for ease of reading.

Discussion

This study updates the state of knowledge with regard to the benefits of Hippotherapy for the elderly, using methodological procedures that are similar to those existing in the scientific literature[23-25], identifying and classifying the most relevant information. Furthermore, it serves as a basis for future reviews while also making it possible to draw relevant conclusions. On the other hand, it has made it possible to analyse the

Figure 3. Main keywords relating to the benefits of Hippotherapy in the elderly.

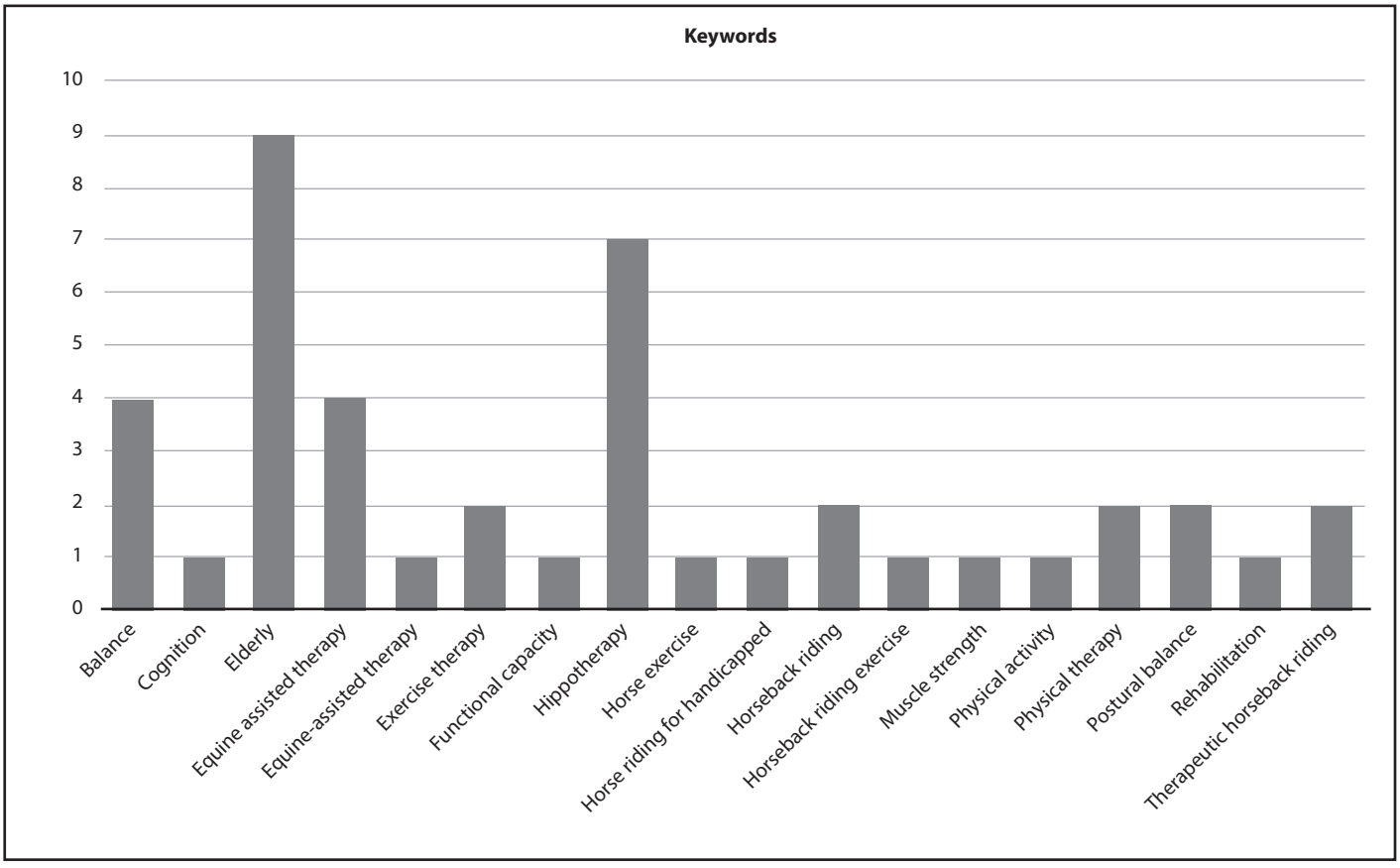


Figure 4. Number of documents selected based on the year of publication.

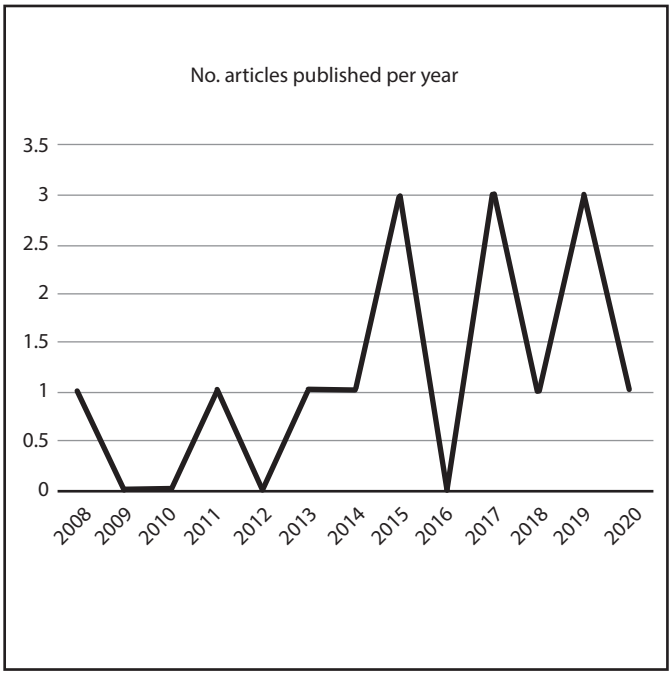


Figure 4. Number of documents selected based on the database.

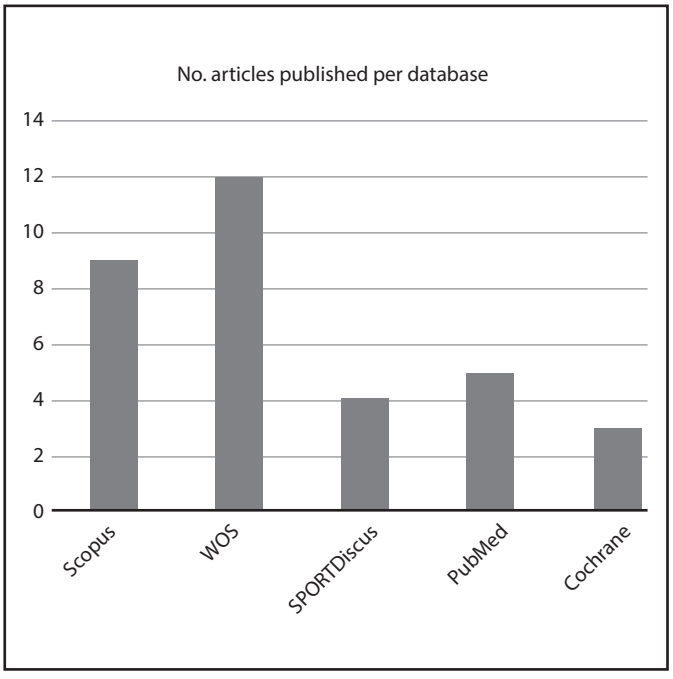


Table 3. Article quality criteria.

