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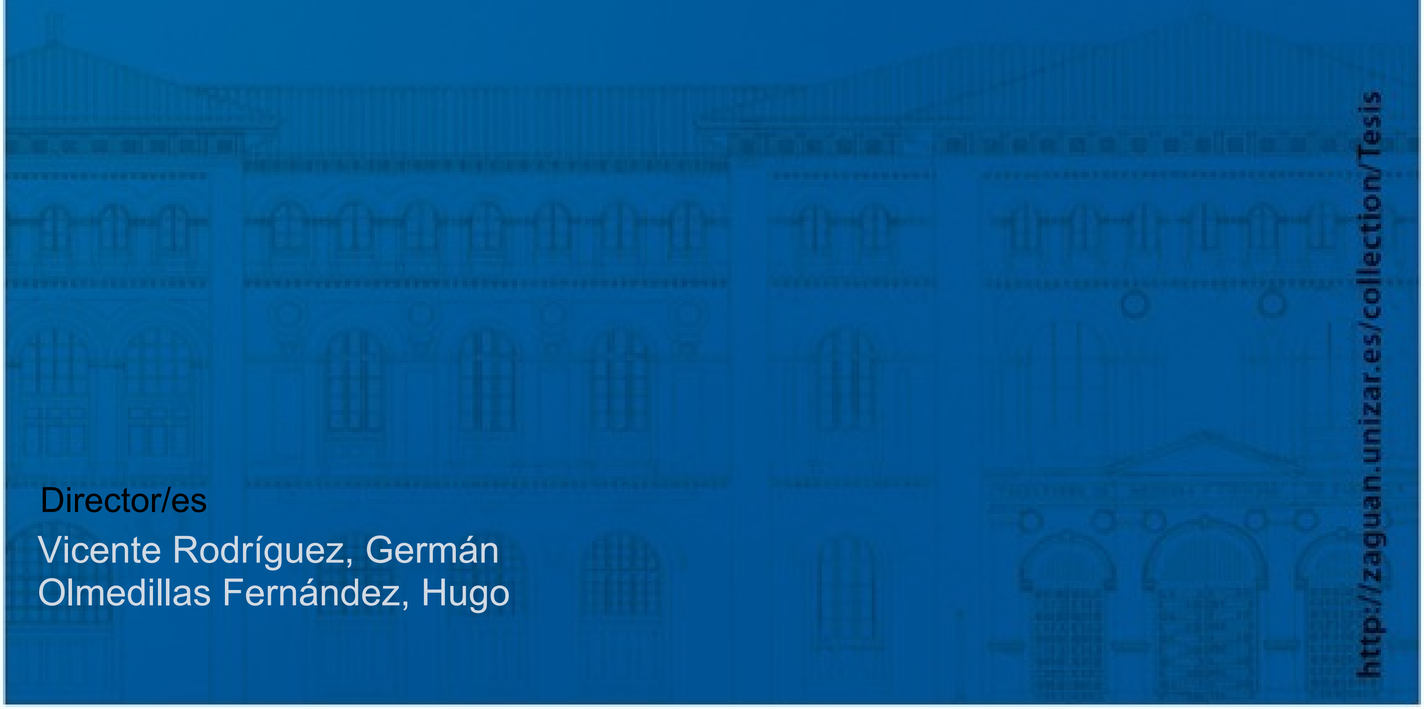
Rony Fares

Effect of recovery on the treatment of delayed onset muscle soreness and muscle performance



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EFFECT OF RECOVERY ON THE TREATMENT OF DELAYED ONSET MUSCLE SORENESS AND MUSCLE PERFORMANCE

Autor

Rony Fares

Director/es

Vicente Rodríguez, Germán
Olmedillas Fernández, Hugo

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TESIS DOCTORAL

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EFFECT OF RECOVERY ON THE TREATMENT OF DELAYED ONSET MUSCLE SORENESS AND MUSCLE PERFORMANCE

RONY FARES

Programa de Doctorado en Ciencias de la Salud y del Deporte

Facultad de Ciencias de la Salud y del Deporte

Universidad de Zaragoza

España

EFFECT OF RECOVERY ON THE TREATMENT OF DELAYED ONSET MUSCLE SORENESS AND MUSCLE PERFORMANCE

EFECTO DE LA RECUPERACIÓN EN EL TRATAMIENTO DEL DOLOR MUSCULAR DE INICIO RETARDADO Y EL RENDIMIENTO MUSCULAR

Rony Fares

الى الذي علمني معنى الحياة و الايمان ، الى الذي طبع في شخصيتي الكرامة و العنفوان ،
الى من كان يدعوني عند عودتي الى البيت بعد نهار عمل طويل"ايها المناضل" ،
الى الذي افتخر و ارفع رأسي لاني احمل اسمه ، الى الذي كنت دائماً اتطلع ان اصبح في احسن الاحوال نصف ما هو عليه، الى أبي.

A celle qui m'a appris à voir le monde plus beau à travers ses yeux bleus, à celle qui grâce à son altruisme a gravé dans mon âme l'amour de la vie et de l'autrui, à celle qui m'a transmis la valeur des rêves et des ambitions, à celle qui malgré tout, reste toujours optimiste et gaie, à mon premier amour, à Maman.

A mis supervisores y directores German y Hugo, su ayuda y apoyo marcaron la diferencia y elevaron el valor de mi trabajo.

“God, grant me the serenity to accept the things I cannot change, courage to change the things I can, and wisdom to know the difference.”
— Reinhold Niebuhr

“Education is the most powerful weapon which you can use to change the world.”
— Nelson Mandela

“You only live once, but if you do it right, once is enough.”
— Mae West

EFFECT OF RECOVERY ON THE TREATMENT OF DELAYED ONSET MUSCLE SORENESS AND MUSCLE PERFORMANCE

DIRECTORES DE TESIS:

Dr. Germán Vicente Rodríguez	**Dr. Hugo Olmedillas Fernández**
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Universidad de Zaragoza Email: joseant@unizar.es	Universidad de Oviedo Email: crespoirene@uniovi.es	Universidad de Caceres Email: golcina@unex.es

Suplente 1º	**Suplente 2º**
Dr. Miguel Enrique Del Valle Soto	**Dr. Jorge Pérez Gómez**
Departamento de Morfología y Biología Celular	*Departamento didáctica de la expresión musical, plástica y corporal.*
Universidad de Oviedo Email: miva@uniovi.es	Universidad de Caceres Email: jorgepg100@gmail.com

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Publications included in the doctoral thesis

A. Chapter 4.1.

Fares, R, Vicente-Rodríguez, G, and Olmedillas, H. Effect of active recovery protocols on the management of symptoms related to exercise-induced muscle damage (EIMD): A systematic review. ***Strength Cond J*** In press, 2021. [Published]

B. Chapter 4.2.

Fares, R, Kairouz, K, Rodríguez, MÁ, Vicente-Rodríguez, G, Crespo, I, Del Valle, M, and Olmedillas, H. Effect of massage and cryotherapy on the management and treatment of delayed onset muscle soreness. [Prepared for submission]

C. Chapter 4.3.

Fares, R, Rodríguez, MÁ, Kairouz, K, Vicente-Rodríguez, G, and Olmedillas, H. Effects of uphill high-intensity interval exercise on muscle damage and exercise performance during recovery. ***J Sports Med Phys Fitness***, 2020. [Published]

Conference papers

- **"Effect of a high speed running protocol on Delayed Onset Muscle Soreness (DOMS) and muscle performance among healthy and active adults"** presented in European College of Sports Science (ECSS) congress, in 2019, Prague – Czech Republic.