Q1	Was the purpose of the study clearly indicated?	1=Yes	0=No
Q2	Did the authors review the relevant background literature?	1=Yes	0=No
Q3	Was the design appropriate for the investigation question?	1=Yes	0=No
Q4	Was the sample described in detail?	1=Yes	0=No
Q5	Was the sample size accounted for?	1=Yes	0=No
Q6	Was informed consent obtained? (If not described, assume that this was not so)	1=Yes	0=No
Q7	Were the result measurements reliable? (If not described, assume that this was not so)	1=Yes	0=No
Q8	Were the result measurements valid? (If not described, assume that this was not so)	1=Yes	0=No
Q9	Was the method described in detail?	1=Yes	0=No
Q10	Were the results reported in terms of statistical significance?	1=Yes	0=No
Q11	Were the analysis methods approved?	1=Yes	0=No
Q12	Was the importance of the practice reported?	1=Yes	0=No
Q13	Was the drop-out rate reported?	1=Yes	0=No
Q14	Were the conclusions appropriate given the study methods?	1=Yes	0=No
Q15	Are there any implications for the practice given the results of the study?	1=Yes	0=No
Q16	Are the study limitations recognised and described by the authors?	1=Yes	0=No

Table 4. Article quality analysis

Documents	Observer 1	Observer 2	Observer 3	Mean	Quality
1	62.5	62.5	68.75	64.583	C
2	81.25	87.5	75	81.250	A
3	75	75	87.5	79.167	A
4	87.5	87.5	87.5	87.500	A
5	75	81.25	81.25	79.167	A
6	81.25	75	75	77.083	A
7	100	100	100	100,000	A
8	100	100	100	100,000	A
9	100	100	100	100,000	A
10	81,25	81,25	81.25	81,250	A
11	87,5	87,5	87.5	87,500	A
12	93,75	87,5	87.5	89,583	A
13	87,5	87,5	87.5	87,500	A
14	87,5	93,75	93.75	91,667	A
15	87,5	87,5	87.5	87,500	A

A: Excellent methodological quality; B: Good methodological quality; C: Poor methodological quality.

main components of Hippotherapy and to determine their benefits, identifying how the sessions should be addressed in order to achieve a positive effect on the elderly. For this purpose, different techniques to access the information were used, preparing a bibliographic review of the documents selected. Following the review process, a wide variety of study Types were found, ranging from *theoretical* to *quantitative*. All the studies agree that the main problems caused by ageing are loss of balance, strength and muscle mass, as well as the risk of falls. On the other hand, account should be taken of the individual characteristics of each participant, given that each person is different and will have a different response, also considering the "active and healthy ageing" approach[29], which considers that each subject will have a different rate of senescence.

The *theoretical studies* conducted[13,30,31] concluded that Hippotherapy or therapeutic horse-riding is beneficial to the elderly. All underscore improved balance and postural control, with the subsequent decrease in the risk of falls. However, a more recent review[32] suggests that the current studies on Equine-Assisted Therapies (hereinafter EAT) are methodologically weak, poorly designed, have a small sample and many of these studies lack control groups and details on the intervention

Table 5. Principal investigations and characteristics regarding the benefits of Hippotherapy in the elderly.

Title	Author	Year	Keywords	B	Abstract	Type	Sample	Benefits	Quality
The use of hippotherapy as therapeutic resource to improve the static balance in elderly individuals	Toigo, Júnior, Pinto & Ávila	2008	Physical Therapy Musculoskeletal, Equilibrium, Exercise movement, Epidemiology experimental, Women, Middle aged, Aged	WOS	Hippotherapy as a means to improve static balance in the elderly. Experimental study with a pre- and post-test Healthy, elderly individuals experience balance alterations, Hippotherapy serves to improve balance.	Quantitative study	10 women aged from 60 to 74 years	Improvements in static balance and reduction in risk of falls.	64,583
Effect of equine-assisted therapy on the postural balance of the elderly	Araujo, Silva, Costa, Pereira & Safons	2011	Equine-assisted therapy, Postural balance, Elderly, Physical therapy, Rehabilitation	WOS/ Scopus/ PubMed/ SPORT Discus	Determine whether Hippotherapy produces alterations in the balance of the elderly. Old age tends to normalise stabilometric measurements, however horse assisted interventions lead to a significant improvement in balance as well as a reduction in the risk of falls.	Quantitative study	17 elderly individuals	Reduces the risks of falls in the elderly.	81,250
Effects of hippotherapy on mobility, strength and balance in elderly	Araújo, De Oliveira, Martins, De Moura-Pereira, Copetti & Safons	2013	Hippotherapy, Muscle strength, Postural balance, Gait, Elderly.	WOS/ Scopus/ PubMed/ Cochrane	Evaluates the chronic effects of Hippotherapy on functional mobility, muscle strength and balance in elderly individuals.	Quantitative study	28 individuals aged from 60 to 84 years, men and women	Improves the strength of the lower limbs and balance in the elderly.	79,167
The Effects of Hippotherapy on Elderly Persons' Static Balance and Gait	Kim & Lee	2014	Elderly, Balance, Hippotherapy	WOS/ Scopus/ PubMed/ Cochrane	Examines the effects of Hippotherapy on the static balance and gait of the elderly.	Quantitative study	30 elderly individuals	Improves the static and dynamic balance of the elderly.	87,500
Effects of horseback riding exercise therapy on hormone levels in elderly persons	Sung-Hyoun, Jin-Woo, Seon-Rye & Byung-Jun	2015	Hormone, Exercise therapy, Horseback riding	WOS	Determines the effects of horse-riding on the normal hormone levels of the elderly. Horse therapy produces a significant increase in serotonin and cortisol	Quantitative study	20 elderly individuals	Increased serotonin and cortisol levels.	79,167
Effects of horseback riding exercise therapy on background electroencephalograms of elderly people	Kim, Cho, Kim, Lee, Brienen & Cho	2015	Exercise therapy, Electroencephalogra, Horseback riding	WOS	Analyses the effect of horse-riding therapy on the electroencephalograms of the elderly. It suggests that horse-riding therapy improves it.	Quantitative study	20 elderly individuals	The alpha power index increased significantly after horse riding, suggesting that the exercise improved the electroencephalogram.	77,083

(keep going)

Title	Author	Year	Keywords	B	Abstract	Type	Sample	Benefits	Quality
Comparative Effects of Horse Exercise Versus Traditional Exercise Programs on Gait, Muscle Strength, and Body Balance in Healthy Older Adults	Aranda-García, Iricibar, Planas, Prat-Subirana, &. Angulo-Barroso	2015	Elderly, Physical Activity, Horse Exercise, Follow-Up Study, Rural Community	WOS	Evaluates and compares the effect of 2 physical exercise programs, one traditional and the other on horseback, with regard to the physical and functional capacity of healthy elderly individuals. Horse exercises could be an alternative to traditional physical exercises for the elderly.	Quantitative study	38 healthy individuals aged over 60 years (TE= 17, HE=10, CG=11)	Horse exercise is a viable activity to maintain or improve the physical functions of the elderly. It leads to improvements in gait speed, maximum isometric force of the knee extensor muscles.	100,000
Equine-assisted therapy intervention studies targeting physical symptoms in adults: A systematic review	White-Lewis, Russell, Johnson, Cheng & McClain	2017	Equine assisted therapy, Therapeutic horse riding, Therapeutic horseback riding, Hippotherapy, Equine psychotherapy, Equine facilitated therapy, Horse riding for handicapped, Equus.	Scopus	Systematic review analysing the evidence and quality of Hippotherapy studies.	Theoretical study		Improved balance, plasticity, muscle strength, gait and cadence as well as quality of life. Improvements at a biological, psychological and social level.	100,000
Therapeutic Effects of Horseback Riding Interventions: A Systematic Review and Meta-analysis	Stergiou, Tzoufi, Ntzani, Varvarousis, Beris & Ploumis	2017	Therapeutic Horseback Riding, Hippotherapy, Cerebral Palsy, Multiple Sclerosis, Neuromuscular Disease, Elderly, Stroke, Neuromotor; Physical Disabilities.	Scopus/ SPORT Discus	Studies the possible positive effects of EAT, both at a physical and mental level. The EAT are feasible interventions for patients with balance, gait and psychomotor problems.	Theoretical study		Improves balance, gait and psychomotor disorders.	100,000
Effects of horseback riding exercise on the relative alpha power spectrum in the elderly	Sung-Hyoun Cho	2017	Horseback riding exercise Relative a-power spectrum Elderly Slow alpha power Fast alpha power	Scopus/ WOS/ Cochrane	Identification of the effects of horse-riding and the mechanical simulator on the alpha power spectrum in the elderly. Both interventions have a positive effect on the psychological stability of the elderly.	Quantitative study	31 individuals aged over 65 years (CG=15; SG=16)	Improvements in the high power electroencephalogram, activation of all areas of the electroencephalogram, improving concentration and rest. Benefits to psychological stability.	81,250
Effect of hippotherapy on older balance: a systematic review with methanalysis	Araújo, Martins, Blasczyk, Feng, Oliveira, Copetti & Safons	2018	Hippotherapy, Elderly, Balance	WOS/ SPORT Discus	Studies the existing signs of Hippotherapy in relation to the balance of the elderly, and concludes that it has a significant effect on improving the postural balance of the elderly.	Theoretical study		Improvement in the postural balance of the elderly.	87,500

(keep going)

Title	Author	Year	Keywords	B	Abstract	Type	Sample	Benefits	Quality
Impact of hippotherapy for balance improvement and flexibility in elderly people	Diniz, De Mello, Ribeiro, Lage, Júnior, Ferreira, Da Fonseca, Rosa, Teixeisa, & Espindula	2019	Balance, Flexibility, Elderly, Horse-assisted therapy.	WOS/ Scopus/ PubMed/ SPORT Discus	Information on the impact of Hippotherapy on the elderly. Ageing leads to a decrease in functional ability, strength, balance, flexibility, agility and coordination, due to neurological and muscular changes. Hippotherapy improves the functional mobility, dynamic balance and flexibility of the elderly.	Quantitative study	30 elderly individuals	Improves the functional mobility, dynamic balance and flexibility of the elderly.	89,583
An umbrella review of the evidence for equine-assisted interventions	Stern & Chur-Hansen.	2019	Animal-assisted interventions; Equine-assisted interventions; Hippotherapy; Systematic reviews; Umbrella review.	WOS	Review of current EAT documentation. The evidence from the EAT may be incorrect. The basis for the current evidence is methodologically weak. Therefore, at present, therapeutic horse-riding interventions cannot be recommended as the best practice. Higher quality studies are necessary.	Theoretical study		There are a number of benefits. However, there is a lack of scientific evidence.	87,500
An Exploration of Equine-Assisted Therapy to Improve Balance, Functional Capacity, and Cognition in Older Adults with Alzheimer Disease	Borges, Martins, Freitas, Camargos, Mota & Safons	2019	Alzheimer disease, balance, cognition, equineassisted therapy, unctional capacity	Scopus	Studies the benefits of EAT in elderly individuals with Alzheimer's, given that physical and cognitive aspects are involved. The objectives are to describe the effects of the EAT on the balance, functional capacity and cognitive level of elderly individuals diagnosed with Alzheimer's. The results show significant improvements in the Wilcoxon test.	Quantitative study	9 elderly individuals (79.7 ± 7.8 years) with Alzheimer's	Improvements in the balance and functional capacity. There is no cognitive decline.	91,667
Electromyographic analysis of stomatognathic muscles in elderly after hippotherapy	De Mello Regalo, Diniz, Lage, Ribeiro, Bevilacqua Junior *et al.,*	2020	Hippotherapy, elerdly, Electromyographic analysis, stomatognathic muscles.	WOS/ Scopus/ PubMed	Uses electromyography to evaluate the muscles of the stomatognathic system (masseter and temporalis) in the elderly before and after participation in hippotherapy. Hippotherapy promotes a reduction in the myoelectric activity of the mastication muscles in the elderly.	Quantitative study	17 elderly individuals (66.5 ± 7 years)	Reduction in the myoelectric activity of the muscles involved in mastication. (In healthy subjects there is less fibre recruitment to perform the same mastication process, compared to persons with morpho-functional changes that generate stress and fatigue).	87,500

A: Year of publication; B: Database; EAT: Equine Assisted Therapies.

made. It would therefore be recommendable to conduct longitudinal studies for the purpose of checking the durability of the benefits of this technique in the elderly.

On the other hand, the *Quantitative Studies* included in this review have a small sample, the largest one being the work by[33], with 38 subjects, and which moreover had a control group, while the smallest sample appears in a study conducted by[34], which only had a sample of 9 elderly persons with Alzheimer's. Most of the Quantitative Studies included in this review[12,33,35] focus on the beneficial effects of Hippotherapy with regard to balance, gait and the risk of falling in the elderly. It would therefore be recommendable to look at other benefits and to use other data recording tools for the investigations, such as inertial devices. These tools make it possible to quantify the internal and external load placed on users.

The studies conducted by[36,37], based on a sample of 20 participants, of which 10 were in the control group and 10 in the experimental group, and by [38], with a sample of 31 participants, 15 in the control group and 16 in the experimental group, both detail the procedure used during equestrian therapies for the purpose of identifying neurological and hormonal changes. Studies[37,39] conclude that the practice of therapeutic riding increases the alpha wave index and the electromagnetic oscillations which are indicative of stability and relaxation, promoting improved brain function and, therefore, useful in the prevention of ageing-associated neurodegenerative diseases. Furthermore, the study by[38] analyses the effects of therapeutic riding on hormone levels, which promote psychological benefits by reducing depression levels, stress and behavioural problems. This exercises a positive effect on frame of mind, sleep and agitation due to the increased levels of serotonin and cortisol. Therefore, the use of different animals to interact with the elderly for therapeutic purposes is fundamental in order to study the potential physical, psychological and social benefits.

Due to the usefulness of EAT at a physical and cognitive level, the study conducted by[34] focuses on the benefits of Hippotherapy in elderly persons with Alzheimer's, being the only study in our analysis to have a sample of individuals with a chronic degenerative disease. It shows the benefits of EAT for this group. Therefore, there is a need for Physical Activity and Sport Science investigators to conduct studies relating to Hippotherapy as a beneficial alternative to physical activity for different users, with and without a disability or previous pathologies. With regard to the study conducted by40, this was the only work analysed to use electromyography to evaluate the activation of the stomatognathic muscles (masseter and temporalis) in the elderly before and after participation in Hippotherapy sessions. These muscles, involved in mastication, increase their tension and activation (muscle fibre recruitment) with age-related morphofunctional changes, generating stress and fatigue. The study demonstrates that the Hippotherapy session leads to a reduction in the myoelectric activation of these muscles, which is beneficial. This type of work makes it clear that there is still a long way to go with regard to Hippotherapy-related investigations.

With regard to the experimental study interventions, the sessions had an approximate duration of 30 minutes[12,30,36]. However, in other Hippotherapy studies related to persons with cerebral palsy, the sessions were conducted once a week and with a duration of 45 minutes per session[7]. It would therefore be recommendable to conduct in-depth studies to compare the benefits achieved based on the duration of the sessions and their maintenance over time. Finally, there is a need to conduct further investigations on the benefits of Hippotherapy and therapeutic riding in the elderly, with larger samples, greater detail on the interventions performed, over longer periods of time and which contain quantifiable and contrastable evaluations, for the purpose of providing greater evidence that will make it possible to recognise Hippotherapy as an effective treatment.

Conclusions

Following this review of the literature, it can be concluded that Equine Assisted Therapies and Hippotherapy have beneficial therapeutic effects for the elderly if performed progressively and correctly. It is essential for these therapies to be performed by a suitably trained professional, multi-disciplinary team.

Hippotherapy interventions improve static and dynamic balance, postural balance, functional mobility, flexibility, muscle strength, gait, cadence and reduce plasticity. These beneficial effects lead to a lower risk of falls, improving the quality of life of the elderly. Furthermore, they lead to enhanced brain function and increased hormone levels, such as serotonin and cortisol, providing psychological benefits, reducing stress levels, depression and behavioural problems, also improving the quality of sleep and exerting a positive influence on the frame of mind.

Despite the fact that there are few EAT studies and that these are methodologically weak, this type of therapy is recommended in order to achieve biological, psychological and biological improvements.

Finally, the main limitation of the quantitative studies is the small sample size, lack of a control group and no follow-up of the participants, as well as the short duration of the sessions, making it impossible to generalise the results. In another respect, it would be of interest to have in-depth information on the daily habits of the subjects, as this could affect the results of the investigations.

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Conflict of interests

Work conducted within the Group for the Optimisation of Sport Performance and Training (GOERD) of the Faculty of Sport Sciences of

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Cancer-related fatigue: trigger factors and function of exercise

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Summary

Introduction: Several publications have theorized about the triggers of cancer-related fatigue, one of the side effects of the disease and its treatments that most stress cancer survivors. On the other hand, physical exercise has been analyzed as a therapy to reduce the impact of this sequel, and several institutions support its inclusion within care programs for the oncological population. However, cancer fatigue and the role that exercise plays in its control has been exposed without an overall assessment that shows its complexity and why physical exercise is so valuable to reducing it.
Objectives: The objective of this work was to review the existing evidence about triggers of fatigue in cancer, to expose how physical exercise acts on each of them to control their symptoms and achieve a comprehensive therapeutic effect.
Material and method: Several bibliographic searches were carried out to find out which were the triggers of fatigue proposed by the research, how they develop and affect the oncological patient and, finally, to what extent physical exercise would be a viable tool to control its effects.
Results: Exposed to more than twenty triggers and aggravating factors of cancer-related fatigue, we found that most of them could be prevented or at least controlled through physical exercise.
Conclusions: It is impossible to isolate some triggers from others, and some of them are inevitable as they are part of the medical treatment of the disease. Understanding the relationships between triggers and knowing the positive effects of physical exercise on each one of them is clearly useful to control this side effect.