- **"Intermittent Pneumatic Compression Effect on Eccentric Exercise-Induced Strength Loss",** presented in ECSS virtual congress, in 2020.

- **"Effect of active recovery protocols on the management of symptoms related to exercise-induced muscle damage (EIMD): A systematic review",** presented in 1st Sports Science International Congress, in 2020, in Cáceres - Spain.

- **"Combined effect of Massage and Cold Water Immersion (CWI) on the treatment of symptoms related to Exercise Induced Muscle Damage (EIMD)"**, presented in ECSS virtual congress, in 2021.

List of Abbreviations

1RM: 1 maximal repetition.
ANOVA: Analysis of variance.
ATP: Adenosine triphosphate.
Ca^{2+}: Calcium.
CK: Creatine kinase.
CMJ: Counter movement jump.
CNS: Central nervous system.
CRP: C-reactive protein.
CS: Compression sleeves.
CTR: Control.
CV: Coefficient of variation.
CWI: Cold water immersion.
DOMS: Delayed onset muscle soreness.
E-C: Excitation-contraction.
EIMD: Exercise induced muscle damage.
FO: Functional overreaching.
FPS: Foot-pound-second.
HIIT: High intensity interval training
HR: Heart rate.
Hz: Hertz.
IL: Interleukin.
IPC: Intermittent pneumatic compression.
K^{+}: Potassium.
LCE: Light concentric exercise.
LDH: Lactate dehydrogenase.
LT: Lactate threshold.
MB: Myoglobin.
MRI: Magnetic resonance imaging.
MU: Motor units.
MV: Maximal velocity.
MVC: Maximal voluntary contraction.
MVIC: Maximal voluntary isometric contraction.
NFO: Non-functional overreaching.
OTS: Over training syndrome.
$PGE_{2:}$ Prostaglandin.
Pi: Inorganic phosphate.
PPT: Pressure point threshold.
PR: Passive rest.
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses.
PT: Peak torque.
RCT: Randomized controlled trial.
ROM: Range of motion.

ROS: Reactive oxygen species.
RPE: Rating of perceived exertion.
RPF: Rating of perceived fatigue.
SD: Standard deviation.
SPSS: Statistical Package for the Social Sciences.
SR: Sarcoplasmic reticulum.
SSC: Stretch-shortening cycle.
TNF: Tumor necrosis factor.
TQR: Total quality recovery.
TW: Total work.
u-HIIE: Uphill high-intensity interval exercise.
VAS: Visual analogue scale.

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General Abstract

The practice of intensive physical exercise requires an appropriate recovery in order to avoid overtraining syndrome and the emergence of sports injuries. Recovery is highly essential in helping athletes to deal with mental and physical fatigue without compromising their performance level when practice and training are resumed. Following any unaccustomed activity, it has been demonstrated that the choice of the proper recovery plays an important role in athletes' performance, and the management of soreness and other related symptoms such as inflammation, swelling and decrease in range of motion, strength, speed, and flexibility.

The selection of a specific recovery protocol and the corresponding subsequent parameters, such as intensity, duration, and frequency, is still unclear, and its impact and efficiency on muscle disorder, weakness, pain, and performance remains controversial and inconclusive. Consequently, this doctoral thesis aims to highlight and to develop a deep insight into the scientific background and validity of recovery protocols reported in the literature. Moreover, the main objective is to demonstrate the effect of active and passive recovery protocols on pain and muscle performance among young active individuals.

To respond to these objectives, a systematic review, a randomized controlled trial, and a quasi-experimental study were performed. The first study systematically reviewed the literature from five databases according to the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. The benefits and limitations are identified in this paper, providing a practical approach for active individuals, coaches, and therapists regarding what type of active recovery could enhance performance level following strenuous activities. Moreover, a quasi-experimental study in which a sample of 35 participants was examined for three days. The methodology in this study was based on an intra-subject

comparison of both legs, to investigate the effectiveness of a combination of massage and cold water immersion (CWI) on pain, jump height, maximum isometric force, and gait kinematic variables. Finally, a randomized controlled trial with a crossover design included 31 young active participants. A four-day experiment was conducted in two identical sessions separated by a three-week period, to test an active recovery protocol consisting of an uphill high-intensity interval exercise. In this study, pain, creatine kinase (CK), muscle inflammation, jump height, sprint speed, and one repetition maximum (1RM) were assessed and analyzed.

The results of this doctoral thesis show that active recovery in general, including running and jogging, exercise in water, yoga, and isolated muscle contractions offers limited management on soreness. Furthermore, inflammation and muscle stiffness following intensive exercise were reduced by general physical activity and yoga, respectively, and the decrease in muscular strength is less following exercise in water. Additionally, a combination of massage and CWI does not seem to significantly decrease soreness, increase muscle performance, or improve gait parameters compared to no treatment. Finally, an active recovery protocol consisting of uphill high-intensity interval exercise does not offer a remarkable benefit in comparison with passive rest, however its implementation does not increase soreness nor aggravate muscle performance, thus it can be performed without any harm.

Resumen General

La práctica de ejercicio físico intenso requiere de una adecuada recuperación para evitar el síndrome de sobre entrenamiento y la aparición de lesiones deportivas. La recuperación es esencial para ayudar a los atletas a manejar la fatiga mental y física sin comprometer el nivel de rendimiento cuando se reanuda la práctica y el entrenamiento. Se ha demostrado que la elección de una correcta recuperación posterior a un ejercicio intenso no habitual, juega un papel importante en el rendimiento de los deportistas y en la forma en que son capaces de manejar el dolor y otros síntomas relacionados como la inflamación, la disminución del rango de movimiento, de la fuerza, de la velocidad, y de la flexibilidad.

La selección de un protocolo de recuperación específico y los correspondientes parámetros (intensidad, duración, frecuencia…) aún no está clara, y su impacto y eficacia en el trastorno muscular, la debilidad, el dolor y el rendimiento siguen siendo controvertidos y no concluyentes. En consecuencia, esta tesis doctoral tiene como objetivo identificar y desarrollar una visión profunda sobre los antecedentes científicos y la validez de los protocolos de recuperación reportados en la literatura y mostrar el efecto de protocolos de recuperación activos y pasivos sobre el dolor y el rendimiento muscular entre individuos jóvenes activos.

Para dar respuesta a estos objetivos, se realizó una revisión sistemática, un ensayo de control aleatorizado y un estudio cuasi experimental. En el primer estudio se realizó una revisión sistemática de la literatura en cinco bases de datos, de acuerdo con las pautas descritas en la declaración de elementos de informes preferidos para revisiones sistemáticas y meta-análisis (PRISMA). En este trabajo se identifican los beneficios, y limitaciones, proporcionando un enfoque práctico para individuos activos, entrenadores y terapeutas acerca de qué tipo de

recuperación activa podría mejorar el nivel de rendimiento después de actividades extenuantes. Adicionalmente, un estudio cuasi-experimental, en el que se examinó una muestra de 35 participantes durante tres días. La metodología del estudio se basó en la comparación intra-sujeto de ambas piernas, que permitiera demostrar la eficacia de una combinación de masaje e inmersión en agua fría sobre la percepción del dolor, la altura del salto, la fuerza isométrica máxima y variables cinemáticas de la marcha. Finalmente se diseñó un ensayo controlado aleatorio con un diseño cruzado incluyó a 31 jóvenes participantes activos. Se llevó a cabo un experimento de cuatro días, en dos sesiones idénticas separadas por un período de tres semanas, para probar un protocolo de recuperación activa que consistía en un ejercicio de intervalos de alta intensidad en pendiente positiva. En este estudio, se evaluaron y analizaron el dolor, la creatina-quinasa, la inflamación muscular, la altura del salto, la velocidad del sprint y la repetición máxima (1RM).