Key words:
Cancer-related fatigue. Exhaustion. Tiredness. Therapeutic exercise.

Fatiga relativa al cáncer: factores desencadenantes y función del ejercicio físico

Resumen

Introducción: Diversas publicaciones han teorizado sobre los desencadenantes de la fatiga relativa al cáncer, uno de los efectos secundarios de la enfermedad y sus tratamientos que más estresa a los supervivientes de esa enfermedad. Por otro lado, el ejercicio físico ha sido analizado como terapia para reducir el impacto de esta secuela, y diversas instituciones apoyan su inclusión dentro de los programas de cuidado para población oncológica. No obstante, la fatiga en cáncer y el papel que el entrenamiento tiene para su control, se ha expuesto sin realizar una valoración global que muestre su complejidad y por qué el ejercicio físico resulta de tanto valor para reducirla.
Objetivos: El objetivo de este trabajo fue revisar la evidencia existente sobre los desencadenantes de fatiga en cáncer, para exponer en qué modo el ejercicio físico actúa sobre cada uno de ellos para controlar su sintomatología y conseguir un efecto terapéutico integral.
Material y método: Se realizaron diversas búsquedas bibliográficas que permitieran conocer cuáles eran los desencadenantes de fatiga propuestos por la investigación, cómo se desarrollan y afectan al paciente oncológico y, por último, en qué grado el ejercicio físico sería una herramienta viable para controlar sus efectos.
Resultados: Expuestos más de una veintena de desencadenantes y agravantes de la fatiga relativa al cáncer, encontramos que la mayoría de ellos podrían ser prevenidos o al menos controlados a través del ejercicio físico.
Conclusiones: Resulta imposible aislar unos desencadenantes de otros, existiendo, además, algunos de ellos que son inevitables al ser parte del tratamiento médico de la enfermedad. Entender las relaciones que se producen entre desencadenantes y conocer los efectos positivos del ejercicio físico sobre cada uno de ellos, es claramente útil para controlar este efecto secundario.

Palabras clave:
Fatiga relativa al cáncer. Cansancio. Astenia. Ejercicio terapéutico.

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Introduction

Defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness[1], cancer-related fatigue (CRF) is one of the consequences of the disease and its treatment which most distresses survivors[1-3]. Its pathophysiology is multifactorial, and the trigger factors proposed include: psychological disturbances, endocrine and energy metabolism dysfunctions, pain, pro-inflammatory cytokine production, and rheumatic complications[2-5].

The treatments to reduce CRF include both pharmacological and non-pharmacological interventions[1]. Of the latter, physical exercise (PE) has proven effective for reducing CRF[4-6] and is, compared with psychosocial therapies, the type of non-pharmacological intervention which leads to the greatest improvement during cancer treatment, which is precisely when CRF is at its most intense[7]. For some authors, PE affects fatigue because it improves one of its triggers, thereby reducing the overall intensity of the fatigue[8]. Many of the studies conducted have analysed the level of CRF in relation to variables such as the level of muscle strength[6], inflammatory markers[9], anaemia[10], and cardiovascular capacity[11].

The aim of this paper is to provide a narrative review of the evidence of reducing CRF through PE, analysing each trigger factor, its individual influence on the other factors, and the therapeutic effect of PE on each.

Materials and method

Three independent literature searches were carried out on the *PubMed, Google Scholar, Springer Link, SciELO*, and *Dialnet* databases. In the first search, the terms used were *Cancer-Related Fatigue* and similar *(fatigue cancer, oncologic fatigue),* selecting those publications containing information on its pathophysiology, symptoms, and/or trigger factors.

Secondly, a search was made to select publications describing each CRF trigger factor and its symptoms in cancer populations. Research conducted on healthy populations was also analysed in order to further study certain trigger factors which have not been studied too much in relation to cancer. Those sources which did not provide information on the development, physiological processes, and symptoms of the proposed trigger factors were excluded.

Finally, those publications analysing physical exercise as a tool to mitigate CRF or improve any of its trigger factors were reviewed, selecting those research and review papers giving results on the level of fatigue in cancer patients or survivors.

Results

Figure 1A shows the CRF triggers described in the literature and the direct relationships between them. On the *Y* axis, they are ordered from most to least influential on other trigger factors; and on the *X* axis, from least to most affected by other CRF factors. So, for example, chemotherapy is the first trigger factor on the *Y* axis, because it leads to alterations in more factors, but it is in eighth place on the *X* axis, because only three trigger factors can influence it. As can be seen, on average, each trigger factor is directly related to another seven, either because it affects them or is influenced by them. Those trigger factors whose degree of relationship is greater than this average are highlighted in Figure 1A.

Beyond direct relationships, trigger factors may also have indirect effects on other triggers. For example, Figure 1B shows not only the relationship between chemotherapy and nutritional problems (direct) but also how psycho-emotional complications could potentially affect the treatment by worsening the nutritional condition of the patient (indirect).

Of the trigger factors with the greatest impact, some are inevitable, such as treatment, and others are difficult to tackle. So, knowing the effects of PE on each trigger factor provides a perspective on the therapeutic potential of exercise on CRF.

Decreased activity and physical deconditioning

Because they are also key factors in the development of chronic fatigue, it has been suggested that decreased activity and the consequent drop in fitness are precursors to CRF[8]. It has been observed that decreased activity in breast cancer survivors (BCS) contributes to the development of osteoporosis[12], poorer cardiovascular health[13], and the loss of muscle mass and strength[12,14], thus aggravating CRF[3].

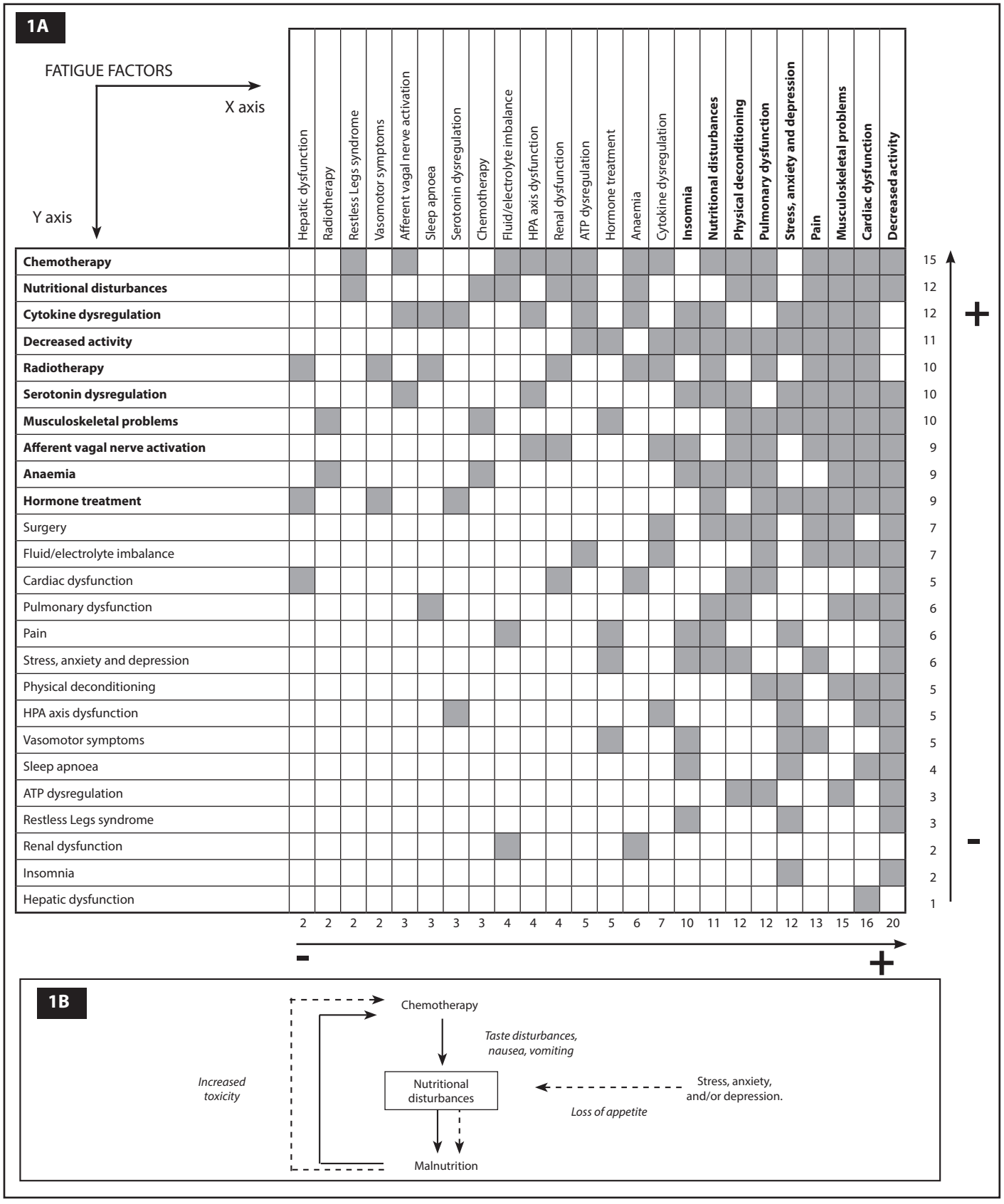
The research conducted on the effects of physical exercise on these trigger factors argues that exercise is associated with a higher level of non-sporting activity both during and after treatment[15], and can also induce further improvements in up to ten CRF triggers. Nevertheless, there are still barriers to cancer survivors (CS) acquiring exercise-related habits[16,17]. On the one hand, patients are faced with external limitations, such as a lack of information and advice on what exercise they can do, and at what intensity they can do it[16]. On the other, patients are also limited by intrinsic factors, such as muscle and joint pain, fatigue itself, the side effects specific to the type of cancer[16], and not having enough time[17].