Los resultados de esta tesis doctoral mostraron que la recuperación activa en general, incluyendo correr y trotar, ejercicio en el agua, yoga y contracciones musculares aisladas ofrece un manejo limitado del dolor. Además, la inflamación y la rigidez muscular después del ejercicio intensivo se redujeron con la actividad física general y el yoga, respectivamente, y la disminución de la fuerza muscular es menor después del ejercicio en el agua. Además, una combinación de masaje e inmersión en agua fría no parece disminuir significativamente el dolor, aumentar el rendimiento muscular o mejorar los parámetros de la marcha en comparación con ningún tratamiento. Y finalmente, un protocolo de recuperación activa que consiste en ejercicio en intervalos de alta intensidad cuesta arriba no ofrece un beneficio destacable en comparación con el descanso pasivo, sin embargo su implementación no aumenta el dolor ni agrava el rendimiento muscular, por lo que se puede realizar sin ningún daño.

Chapter 1: Introduction and Justification

1.1. Fatigue and associated symptoms

Exercise-induced fatigue or muscle fatigue is expressed by a reversible decrease in the capacity to generate power during and following prolonged or repeated muscle activity[1], with recovery occurring immediately within the first hour, and partially, at a slower rate up to several days to become completely reversible[2]. Assessing maximal voluntary contraction (MVC) under isometric conditions is crucial, if muscle strength remains decreased compared to the value before the activity, then a state of muscle fatigue is witnessed[3]. For example, a significant decrease in both voluntary isometric and concentric activation of the quadriceps femoris was found following 2000 m of rowing[4]. Athletic performance and other intensive prolonged activities are also limited.

A linear relationship has been shown between the perception of fatigue, measured by a scale representing the rate of perceived fatigue (RPF) and the decline in MVC following two bouts of fatiguing exercise[5]. Performance and perceived fatigability are both associated and can affect physical and cognitive functions[6]. Consequently, physiological and psychological parameters are both involved in the phenomenon of fatigue. A strong correlation was observed between RPF and objective measurements, such as heart rate, blood lactate concentration, oxygen uptake, carbon dioxide production, respiratory exchange ratio, and ventilation rate, measured during intensive bouts of exercise and the following periods of rest[7].

Muscle fatigue originates both at a central and a peripheral level[3,8,9]. When changes are taking place at the neuromuscular junction, fatigue is considered peripheral, however, when it is caused by a decline in motoneuronal output leading to decrease in muscle force, the central nervous system (CNS) becomes the origin and fatigue is considered central. In this case, the contractile filaments are affected by the metabolic changes that accompany fatigue, the capacity of oxygen transport is influenced, afferent nerves and efferent motor commands from the brain are disturbed, and the interaction of contractile proteins within the muscle fibers is perturbed inducing a decline in muscle strength[1,3,8,9].

The decline in muscle force following high intensity exercise has been thoroughly investigated. However, it is crucial to mention that considering acidosis behind the contractile failure and particularly, considering it arising from the formation of lactate, which is a single molecule, is no longer a valid theory, therefore, acidosis and lactate production cannot be treated as fatigue-inducing events[10]. In fact, it is also believed that acidosis might have a protective effect against fatigue[11]. Research has explained that the decline in force production is caused by an increase in the concentration of inorganic phosphate (Pi), inhibiting the fiber maximal force. This inhibition is caused by reducing the release of calcium (Ca^{2+}) from the sarcoplasmic reticulum (SR), the precipitation of CaPi reducing the number of active crossbridges and the sensitivity of the myofibrillar membrane to Ca^{2+}. Furthermore, twitch relaxation velocity is decreased by reducing the detachment of isometric crossbridge rate caused by a slow myofibrillar ATPase following the increased concentration in Pi[8]. In a study using single fibers isolated from a mouse muscle, fibers were stretched to 125% of their optimal length following ten eccentric contractions, it was shown that maximal Ca^{2+}-activated force was not significantly affected and that maximal isometric force decreased by a 28%[12]. Moreover, large and rapid fluxes of potassium ion (K^+) concentration including an increase in intracellular K^+ with a decrease in extracellular K^+ were also reported during an intensive exercise and were considered responsible for muscular fatigue. Following this disruption in K^+ homeostasis, depolarization of transverse tubules and the sarcolemmal membrane occurs, causing a slowing of the conduction velocity of the muscle fiber action potential and affecting the onset of muscle contraction. Consequently, peripheral fatigue is induced by metabolite accumulation through compromised neuromuscular propagation and reduced contractile activity[9].

In addition to the metabolic factors mentioned above, fatigue and decrease in muscular contraction are also caused by neural factors. Concentrations of several neurotransmitters: 5-hydroxytryptamine (Serotonin), Dopamine, and Noradrenaline in the brain are modified by exercise, and accompanied by changes in the CNS leading to a central fatigue state. Motor units (MUs) are activated as a result of excitation and inhibition from the CNS on the spinal motoneurons through a central neurotransmitter. Each muscle contraction is controlled in terms of strength and timing by the firing of the motoneurons. MUs normally fire at a rate of 5-8 Hz when they are recruited in healthy conditions, when non-fatiguing voluntary contractions take place in humans, this firing rate increases and reaches a mean of 50-60 Hz[13]. The amount of activated muscle tissue is controlled by an orderly fashion of recruitment/derecruitment of the MUs on the basis of the motoneuron size[14]. During fatiguing maximal contractions, a decrease in the firing rate of MUs is noticed, and this is due to several factors: 1) A decrease in the excitability of the motoneurons to excitatory synaptic input caused by repetitive firing, 2) a lower excitatory drive from the motor cortex or other supraspinal area to the motoneurons, 3) an increase in the firing of group III/IV muscle afferents leading to a decrease in motoneuron firing, 4) a decrease in the firing of sensory receptors of muscle spindles leading to a decrease in the firing of group Ia muscle afferents, an increase in the presynaptic inhibition, and a decrease in motoneuron firing, and 5) the presence of a feedback interaction of group III/IV muscle afferents with cardiovascular and respiratory processes through the autonomic nervous system, in order to improve blood flow and oxygenation, thus delaying the emergence of muscular fatigue[15–17].

The type of exercise leading to muscular fatigue plays an important role in determining the neuromuscular alterations. Generally, fatigue is evaluated under two types of prolonged exercise: isometric or global dynamic exercise. During isometric exercise, sustained isometric contractions are performed until voluntary exhaustion or for a certain time, targeting a particular muscle group, whereas global dynamic exercises include general activities such as running, cycling, or skiing, involving different muscle groups and are practiced under dynamic conditions[3]. Dynamic prolonged exercises are considered to be closer in nature to everyday sports activities than isometric contractions, making it beneficial in identifying all the mechanisms responsible of fatigue and contributing to better training outcomes and performance optimization. As for isometric sustained contractions, central fatigue is greater in the case of long duration bouts exceeding two hours than in the case of shorter more intensive bouts[18].

1.2. Muscle Damage versus muscle fatigue

Muscle fatigue might lead to muscle damage, in some cases, but one phenomenon might be present without the second. Following isometric or concentric dynamic exercises, muscular fatigue might occur, without being necessarily associated with contractile alterations and damage. Likely, muscle damage is not always the result of muscle fatigue and might happen without being linked to an intensive exercise such as in some pathological conditions like rhabdomyolysis, contusion or excessive stretching[19]. After a single eccentric bout of exhaustive high intensity exercise, fatigue occurs and a decrease in muscle force is observed, this is stated as exercise-induced fatigue. Exercise-induced fatigue leads to better performance and muscular adaptations by creating an acute overload or training stimulus to the athletes, and it is defined as a protective mechanism prior to any potential damage[20]. In case fatigue was absent or even delayed, muscle cells and supportive tissues would experience structural contractile alterations during exercise, leading to exercise-induced muscle damage (EIMD) or any other type of injury[19]. EIMD is mainly characterized by stretched muscle fibers, which increases the risk of muscle damage and leads to very slow recovery compared to exercise-induced fatigue[2,20]. For a better understanding, this situation is divided into an initial phase, which is well established during the intensive bout, and a secondary that is associated with a delayed inflammatory reaction. Both phases lead at a later stage to tissue remodeling[19,21,22]. In addition to myofibrillar disruption, strength loss and inflammatory reaction, EIMD is also accompanied by delayed onset muscle soreness (DOMS), swelling of the muscle and a limited range of motion[23].

1.3. Muscle damage and strength loss

In the following section, strength loss will be discussed and explained as a symptom associated with muscular alterations. The decrease in muscular strength is considered the most valid indirect marker of muscle damage, and the representative of the magnitude of histological damage[24,25]. From a histopathological point of view, strength loss can be explained by many factors[26]:

1. In reference to the muscle fibers, internal and external damages to force-bearing structures have been considered to be for the most part responsible for strength loss after eccentric contractions. The damage caused is considered a major marker of muscle injury however studies did not show a strong association with strength loss when the amount of damage and the time of injury were taken into account[26]. Therefore, a damage of 80% of muscle fibers was found in elbow flexors immediately and two days following an eccentric bout of exercise, whereas strength loss was only 32% and 39%, respectively, at these time

points[27]. Similarly, after a second bout of eccentric contractions, the longitudinal sections of the vastus lateralis of participating subjects showed a damage of 23% of the muscle area with no reported decrease in quadriceps strength[28].

2. Failure of excitation-contraction (E-C) coupling as a result of disruption of the contractile and structural proteins is another factor behind strength loss[29]. E-C coupling is defined as the sequence of events starting from the acetylcholine release at the neuromuscular junction to calcium release from the SR. It was shown that the failure of E–C coupling is a major factor in the decrease in isometric strength; nonetheless, the contributions from damage to force-bearing elements, intrinsic SR dysfunction, or both showed minimal evidence[21].
3. Force-bearing protein structures have also been lightly linked to strength loss. Studies have shown that immediately and in the next six hours following an in vivo muscle injury neither muscle protein degradation rate nor the amount of total and contractile protein were elevated. However, protein content was found to be modified over the days following the injury, the degradation rate was increasing and maintained a rate of 60% above the normal value by the second day, as a result, actin and myosin heavy chain content were reduced by 20% around day five. This protein degradation was not associated with any loss of muscle strength. Three to five days following the initial injury, strength was recovering but protein content continued to decline. Consequently, the decrease in strength cannot be associated to any modifications in the protein content. Only after two weeks post injury, some residual decrease in strength can be attributed to a decrease in protein content[30,31].

As mentioned above, the type and intensity of exercise are also considered an important factor in the decrease in strength. Eccentric contractions even at a low intensity and isometric contractions at a long muscle length produce more ultrastructural disruptions and strength loss, leading to EIMD rather than concentric contractions[20,32,33]. Thus, for the fibers that are being lengthened, the force produced is greater by 80-100% to the one produced during an isometric or a concentric contraction. In this case, the reported strength loss reached 10 to 30% following an eccentric downhill running exercise[34,35], 50 to 60% following an acute bout of eccentric contraction for the biceps brachii[36] and exceeding 70% following a high force eccentric exercise without a return to baseline for more than two weeks post-exercise[37].

The complete recovery of muscle strength can take more than a month in humans following eccentric activity, whereas following a concentric activity, strength can be restored in only a few hours following the exercise[26,38]. Subsequently, a depletion of Adenosine triphosphate (ATP) and a leakage of extracellular Ca^{2+} ions to the intracellular space are noticed because of a dysfunction in the pumps of both Na-K-ATPase and Ca^{2+}-ATPase. Therefore, degradation of muscle protein and increased cell permeability occur because of the activity of an intracellular proteolytic enzyme leads to a leakage of cell content into the circulation[39,40].

The speed and tension imposed on muscles that are being lengthened during eccentric contractions offer a possible explanation for the resulting strength loss. If the stretching speed is slow, sarcomeres are lengthening in uniformity while muscle tension is increasing; however, when this tension is forceful or unexpected, in case of eccentric bouts, sarcomeres might stretch in a non-uniform manner to a certain point where stretching is too far and damage occurs. At this point, sarcomeres are only supported by muscle passive elements, the muscle series elastic elements are affected by the damage, causing the popping of sarcomeres and leading to strength loss in the muscle[41,42].

In summary, 75% of the loss of strength occurring during the first three days after the injury is attributed to a failure of the E-C coupling pathway. The remainder of the loss, for the first two days, is associated to alterations of the myofilaments and connective tissues within the fibers of the muscle; by day three, the main factor attributed to strength loss is a decrease in the contractile protein content. E-C coupling failure starts diminishing from day five and disappears at day 14 after the injury, over this period, the percentage of force deficit causing the loss in contractile protein, increases from 40-45% to 100%[26]. Therefore, a complex interaction of mechanisms seems to be involved in the phenomenon of strength loss and the process of recovery after muscle damage. Apparently, the relation between EIMD and strength is clear and well determined, but it has also been shown that EIMD can partially be considered efficient, offering positive stimulus in the case of strength training which in turn is also responsible for muscle restructuring, hypertrophy and increase in strength[21,43].

1.4. Muscle damage and DOMS

Along with strength loss following eccentric activity, alterations in the muscle contractile properties and soreness have also been linked to EIMD. Studies have shown that soreness emerges following an intensive activity, typically eccentric contractions[38], it peaks between 24-48 h and start decreasing around day five to seven post exercise[25]. Soreness is considered delayed because it is greatly perceived between 24-48 h and not immediately following the intensive exercise; moreover, it is not tightly correlated with the muscular damage observed in biopsies, in convergence with strength loss[25].

Two classical experiments, which utilized a repeated stair descent and a backward cycling exercise, provided the first evidence of ultrastructure myofibrillar disruptions following intense exercise[44,45]. Both studies have revealed myofibrillar disturbances of 12 to 52% of the fibers of the studied muscle[44,45]. Therefore, the external load during eccentric contractions is greater than the force generated by the muscles during concentric contractions, because muscles produce more force at the same angular velocity[46–48]. Ultra-structural integrity modifications were also noticed: Z-lines out of register, Z-lines streaming, loss in thick myofilaments, disruption of sarcomeres in the myofibrils leading to protein degradation, autophagy and a local inflammatory response[49]. Type II muscles with fast twitch motor units were mainly recruited and showed more damage than type I fibers following eccentric contractions[49,50].