Organ dysfunctions

The main organ dysfunctions related to cancer are cardiac, pulmonary, renal and hepatic dysfunctions. These are related to other CRF triggers in varying degrees.

- *Heart conditions:* The cardiovascular system can be affected by physical deconditioning[18], weight gain[19], dysfunctions in other organs[20], and treatment[18,19]. This type of condition is a major risk in CS and is, in fact, the leading cause of death in CS aged 65 and over[21].
- *Lung conditions:* Radiotherapy to the chest influences the development of pulmonary complications, with an increased risk of developing pulmonary fibrosis, pneumonitis, and alterations of the respiratory function[22]. In the case of chemotherapy, the mani-

Figure 1. Interactions between cancer-related fatigue triggers.



festations of toxicity are often delayed and come with coughing, fever, and fatigue[23].

– *Kidney and liver conditions:* The kidneys, which are key to eliminating the drugs used in chemotherapy, are exposed to the risk of renal failure, nephrotic syndrome, and tubulopathies[23]. Similarly, radiotherapy can produce acute hyporeninaemic hypertension and nephropathy[22]. Chemotherapy is not considered problematic for the liver unless the patient has a previous condition[23]. However, radiotherapy can alter the values of transaminases and liver disease markers such as gamma-glutamyl transpeptidase[22].

Although PE is part of rehabilitation therapies for different cardiopulmonary conditions, in cancer its use has not yet been standardised[11]. However, the general consensus is that PE is safe and tolerable for CS[11,19], and PE programmes with BCS have been observed to produce improvements in cardiovascular efficiency[9,11] and blood circulation, and reductions in cholesterol levels, blood pressure[24], attendant symptoms (including CRF), and risk of mortality from all causes[11].

Similarly, PE has proven effective in increasing maximal oxygen consumption (VO_{2max}) both during and after chemotherapy in patients with Hodgkin lymphoma[25], breast cancer[26], and solid tumours, even when being treated for anaemia[27]. Nevertheless, it is yet to be demonstrated whether PE acts on other cardiovascular health markers[11,19], such as cardiac output, the differences in oxygen content between venous and arterial blood, or defects in oxygen pathways[11].

Musculoskeletal problems

– *Cancer cachexia:* Although some authors state that a reduction in fatty tissue does not necessarily accompany cancer cachexia, there is a loss of muscle tissue, associated with a lower tolerance to the treatment, a reduction in the effectiveness of the treatment, and loss of quality of life (QOL)[28]. The cachectic state is particularly serious because it is very difficult to reverse through conventional nutritional support[28,29]. Cachexia is usually accompanied by anaemia, fatigue, and malnutrition[30], affecting protein metabolism[30,31] and, therefore, the possibility of ATP regeneration[31]. It is also associated with the development of osteoporosis[32] and can induce cardiac atrophy and dysfunction[33].

– *Bone loss:* Bone health is especially important for BCS and prostate cancer survivors (PCS)[34] because they often need androgen deprivation therapy. This indirectly affects the process of bone formation and resorption, and can increase the risk of fracture in PCS by up to five times compared to healthy men[34]. In BCS, the consequences of treatment on bone mineral density (BMD) may appear as of chemotherapy[34]. Osteoporosis means a loss of independence for older subjects and, of course, both increases the risk of fracture and impairs QoL[32].

It has been confirmed that regular exercise reduces the risk of bone problems in PCS[34]. It is also known that increased lower limb strength prevents loss of muscle mass, reduces fat percentage increases during treatment[29], and decreases the level of CRF in BCS[35]. Resistance training (RT) can, therefore, be an effective tool for PCS with androgen deprivation, due to its effects on muscle function, lean mass, and BMD[15]. The effectiveness of programmes that include impact and resistance training for the bone health of BCS has also been demonstrated[36].

Pain

Pain in cancer patients can be basal[37], appear suddenly, or be caused by neuropathic problems[37-40] due to nerve compression caused by infiltration of the tumour or treatment toxicity[39]. It is considered a contributing factor to the development of CRF[3] because it affects the patient's appetite, sleep quality, treatment adherence, mood[38], and level of activity to such an extent as to produce kinesiophobia[41].

Although pain hinders PE adherence[42], regular physical activity is known to help relieve it in various diseases, including those involving chronic pain[42,43]. Though different analgesia pathways are associated with exercise[43], it is held that the effects achieved are proportionally related to the length and intensity of the exercise, and the isometric contractions[43] associated with the modulation of the nervous system with respect to pain[42].

In BCS, it has been observed that combined PE protocols (aerobic, resistance, and flexibility)[44], Pilates[45], Qigong[46], specific exercises mobilising the arm on the affected side[47], and simply a higher level of physical activity (even while under treatment)[48] reduce the intensity of pain and its impact on daily life. Similarly, lumbopelvic stabilisation exercises in colon cancer survivors can lead to improvements in pain perception, CRF, and mood[49].

Nutritional disturbances

– *Malnutrition:* The presence of a tumour increases protein catabolism, lipolysis, insulin resistance, and energy expenditure in CS[28]. We also know that when the digestive system is affected or when patients are undergoing treatment, caloric intake falls[2,28]. If malnutrition ensues, the competition between the tumour and healthy cells for nutrients triggers hypermetabolism, leading to loss of efficiency in replenishing ATP and reducing the level of complete blood protein[30]. Malnutrition has consequences related to CRF: dysfunctional breathing patterns due to respiratory muscle atrophy, inactivity as a result of reduced functional capacity, heart muscle disorders, reduced glomerular filtration, depression, increased toxicity of the treatments[28], and damage to the peripheral nervous system[50]. Anaemia[31,51], cachexia [2,28,30,31], and electrolyte imbalances[28] may also develop. Finally, vitamin D deficiency influences the intensity of muscle pain and arthralgia, typical of hormonal treatment with aromatase inhibitors in BCS[52], while iron deficiency is associated with restless legs syndrome[53], related to CRF[3].

– *Electrolyte imbalances:* The most common alterations in CS are decreases in sodium and magnesium, and increases in potassium,

phosphates, and calcium[54]. Chemotherapy, however, especially with cisplatin, can reduce the levels of all the minerals mentioned[55]. Some of the consequences of these imbalances affect CRF. Magnesium deficiency has a negative effect on fatigue, neuromuscular excitability[55], cardiovascular health, energy production in cells, and inflammatory response[56]. Hyponatremia causes fatigue, cognitive impairment and, in severe cases, pulmonary oedema and increased risk of bone fracture[54]. Finally, hypercalcemia increases bone resorption and affects bone health[55].