Studies have shown that Z-lines were the weak link in the myofibrillar chain, where disturbances have been found in muscle biopsies taken 24 h to 72 h post exercise compared to those taken immediately[36,38,46]. The reason of those disturbances was attributed to the loss of desmin, a cytoskeletal protein connecting the Z-lines, which was noticed in muscle fibers following eccentric exercise[51]. Desmin can be also considered a marker for active muscle regeneration, since an increase in desmin staining has been reported following an eccentric cycling exercise[52]. Additionally, biceps brachii biopsy taken at 48 h following an eccentric exercise, have shown mast-cell degranulation in the perimysium near the blood vessels and mononuclear cells in the perimysium and endomysium. A widened interstitial space pulled away the extracellular matrix from the fibers, fibrinogen and albumin were found in the endomysial and perimysial spaces, confirming damage to the extracellular matrix and in the capillaries[38]. This is witnessed in the case of repeated non-uniform lengthening model during eccentric exercise giving rise to an inflammatory reaction serving at a later stage for regeneration and repair of the cells[33]. Furthermore, older adults have expressed a greater magnitude of muscle damage than younger individuals following an intensive exercise; similarly, older women have shown more strength decrease 24 h following eccentric exercise[53,54].

The damage occurring to the exercised muscle might lead to a better understanding of the concept of muscle soreness after an intensive eccentric exercise. The degree of soreness perceived is related to the intensity of the exercise itself and the resulting damage. Following downhill running or isokinetic eccentric knee extension with less muscle damage, the level of soreness measured by a scale is low. If eccentric contractions are maximal, soreness level will significantly increase and the reason can be attributed to swelling and pressure in the muscle[55]. Two different studies conducted respectively on tibialis anterior muscle and knee extensor muscle following an eccentric activity have shown an increase in the size of the fibers and in the intramuscular fluid pressure[56]. Although both swelling and soreness are related, they don't occur at the same time; soreness reaches its highest level long before swelling does according to the authors[55]. It has been also demonstrated that the sensation of soreness was related to the subcutaneous swelling that has moved from within the muscle at five days after intensive exercise. Free nerve endings were activated as a result leading to the sensation of soreness. Pain was attributed to chemical factors, when noxious mediators such as histamines, bradykinins and prostaglandins are released in the presence of muscle damage. Type III and IV nerve afferents are activated carrying the pain message from the muscle to the CNS. Consequently, the pain threshold is reduced because of the excitatory action of these mediators on the muscle nociceptors, making it more sensitive to other stimuli such as swelling[57].

1.5. Muscle damage and inflammation

Inflammation is defined as a cellular response of the organ to damage, and is considered crucial for appropriate tissue repair, and for complete functional remodeling and return to homeostasis particularly when muscle damage and peripheral muscle fatigue coexist such as following a muscle injury caused by an intensive exercise[21,23,58].

In vivo[24] and in vitro studies[59] have stated the role of neutrophils in muscle damage and the following inflammatory reaction. As a result, satellite cells are activated, debris from the affected area is cleared preparing for muscle regeneration, by infiltrating plasma proteins into the injured site, releasing cytokines and increasing inflammatory cell population[2,60,61]. The role of cytokines, also called myokines, when expressed by the skeletal muscle, is very particular in activating and modulating the inflammatory reaction in a regulated fashion[24,62]. As part of the neutrophils contribution to the degradation of the altered muscle tissue, the release of reactive oxygen species (ROS) will increase, macrophages are then attracted, and phospholipases and proteases will be activated in the injured site, magnifying the initial muscle injury[21]. Following the initial injury by 24 h, neutrophils are replaced by macrophages and remain present for the following 14 days post-exercise. Along with the monocytes, macrophages infiltrate the endomysium and particularly the perimysium of the injured area of the muscle. The accumulation of leucocytes and muscle remodeling processes are both regulated by and depend on the extent of muscle damage[21,24,63]. Cytokines are categorized as: 1) Pro-inflammatory cytokines, such as interleukin (IL)-1α, IL-1β and tumor necrosis factor (TNF), whose role is to promote inflammation and 2) anti-inflammatory cytokines, such as IL-4, IL-10 and IL-13, whose role is to inhibit inflammation, and chemokines such as chemokine (C–C motif) ligand 2 (CCL2), whose role is to permit the migration of the leucocytes from the blood to the injury site[21,24,64]. Furthermore, some cytokines such as IL-6 retain both roles, pro and anti-inflammatory, depending on the environment[65]. Several cell types such as fibroblasts, muscle fibers, neutrophils and macrophages give rise to the release of most of cytokines. Following an intensive exercise, muscle cytokines are expressed as pro-inflammatory and TNF is expressed by the invading neutrophils and macrophages at the early stage of inflammation. Additionally, TNF plays a major role in initiating the muscle remodeling process[66,67]. The inflammatory reaction is variable and dependent of many factors such as exercise intensity, duration, involved muscles and mode[68]. Muscles experience cell necrosis and tissue damage and a loss of the soluble enzymes such as CK that can be detected by measuring its level in the blood[2,69]. CK is considered a very common indirect marker for muscle damage. In general population, it ranges between 35 and 175 U/L. When this value exceeds 5000 U/L without any myocardial incident, stroke, disease, or physical trauma, serious muscle disturbances might be behind this increase[40,70].

The type of activity is directly related to changes in inflammatory markers. Following low-to-moderate intensity exercise and strength training, CK release in the blood is increased[43].
In track and field events, movements involve repeated eccentric contractions over a prolonged period of time, causing more stress and damage to the musculoskeletal system, consequently, inflammation arises producing more oxidative stress[71], compared to endurance activities[72]. An increase in plasma myoglobin (Mb) concentration and CK was also noticed following an endurance exercise causing moderate muscle damage, (cycling followed by running), confirming an early migration of leucocytes to the muscle site 3h after the exercise[73]. Following downhill running, plasma CK activity was found increased compared to uphill running, without any significant changes in IL-6 and IL-1β in both running trails[74]. Moreover, following three sets of maximal eccentric leg flexion, CK significantly increased at 24 h following the exercise, and then decreased the next two days[75].

Exercise intensity and duration are also important elements in the inflammatory response. Two groups of subjects with the same training volume were divided into low and high intensities of eccentric leg extensions, CK showed higher increase in the high intensity group yet the result was not significant, but, this group has shown more strength decrease and a slower recovery[76]. Similarly, in a study investigating a group of soldiers following a bench press protocol, prostaglandin was found increased following 110% one-repetition (1RM) of eccentric contraction compared with other groups (50%, 75% and 90% 1RM of both concentric and eccentric contractions), though, CK increased for all groups without any significant result[77]. Consequently, studies confirm more increase of CK following high intensity exercises where more disruption of cell membrane is present, leading to potentially highest adaptations to exercise in a short amount of time[76,77].

Levels of CK vary in general among individuals. When practicing the same type of activity, some people have shown higher levels of CK than others. This difference remained the same even when other factors were taken into consideration such as gender, age and training status. The reason behind that remains unknown[78]. Gender differences in CK were also noticed. Lower levels were found in blood samples of women in resting conditions when compared to men[79,80], however, following intensive exercise results have shown many discrepancies: no differences were noticed after downhill running[34,81], nevertheless, CK showed a relative increase in women following maximal eccentric contractions[80] and following a stepping exercise[82]. It is also crucial to mention that baseline CK levels are generally higher in people involved in high intensity and volume exercises compared with sedentary or moderately active individuals[83]. Finally, exercising on land induced more increase in CK than exercising in water at 48 h. This fact might be attributed to less eccentric contractions in water leading to a decrease in the magnitude of the resulting muscle damage[84]. Other inflammatory markers, Mb and C-reactive protein (CRP), were also investigated following training on soft sand and grass surfaces with matched intensities[85]. Results have shown a significant increase of Mb following running on grass, and no significant difference for CRP. This finding concludes that grass surface induces more muscle damage and Mb increases as an adaptation to this direct damage with increased deceleration forces compared to running on soft sand. It also concludes that soft sand offers a potential shock absorbing feature compared to grass. An explanation of this result might be related to the absolute running speed and distance covered, where a higher velocity resulted in an increased number of ground contacts on grass, inducing more muscle damage[85].

Following the inflammatory phase, the remodeling phase with regeneration of the skeletal muscle occurs. This phase is facilitated by the satellite cells which are mononucleated stem cells located between the basal lamina and the sarcolemma on the surface of the muscle fiber. These cells are usually inactive, and become activated when muscle damage occurs[21]. Their proliferation takes place 24-48 h later and they either return inactive while restoring the population of satellite cells, or ensure the migration to the site of injury and the repair process by an increase of the nuclei-to-cytoplasm ratio, or finally form myotubes as a result of fusing with other myogenic cells, in order to generate new fibers and replace other damaged ones[86,87]. Additionally, extracellular matrix components such as collagen is also believed to be synthesized within the endomysium and the perimysium following EIMD[88,89].

The physiological response to EIMD has shown discrepancies in the results between studies, and those could be related to the population, age, gender and small sample size[90,91], or within the same studies, with differences among the participants, showing a potential genetic variability[92,93]. However, this genetic association between muscle damage and muscle regeneration in response to intensive exercise, among old or young subjects, is still to date unclear, and the responsible mechanisms are yet to be identified[21].

In conclusion, inflammatory response plays an important role in muscle regeneration and adaptive remodeling, thus, such a phenomenon shall not be blocked nor reduced in order to facilitate the functional recovery process[32].

1.6. Assessment of muscular alterations

Various ways of assessment are necessary to mention in order to evaluate the corresponding changes and differences in muscle performance. Maximal strength and power of the lower limbs have been significantly associated to jump height, acceleration, and sprint performance[94]. In the following section, we are discussing the main variables related to muscle performance, muscle damage and inflammation, commonly assessed in the literature.

In order to determine the changes in muscle structures following an eccentric activity, magnetic resonance imaging (MRI) is used as a tool by assessing signal intensity T2 or relaxation time. T2 was found to be prolonged, and since any increase in T2 also reflects the increase in water within the muscle, this finding helped to determine the presence of edema in the damaged muscle[95]. The increase in T2 depended also on the sections within the same damaged muscle, for example, the distal part of the semitendinosus and short head of biceps femoris and the proximal part of the semitendinosus and gracilis, both showed more increase in T2 at 60 h following a knee flexion-extension exercise, though this was not linked with the fibers recruited in these sections following eccentric contractions[38,96].

As mentioned previously, the decrease in muscular strength is considered the most valid indirect marker of muscle damage, therefore, its evaluation was mentioned in several studies: the 1RM test (against weights or plate-loaded machines) is considered a gold standard measure and is defined as the maximal weight lifted for a single repetition executed with a correct lifting technique[97,98]. Several attempts per testing session are required before estimating the 1RM, ranging usually between 3 and 8, with a rest of 1 to 5 min between attempts[99]. Notably, 1RM has an excellent test–retest reliability, regardless of sex, age, the previous resistance training experience, and whether it is assessed on muscles of the upper- or lower-body[99]. Similarly, isometric and isokinetic strength are both evaluated in the objective of monitoring muscle performance. This is usually performed using a dynamometer or force platform in the case of isometric strength, where a subject is required to push or pull against a fixed object. In the case of isokinetic strength, an isokinetic dynamometer is used and the corresponding muscle group is moved at a constant joint angular velocity[100]. In both cases, MVC is considered the best indirect marker of EIMD[101] and its decline is caused by central fatigue, whereas peripheral fatigue is more involved in muscle damage and inflammation[102].

Numerous studies have shown a strong correlation between maximal strength and both jump height and sprint time, often used in sports where the production of muscular strength and power is an important factor and where performance is influenced following explosive intensive efforts[20,103]. Jump height measured by Counter Movement Jump (CMJ) test and 10-m, 20-m and 30 m sprint time were all correlated with maximal strength in half squat[94,104]. In a study examining the neuromuscular fatigue following an intensive 3-day baseline repeatability protocol, CMJ showed high intra- and inter-day reliability and detected with high accuracy alterations in neuromuscular function following fatiguing exercise, lasting up-to more than 72 h for full recovery[105]. Moreover, 20-m sprint time was found to be decreased when strength of lower body was increased following an 8-week training period[106]. Other studies have also shown a strong inverse relationship between CMJ and 20-m, 30-m and 40-m sprint[107–111]. Finally, following an intensive rugby training session, a study showed an increase in 30-m sprint and a negative significant correlation with the changes in distance covered above maximum aerobic speed[112].

Additionally, inflammation was assessed in many previous studies investigating specific protein markers for determining and monitoring muscle fatigue and muscle damage[19]: CK, Mb and α-actin, which are commonly used to indicate exercise-induced muscle damage[21,40,113], and Tenascin-C, which is considered an indicator for connective tissue and extracellular matrix disruption[21,114].

1.7. Recovery and performance

In order to understand the recovery process and all the strategies that might help and contribute to better management of EIMD, a few highlights regarding these topics are necessary.

Recovery is defined as the period of time necessary to reach biological responses taking place after the disturbances to homeostasis created by training, it is also described by a temporary impairment to an athlete's performance. It can be classified according to the corresponding timeframe: immediate, when recovery is between strength training repetitions, short-term, when recovery is between sprinting sets, and long term, when recovery is between training sessions[115]. Following an exhaustive effort, several internal and external factors will affect the recovery status. In this case, a lot of physical and mental efforts are exerted, which results in a state of increased exhaustion or fatigue[116]. When fatigue is induced by an intensive training or a competitive activity, recovery plays a crucial role in the regeneration process by compensating and restoring the organismic allostatic balance. This is normally accomplished through an investment of all individual physiological and psychological resources[117], and an implementation of several strategies and modalities depending on the type of fatigue, offering a positive influence when fatigue is mental or cognitive[118–120]. However, a certain level of fatigue is beneficial and contributes to an enhancement of performance level whenever the recovery process is well established, and this is considered a functional overreaching[117]. Consequently, a short decrease in performance level is witnessed, without any negative signs related to intensive training. However, if recovery is not thoroughly established and customized, an imbalance between recovery and individual physical requirements will eventually result in under-recovery and non-functional overreaching (NFO): under-recovery is more general in nature, whereas NFO is a training related phenomenon; both lead to overtraining syndrome (OTS), which results in physical symptoms such as soreness, pain and muscular alterations[117,121].