On this point, the positive effect of combined exercise and nutrition protocols for improving CRF in PCS[57] and maintaining muscle mass in BCS[58] has been reported. However, there is no evidence that PE might influence appetite in CS[59].

Stress, anxiety and depression

Some authors suggest that depression predisposes patients to chronic fatigue and that it shares a common aetiology with CRF[2]. Psycho-emotional health, which is highly variable between patients, influences the level of fatigue[1,60]; to such an extent that there are studies which suggest that interventions to treat psychological and emotional disturbances could reduce its intensity[60]. Depression also affects adherence to medical treatment, particularly hormone therapy in BCS, with the consequences this might have on a patient's prognosis[61].

The effectiveness of PE to improve the emotional state of CS is recognised by the *National Comprehensive Cancer Network* (NCCN) for its ability to reduce anxiety, perceived stress, and cortisol release[62]. Improvements in psycho-emotional health during chemotherapy in BCS are also greater when physical and psychological interventions are combined, especially when the physical interventions are supervised[63]. Specifically, aerobic exercise interventions (AE)[12] and yoga[64] reduce emotional symptoms in BCS although no significant improvements in physiological parameters have been observed through yoga[64].

Sleep problems

Commonly associated with emotional issues[4], insomnia, daytime sleepiness, and night-time awakening are directly related to fatigue in CS[1,9]. They are produced in part by disruption of the natural circadian cycle, which leads, precisely, to increased susceptibility to emotional disorders[2]. They are also the result of serotonin dysregulation and HPA-axis dysfunction, due to the increase in cortisol, which negatively influences non-REM sleep[2]. Finally, the increased level of cytokines due to chronic inflammation in CS[65] also influences CRF, given their effect on daytime sleepiness, narcolepsy, and idiopathic insomnia[2]. In the case of head and neck CS, radiotherapy favours the onset of sleep apnoea, although the relationship between this sequela and CRF could be due to a higher level of cytokines[65].

Sleep problems, together with pain and CRF, significantly predict the functional decline of CS[66,67], and although not all the research conducted has found a correlation between PE and improved quality of sleep, benefits have been confirmed in BCS, especially after treatment[68]. Although more research is needed, the moderate AE protocols tested with CS[69,70] and the RT protocols tested with BCS during radiotherapy have shown clear benefits regarding this problem compared to relaxation protocols[71].

Cytokine dysregulation

Chronic inflammation causes different symptoms related to CRF[2,72], such as anaemia, depression, and cachexia[51]. The most direct relationship between cytokines and fatigue is caused by the amounts of tumour necrosis factor (TNF) receptor 1 (sTNF-r1), C-reactive protein (CRP), and interleukin IL-6, the latter being of greatest importance when it comes to symptoms such as sleep problems and depression in BCS[5,72]. The AIS protein (Anaemia-Inducing Factor) secreted by cancer tissue depresses the production of erythrocytes and the immune capacity of healthy cells, causes endothelial damage, and increases vascular permeability and the leakage of clotting factors[18], encouraging the development of anaemia. The AIS protein also stimulates lipolytic activity, playing a part in the development of anorexia and cachexia[30].

The development of cachexia depends on catabolic and proinflammatory cytokines (IL-1, TNF-α, IL-6) and anti-inflammatory cytokines (IL-4, IL-10 and IL-12), and their ability to stop or reverse the cachectic process[30]. During exercise, muscle tissue is the main source of cytokine production. However, regular muscle contraction produces myokines (anti-inflammatory) both in muscle tissue and at more distant sites which could suppress proinflammatory activity, meaning that habitual training would reduce their plasma concentration[9]. In fact, more active people, with or without a history of cancer, have lower levels of inflammatory markers (especially TNF-α, IL-6, and CPR)[6,9].

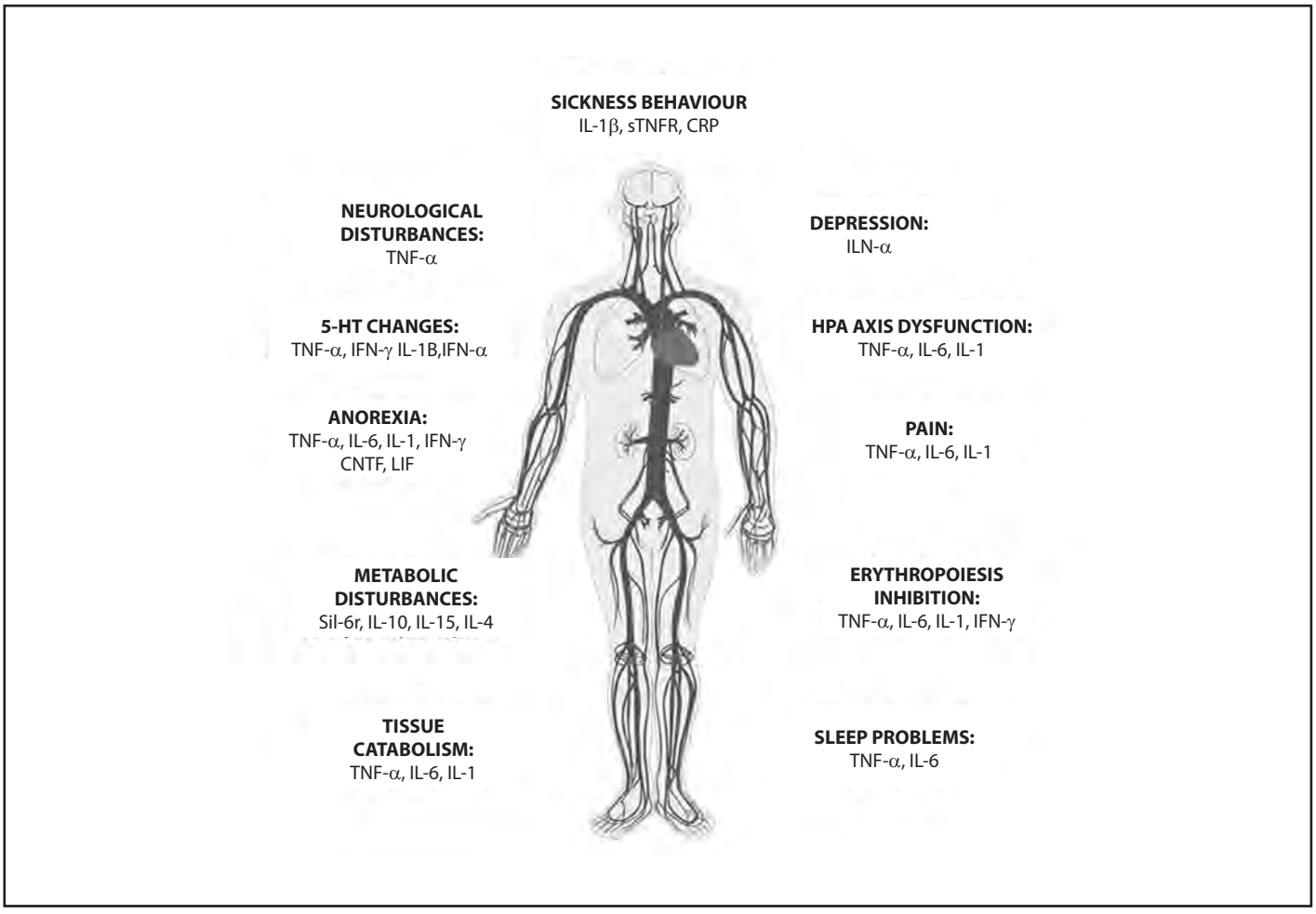
Continued PE is known to cause changes in myokine production. On the one hand, the reduction in myostatin permits less inhibition of the mammalian target-of-rapamycin (mTOR), thereby allowing increased tissue synthesis, less insulin resistance, and a reduction in sarcopenia[73]. On the other, increased secretion of IL-6 due to increased muscle mass recruitment and exercise intensity and duration induces a better response of anti-inflammatory cytokines such as IL-1Ra, IL-10, and sTNF-R, and inhibits the effects of TNF-α[73].