The management of under-recovery and early NFO involve an individualized recovery program and modifications in many aspects of one’s lifestyle, such as diet, hydration, sleep and social skills, all of which are essential factors along with exercise. Inversely, when OTS occurs, the management is quite different and requires long rest and a recovery phase going from weeks to months with a noticeable reduced performance level. The decrease in performance level is caused by physical abilities such as endurance, speed, strength or flexibility and also psychological factors such as concentration, motivation and desire[116,120,122]. Any imbalance between insufficient recovery and sustained fatigue may result in under-recovery, NFO and OTS, thus the assessment of recovery-fatigue concept is an integral part in monitoring the fluctuations in performance levels. The evaluation should be adapted to each activity, the use of specific performance outcomes is a very important issue, other physiological and psychological measures should also be assessed[118]. Monitoring the heart rate (HR) and/or heart variability at rest or after exercise to assess the autonomous nervous system is a very frequent non-invasive method used to evaluate the physiological profile of athletes[119,123–125]. Moreover, a broad variety of psychological measures is also used, reported benefits are mainly related to the perception of the own athlete about her/his readiness making it a primary determinant of recovery. Among these measures, apart from the control of physiological variables associated with fatigue and muscle damage previously explained, the Rating of Perceived Exertion (RPE), the Profile of Mood States, and the Recovery-Stress Questionnaire for Athletes[118,126,127]. These measures are considered sensitive, feasible and an essential element in monitoring the recovery-fatigue continuum[128]. Consequently, the combination of physical and psychological measures in the process of assessing athlete's recovery state is extremely important, and none of these parameters should be assessed separately in order to avoid focusing on one aspect of recovery while overlooking other important aspects[117].

In terms of time, many studies have shown that physical performance and the alterations following intensive training such as muscle damage and inflammation, require more than 72 h to reach the pre-match values in elite, first and second division athletes[119,129–131]. The main problem in recovery is usually the busy schedule of training where the challenge is to regain as fast as possible a good performance level and to prevent any incidence of sports injuries[119].

Therefore, recovery plays a crucial role in maximizing performance level, a proper balance should be maintained between training and recovery in order to prevent the occurrences of all alterations related to an accumulation in psychological and physiological stresses created by an intensive load of training[132–134]. The emergence of recovery is also a determinant factor in training, thus, short-term and long-term recovery strategies should clearly be established. Short-term recovery intervention such as a *power nap* is usually beneficial when training sessions are intense; this allows athletes to maintain good training and performance levels[121,133]. Although recovery between training sessions is essential and can lead to better adaptations and improvements in subsequent training quality, its implementation should be executed with caution as it can also lead to negative effects related to repeated decrease in training adaptations such as a reduction in physiological adaptation to resistance training[119]. Furthermore, when training sessions are intense with an increased volume and recovery time is limited, musculoskeletal, nervous, immune and metabolic systems require huge physiological demands. Thus, athletes are exposed to a high rate of injuries and a negative effect on the performance of subsequent exercises, especially during periods of overloaded trainings and competitions within a limited time frame[135–137]. In contrast, performance benefits and increased physiological responses have been reported in moderate intensity activities[138]. The choice of proper recovery should answer those demands and be customized according to the activity and to the athlete. Therefore, recovery is considered complete when it contributes to a return to homeostasis of all alterations and modifications caused by intensive exercise sessions and to a decrease in all disturbances and damages related to fatigue and created by training[115,132]. The adaptation to fatigue following a training load is a complex mechanism and might be negatively or positively controlled by the choice of the proper recovery technique[139].

Central or peripheral mechanisms are usually targeted by the recovery interventions and the reported beneficial effects depend on the selected type and technique. Generally, the advantages and benefits are common among all recovery methods, reducing inflammation and EIMD. The main mechanism is reducing swelling and edema, thus decreasing the diffusion of fluid into the interstitial space and permitting the transport of metabolites, neutrophils and protein markers from the muscle to the blood[119,132,140].

1.8. Recovery protocols

The literature has defined an exhaustive list of recovery methods, using two main categories in order to thoroughly identify and classify the different protocols; methods are grouped into active and passive interventions[135].

1.8.1. Active recovery

Active recovery has been investigated and hypothesized in several previous studies as an alternative for post-intensive exercise recovery[141–144]. It includes all protocols involving movements performed by athletes such as jogging, sub-maximal running, stretching, isolated muscle contractions, cycling, arm cranking, exercising in water, and yoga[135,141,143,145–151]. The science behind the use of active recovery protocols is those modes of exercise increase blood flow, prevent venous stagnation following intensive activities, restore metabolic perturbations, decrease the emergence of muscle soreness, and improve muscle-damage recovery[136,152,153]. Nevertheless, results of different studies related to this topic are still controversial and divergent. Both early and some recent studies have shown an advantage over passive recovery in terms of clearance of accumulated blood lactate[142,154] and contribution to a faster return to homeostasis, especially when exercise is repeated in a limited time such as less than 30 min[155]. Lactate clearance was even found faster when the intensity of exercise in active recovery reaches approximately the individual lactate threshold (60-100%)[156]. However, there is a controversy about considering lactate removal as a valid indicator of the quality of recovery following intensive exercise because recent studies have suggested that acidosis arising from lactate is not the cause of contractile failure[10]. Moreover, according to a past study, active recovery was found to be beneficial only shortly after an intensive exercise[157].

Active recovery was also assessed by examining CK concentration, which showed a modification depending on the duration of the recovery. Following a rugby game, an hour of low-intensity exercise in water did not show any effect on the circulating CK[158] compared with a better CK clearance following seven min of low intensity exercise[159]. This result was also convergent with other studies[160,161]. Additionally, muscle soreness was temporarily found to be relieved[157,161]. Conversely, different results were found in another study, which revealed that muscle soreness and muscle strength did not show any significant results at 1, 24, 48 and 72 h post exercise following low-intensity exercise recovery[162–164]. Moreover, performance did not show any significant improvement on high intensity treadmill running performed before and after a recovery run at 40% of peak running speed, compared to passive recovery[165]. Moderate intensity (70% of HR max) was also investigated in a cycling protocol following an intensive activity and showed a significant improvement of isometric strength at 72 and 96 h following EIMD[166]. The idea behind the potential positive effect of active recovery was attributed to the effect on blood circulation. Active exercise in the scope of recovery increases blood circulation, by doing so, it helps eliminating waste and toxic products and releasing endorphins which in return lead to an analgesic effect[142,166–168]. The explanation of the decrease in pain is related to the stimulation of the sensitive fibers Ia, Ib and II, similar to the one perceived following massage, which will interfere with the pain sensation transported by fiber types III and IV[169].

1.8.2. Passive recovery

Passive recovery includes all protocols performed on athletes whether by sports practitioners or by themselves but without performing any movement. These protocols include the use of compression sleeves (CS) and intermittent pneumatic compression (IPC)[170–175], the application of massage [147,176–179], magnetic field [180], hyperbaric oxygen therapy [136,181], cryotherapy [182–185], cold-water immersion [138,151,186–192], laser therapy [184,185,193], ultrasound [194–196] and electrical currents [197,198].

Some studies discussed in this section investigated protocols used as a preventive measure before the activity, nevertheless we included them because of their potential benefit following intensive activities. Most of the mentioned protocols have shown to a certain extent, several benefits on different aspects of recovery. Massage and cryotherapy were considered amongst the most frequently used passive therapeutic interventions to cause analgesia and deal with sore and injured muscles [149].

1.8.2.1. Massage

Massage was shown to be efficient in managing muscle soreness at 24 h, if applied for 20 to 30 min or up-to 2 hours following intensive exercise[149]. It was also shown that the decrease of DOMS was reported at 72 and 96 h when massage was applied following EIMD[199]. Similar benefits were found in elite ultra-marathon runners[178]. In fact, massage was found to be the most efficient on reducing perceived fatigue[132]. The positive effect on soreness might be attributed to the stimulation of afferent fibers type Ia, Ib and II, thus reducing the pain sensation transmitted by the afferent fibers type III and IV[149]. The reason behind that is the potential inhibition of pain sensation from the excessive tactile stimulation caused by massage, yet, the result is temporary and not sustained[149]. Other benefits are shared with other recovery methods in general, such as stimulating the blood and lymphatic flow and reducing the swelling and muscle tone, therefore, modulating pain and repairing damaged muscles[200–204]. Additionally, positive results in blood and inflammatory markers were also shown, consequently, an increase of 16% in the concentration of beta-endorphin in the plasma[205] and a decrease in CK and IL-6 concentrations in the blood after exercise, leads to a decrease in pain and muscle damage and thus a faster recovery[206]. The result of massage showed a small positive effect one hour after intensive exercise[149].