The release of pro-inflammatory cytokines during exercise, therefore, would be balanced by the production of anti-inflammatory cytokines and inflammatory response inhibitors[9]. Although the exact mechanisms through which exercise reduces systemic inflammation are unknown, other contributing factors, such as reduced body weight, increased insulin sensitivity, and improved endothelial function, have been suggested[9], not only at a general level but also in relation to CRF[72,74].

Anaemia

According to the NCCN, anaemia is one of the CRF factors which may be treatable[2,75,76]. Although it depends on the type of cancer and stage, its prevalence is very high, reaching 30-80% of patients[77]. It may result from nutritional problems, erythropoiesis inhibition[2], the

Figure 2. Effects of cytokines on the body.



progression of the disease, or the treatment applied[78]. Although in some cases it can cause dyspnoea on exertion, chest pain, tachycardia, depression, anorexia, and sleep disturbances[78], anaemia chiefly manifests as fatigue[76,78]. Additionally, it is important to consider that in some CS, it affects QoL and is associated with a worse prognosis and less effective treatment[78].

Treatment with erythropoiesis-stimulating agents[51,76,77] or packed red blood cell transfusions[76] yields positive results in terms of patient energy levels[75], haemoglobin concentration, QoL, and prognosis[78], although, of course, such treatment entails certain risks[76]. There is, therefore, evidence to suggest that QoL improves when the haemoglobin value improves[78].

PE in the case of anaemia would, therefore, be effective because it stimulates the production of erythrocytes[9]. Specifically, moderate-intensity AE, as occurs in healthy populations, increases blood volume through an early increase in plasma volume and a later increase in erythrocyte volume, normalising the haematocrit[10,79]. This not only improves oxygen transport (by increasing the total haemoglobin mass) but also improves cardiac output by increasing preload during diastole[10], both fundamental in reducing CRF. However, if the anaemia is severe (Hb <6 g/dL), it is advisable to put off exercise until it improves[50], although patients can still perform daily life activities.

Alterations in muscle metabolism

There are several theories about the relationship between muscle metabolism and CRF which could explain, at least in part, the feeling of tiredness that patients describe[2]. One is ATP dysregulation, produced by the damage that the cancer or its treatment causes to the sarcoplasmic reticulum of cells, which increases intracellular calcium levels. This phenomenon has several possible consequences: lower protein synthesis; alterations in calcium release, and reduced calcium sensitivity of actin and myosin[31]. Together with this, most tumours degenerate the muscle tissue, leading to tissue loss (cachexia) and different alterations in the metabolism of its nutrients[30].

In this case, it has been observed that CS have less muscle strength than healthy subjects and that those with greater muscular strength are those with lower levels of CRF[6]. Therefore, it would appear that RT could improve muscle strength and function in CS[6] by improving motor unit synchronisation, central nervous system activity, and motor neuron excitability[44]. AE, meanwhile, produces an increase in mitochondrial volume, density, and enzyme activity, which changes muscle morphology towards a phenotype which is more oxidative and, therefore, better able to synthesise ATP[10].

Treatments

Each treatment applied can influence the onset of symptoms related to CRF (Table 1). It is known that the prevalence and duration of CRF is greater in patients who have undergone chemotherapy compared to those who have not[80]; the effects of radiotherapy on vital organs, sleep disorders, and hot flashes are widely described; and arthralgias are specific to hormonal treatments.

Increases in cytokine levels are considered one of the most determining factors for CRF as a result of treatment[2,9]. Analgesics or medication for comorbidities, such as β-blockers, antidepressants, or antiemetics, can also contribute to increases in the perception of fatigue[1].

Among the effects of treatment directly related to CRF, it is found that:

- Surgery may compromise the nutritional status of patients[28] and damage peripheral or muscle nerves, favouring the onset of pain[23,81].
- Chemotherapy increases the risk of developing heart disease[12,19,82], pulmonary toxicity[83]; and ovarian failure, which accelerates bone loss in BCS[24], and reduces the protective effect of oestrogen on cytokines[52]. It can also cause nervous disturbances which affect muscle force-generating capacity, initiating atrophy and functional decline[12]. Finally, it affects the digestive system, which has nutritional consequences[23].
- Radiotherapy is also related to heart disease[13,18], lung damage[22], nerve damage, due to its effects on blood vessels and tissue fibrosis[81], anaemia[78], and nutritional disturbances[28].
- Finally, hormonal treatment with tamoxifen increases the risk of cardiovascular disease[13], pulmonary toxicity, and hot flashes[84,85]. When aromatase inhibitors are used, there is a higher incidence of hypercholesterolemia[13] (and, therefore, a greater risk of myocardial infarction[86]), joint pain, and increased bone loss and fracture risk[52].

Taking certain considerations into account before planning the training programme[14], PE, even high-intensity exercise[35,87], during chemotherapy has proven to be both safe and beneficial for cancer patients[14,24,88]. We also know that exercise induces the release of anti-inflammatory cytokines[9], and various studies report improvements in cardiorespiratory level[13,14], functionality[14,89], muscle strength, fatigue[14], body composition, and QoL[89].

During radiotherapy, the effect of exercise on CRF is equally significant; interventions which centred exclusively on resistance in BCS[90] and PCS[91] reduced the level of fatigue or prevented the decline that the subjects in the control groups suffered[90,91].

Hypothalamic-pituitary-adrenal (HPA) axis dysfunction

Cancer and/or its treatment have a direct effect on the HPA axis, altering the release of cortisol[2] and androgens[51]. For example, lower decreases in cortisol levels during the day and high concentrations at night[6] have been observed in breast and ovarian CS suffering from CRF, and low testosterone levels related to fatigue have been observed in male CS[75]. Cortisol is also released in situations of psychological or

Table 1. Side effects of the treatments associated with cancer-related fatigue.

	Oncological T.	Analgesic T.	Others
Heart condition	CT, RT, TX & AI		Antidepressants
Lung condition	CT, RT & TX	Buprenorphine, morphine & oxycodone	
Nutritional disturbances	S, CT, RT	Oxycodone	
Anaemia	CT, RT		
Mood swings		Tramadol	
Liver damage	CT, RT		
Nerve damage	S, CT, RT		
Kidney damage	CT, RT		
Fatigue	CT	Oxycodone & tramadol	Anticonvulsants
Insomnia	CT	Corticosteroids & oxycodone	
Kidney failure		Morphine & paracetamol	
Loss of muscle contractility	CT		
Bone loss	CT, AI		
Vasomotor symptoms	TX		
Drowsiness		Codeine, oxycodone & tramadol	Anticonvulsants

S: surgery; CT, chemotherapy; RT, radiotherapy; TX: tamoxifen (hormone treatment); AI: aromatase inhibitors (hormone treatment).

physical stress[2], but when stress becomes chronic, the production of proinflammatory cytokines increases and the functioning of the HPA axis is disrupted, reducing the release of cortisol and leading to symptoms compatible with CRF[31].

Based on the research conducted, we know that the hormone release which takes place in healthy subjects during AE could be altered in BCS[92], it having been observed that the reduction in cortisol that PE produces is less pronounced in BCS compared to healthy women following a single session of moderate-intensity AE[92]. We also know that there is no significant difference in cortisol levels between active and inactive BCS[93]. However, interference with the endocrine system caused by medication, sleep disturbance, psychological stress, and other factors means it is not possible to clearly describe the relationship between PE and cortisol, and further research into the subject is needed[93].

Serotonin dysregulation

Serotonin (5-HT) regulates processes such as the circadian cycle, mood, pain, appetite, and cardiovascular and muscle functions[2], processes which influence the intensity of CRF[3]. It has been described that in cancer patients, the increase in serotonin in the brain appears to decrease the nerve impulse to the muscle fibres[2,3] and affects vagal afferent nerve activation, reducing the ability to carry out PE[2]. The HPA axis is also directly affected by serotonin, with an increased release of corticotropin releasing hormone (CRH), antidiuretic hormone (ADH), and adrenocorticotropic hormone (ACTH)[2].

When healthy subjects perform PE, two mechanisms influence the increase in brain serotonin content and, consequently, the acute increase in fatigue[94]. Firstly, the depletion of glycogen reserves (should it occur), and secondly, the increase in the brain of the concentration of tryptophan, the precursor of 5-HT synthesis[94]. However, decreases in cortisol and serotonin have been reported in older female BCS after 12 weeks of AE (four weekly walking sessions), with a consequent improvement in sleep quality, but not in the level of CRF[95]. Even so, it is not known whether exercise could normalise the metabolism of serotonin in CS in the long term[6].

Vagal afferent nerve activation

It has been studied that a healthy vagus nerve could inhibit the inflammation caused by cancer and that its activity, reflected in the basal heart rhythm, is associated with the prognosis of various types of cancer[96]. For example, a high basal heart rhythm and recovery heart rate (HR rec) are associated with a worse prognosis for people who have been operated on for lung cancer[97]. When there is inflammation, caused by the disease and its treatment, a peripheral release of cytokines occurs, activating vagal afferent nerves signals. This leads, among other things, to suppression of somatic muscle activity, sickness behaviour[2,31], and changes in the hypothalamus[31].

It is known that AE improves the aerobic capacity of cancer patients, their HR_{rec}, and autonomic control of cardiac muscle both during and after treatment, especially in patients with lesser cardiovascular capacity[98]. Although these results are not reflected in the level of CRF, improved vagal tone may also reduce the risk of cardiac arrhythmias, which could have a positive impact on the survival of CS[98].

Vasomotor symptoms: hot flashes

Typical during menopause, these mainly affect survivors who have received hormone therapy, such as BCS[99] and PCS[100]. They are considered fatigue triggers because they are a bothersome symptom which affects daily activities[84], QoL[84,101], treatment adherence[101], and rest[84,101,102], and may augment the perception of pain and fatigue[84].

Although PE is beneficial for controlling hot flashes in healthy women[103], it is generally advised that BCS avoid any increases in body temperature[99]. In these women, breathing exercises and progressive relaxation seem to be effective ways of reducing the frequency of this event[100,104].

Conclusions

Having reviewed the triggers of CRF, it is possible not only to appreciate the complexity of this side effect but also to recognise that it presents a significant number of physiological alterations which also have effects on other processes and increase the risk of developing comorbidities. Similarly, it can be observed that there are fatigue triggers inherent in the disease and, from there, unavoidable triggers and other factors which could be tackled. In this light, it would be appropriate to assess the advisability of applying preventive therapies for CRF, such as physical exercise.

One of the conclusions of this review is that decreased activity and physical deconditioning are not only CRF triggers in themselves but that they are also greatly aggravated by a great many of the factors related to this side effect (Figure 1A). Perhaps the most important conclusion of this review is that physical exercise is capable of reversing these two factors (being directly related to them) and that it also has positive effects on many other CRF triggers.

This review also concludes which CRF triggers could be improved through physical exercise, either during or after treatment. In addition to improving CRF directly as the main outcome, there is evidence that physical exercise improves CRF through its positive effects on organ dysfunctions, musculoskeletal problems, pain, and the effects of treatment (Table 2). There is also evidence that physical exercise has positive effects on other triggers, such as psycho-emotional disturbances, sleep problems, cytokine dysregulation, alterations in muscle metabolism, sleep dysregulation, and vagal afferent nerve activation. The action of physical exercise on CRF in these cases would be indirect but equally effective in reducing their overall intensity. Only in three of the fifteen CRF triggers is there no evidence of physical exercise having a positive effect.

Table 2. Effects of physical exercise on cancer-related fatigue triggers.

Decreased activity and physical deconditioning	CS: ↑ Level of autonomous PA15
Organ dysfunctions	BCS: ↓ blood pressure and cholesterol; → blood circulation[24],↓ CRF symptoms and mortality[11]; ↑ cardiovascular efficiency, VO_{2max}[10] HLS: ↑cardiovascular efficiency, VO_{2max}[10]
Musculoskeletal problems	PCS: ↓ Bone problems[34]; → muscle mass and BMD[15] BCS: RT→ muscle mass and ↓ fat percentage during treatment[29]; ↓ CRF[35]; ↑ lumbar BMD[36]
Pain	BCS: ↓ reduces pain intensity and impact[44-48] CCS: ↓ reduces pain intensity and CRF; ↑ psycho-emotional health[49]
Nutritional disturbances	CS: NE on increased appetite[59] PCS: PE + diet ↓ CRF[57] BCS: PE + diet → muscle mass[58]
Stress, anxiety and depression.	CS: ↓ anxiety, stress and cortisol release[62] BCS: ↓ emotional symptoms[12,64]; ≈ physiological parameters[64]
Sleep problems	CS: AE ↑ sleep quality[59,70] BCS: RT ↑ sleep quality[71]
Cytokine dysregulation	CS: ↑ inflammatory cytokines and myokines[9]
Anaemia	CS: ↑ erythrocyte production[9], → normalisation of haematocrit[10,79]
Alterations in muscle metabolism	CS: RT → motor unit synchronisation, CNS activity[44], ↑ strength and functionality[6] AE↑ mitochondrial ATP synthesis capacity[10]
Treatments	CS: ↑ cardiorespiratory level[13,14], functionality[14,89], muscle strength[14], and QoL[89]; ↓ inflammation[9], CRF[14]; → body composition[89] BCS & PCS: RT ↓ CRF[90,91]
HPA axis dysfunction	CS: NE BCS: → cortisol[92]
Serotonin dysregulation	CS: NE BCS: ↓ 5-HT,↑ sleep quality, ≈ CRF[95]
Vagal afferent nerve activation	CS: ↑ aerobic capacity,→ vagal tone, ↓ cardiac arrhythmia risk, ≈ CRF[98]
Vasomotor symptoms	CS: NE

5-HT: serotonin; PA: physical activity; QoL: quality of life; BMD: bone mineral density; AE: aerobic exercise; PE: physical exercise; RT: resistance training; HPA: hypothalamic-pituitary-adrenal; CS: cancer survivors; CCS: colon cancer survivors; BCS: breast cancer survivors; PCS: prostate cancer survivors; HLS: Hodgkin lymphoma survivors; CNS: central nervous system.
→: effect on; ↑: increases; ↓: decreases; ≈: does not change; NE: no evidence

In all, the findings of this review clearly describe the therapeutic value, at least as a coadjuvant, of physical exercise on the different side effects of cancer, making the inclusion of exercise programmes highly recommendable as preventive therapy for CRF.

Conflict of Interests

The authors do not declare any conflict of interests.

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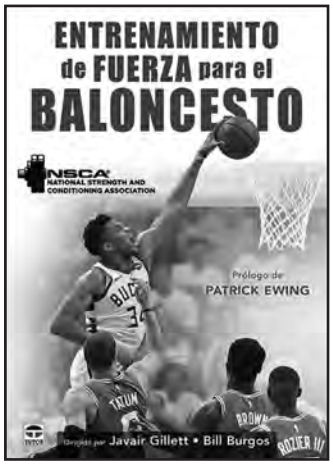

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Desarrollado con la experiencia de la *National Strength and Conditioning Association* (NSCA), este libro muestra cómo diseñar programas de entrenamiento de fuerza, que desarrollarán el potencial de tus deportistas sobre la cancha, basándose en las exigencias físicas de cada posición: base, alapívot, pívot, escolta y alero. También encontrarás lo siguiente: 20 protocolos de pruebas para la fuerza, potencia, velocidad, agilidad y capacidad aeróbica; 18 ejercicios para todo el cuerpo con 2 variantes; 19 ejercicios para la parte inferior del cuerpo con 3 variantes; 17 ejercicios para la parte superior del cuerpo; 11 ejercicios para la zona media (core) con 5 variantes; y 16 ejemplos de programas específicos en relación con la temporada.

Respaldado por la NSCA, y con el conocimiento y la experiencia de exitosos profesionales de la fuerza y el acondicionamiento físico del baloncesto en diferentes niveles, hasta el profesional, este libro es un autorizado recurso para crear programas de entrenamiento de fuerza, específicos del baloncesto, que ayuden a tus deportistas a optimizar su fuerza y transferirla con éxito a la cancha.

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Nueva edición de la fuente definitiva de información relativa a la hipertrofia muscular

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Este libro es el recurso más completo del mundo sobre hipertrofia muscular y su aplicación al diseño de programas de entrenamiento. Escrito por Brad Schoenfeld, reconocido experto internacional de la materia, constituye la explicación definitiva de todo lo relacionado con la hipertrofia muscular: los mecanismos de su desarrollo, la forma en que cambia el cuerpo estructural y hormonalmente cuando se expone a estrés, las maneras de diseñar los programas de entrenamiento más eficaces y las pautas nutricionales para obtener cambios hipertróficos.

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