1.8.2.2. Cryotherapy

Cryotherapy is also considered an initial treatment of choice following traumatic injuries of soft tissues[207]. The method used in most studies is cold water immersion (CWI)[138,151,186,188–192] and local cryotherapy to a lesser extent[182–185]. The reported benefits included a positive result on decreasing muscle soreness at 48 and 72 h following intensive exercise[191,208–210], and results were also persistent along with a decrease in perceived fatigue up-to 96 h[190]. Moreover, when cryotherapy was repeatedly applied on separate times up-to 72 h following intensive exercise, the result on muscle stiffness and recovery was significant[210]. The efficiency of a single session of cryotherapy on muscle soreness, muscle strength and Mb concentration in the blood, immediately following an exercise-induced muscle damage was also reported[209]. The reasons behind the beneficial use of cryotherapy are related to a decrease in the skin, subcutaneous, intramuscular and joint temperature. Cutaneous receptors are then stimulated, creating an excitation of the sympathetic adrenergic fibers, which causes local arterioles and venules to constrict and thereby reducing the inflammatory processes. Consequently, a reduction in the perception of pain as well as muscle swelling are the resulting phenomena[207,211].

1.8.2.3. Compression stockings and intermittent pneumatic compression

Compression stocking (CS) is another type of passive recovery used to deal with symptoms of EIMD as stated earlier. The significance of their use reached 96 h post intensive exercise[170].

Their efficacy was examined as a preventive method during and after a long distance of off-road running that involved uphill and downhill trails. The perception of soreness was significantly less at 1 h and 24 h post-run by 82% and 80%, respectively, when CS where worn during the run Furthermore, a possible beneficial effect of CS was noticed on MVC at 1 h and 24 h post running and on CMJ during the recovery period, when CS were worn during running compared to non-use of CS[212]. Additionally, perceived fatigue was also significantly decreased by wearing a whole body compression garment for 24 h following a heavy resistance training[213]. The positive results of applying compression garments might be due to the decrease, caused by pressure, of the space available for swelling, causing small modifications in osmotic pressure, limiting the diffusion of the fluid in the interstitial space and activating a better venous return[213]. However, the results on inflammatory markers were not similar as a divergence was found in previous studies in that no significant changes were detected in CK, CRP and IL-6 following the use of garments[132,212], whereas a significant decrease of CK concentration was reported in a different study[214]. This contrast might be attributed to several factors such as the duration of the applied pressure, the group of muscles targeted (upper or lower extremities), and the amount of pressure applied[215–218].

Intermittent pneumatic compression (IPC) was investigated following an ultramarathon, for four consecutive treatment days and two weeks of monitoring[172]. Post-race CK and 400 m run time over the two-week period showed no significant difference in 20 min IPC group. Only muscular fatigue expressed subjectively showed an improvement following the race and post-race on day one[172]. In another study on IPC, participants performed for three consecutive days, high intensity interval training (HIIT), followed by an hour of IPC treatment and for the next three days they only had IPC[175]. No significant effect on CK, on 8-isoprostane (a marker of lipid peroxidation), and on hsCRP (a marker of inflammation) was found in IPC group. Similarly, pain threshold, flexibility and 6 km time trial performance did not show any significant improvement throughout the days and when compared with no treatment[175]. In contrast to the previous findings, IPC was found effective in improving the pain threshold of professional athletes involved in different sports activities (free style wrestling, triathlon, track cycling, weightlifting, gymnastics, modern pentathlon and shooting). Athletes underwent two practice sessions, morning and afternoon. Following the morning session, they received 15 min IPC. Both PPT measurements immediately following the treatment and in the afternoon showed an improvement only in IPC group[173].

1.8.2.4. Stretching

In addition to all passive recovery methods, stretching has also been investigated and studied in the literature, as a protocol potentially capable of improving recovery and enhancing performance.

The primary reported benefit was an increase in range of motion[219]. Studies have also shown that stretching caused a decrease in muscle stiffness and spasm following an intensive exercise, induced changes in the muscle spindles function, and presented some effect on the reflex activity[149].

Despite the mentioned benefits, several studies have examined different protocols of stretching, pre- or post-activity, and the program was either a single or a repeated session[220–222]. Results did not show any significant effect on perceived soreness, fatigue and muscle function, regardless of the time of its application. Interestingly, some studies did not even recommend stretching after exercise[223,224] and others claimed that it might produce delayed soreness[225]. Moreover, stretching was examined 60 min before exercise, and showed a negative effect on explosive power[226], the same negative effect was also found on 20-m sprint time in a different study[227], these results clearly show that stretching is not beneficial and should not be practiced in the last 60 min of recovery preceding an explosive event[136]. Furthermore, for activities where running is an essential component, stretching during recovery period did not lead to any long term benefits[228]. A possible explanation of the negative result of stretching might be the potential effect on evacuating edema which is generally accompanying DOMS as part of the inflammation process following an intensive exercise. Knowing that inflammation plays a key role in muscle recovery and adaptation, any attempt or technique aiming to reduce this reaction by removing edema might be detrimental to the recovery process[136].

In summary, results are inconclusive and divergent in many outcomes related to recovery. Duration and intensity are two major elements to be considered in the development of the appropriate protocol aiming at enhancing performance following any intensive activity. The choice of the appropriate recovery protocol should take in consideration the level of pain perceived by the athletes, which might prevent them from recovering faster. Additionally, an optimal inflammatory reaction is crucial for muscular remodeling with respect to an appropriate duration of inactivity in order not to compromise muscle strength and performance.

Chapter 2: Hypotheses and Aims

Hypotheses

A. Active recovery protocols are beneficial in managing exercise-induced muscle damage symptoms, such as soreness, inflammation and muscle strength loss, among others (Chapter 4.1.).

B. A combination of massage and cold water immersion can be used as an efficient passive recovery protocol to improve pain perception, isometric and dynamic strength and gait kinematics (Chapter 4.2.).

C. An active protocol consisting of uphill high-intensity interval exercise offers improvements on muscle damage markers recovery and exercise performance after muscle damage-inducing exercise (Chapter 4.3.).

Hipótesis

A. Los protocolos de recuperación activa son beneficiosos para manejar los síntomas relacionados con el ejercicio que induce daño muscular, como el dolor, la inflamación y la pérdida de fuerza muscular, entre otros (Capítulo 4.1.).

B. La combinación de masaje e inmersión en agua fría se puede utilizar como un protocolo de recuperación pasiva eficaz para mejorar la percepción del dolor, la fuerza máxima tanto isométrica como dinámica y la cinemática de la marcha (Capítulo 4.2.).

C. Un protocolo activo que consiste en intervalos de carrera de alta intensidad en pendiente positiva, ofrece mejoras en la recuperación de marcadores de daño muscular y en el rendimiento, después de un ejercicio que induce daño muscular (Capítulo 4.3.).

Aims

The general aim of the present doctoral thesis is to provide a framework of knowledge about the main recovery protocols carried out following muscle damage inducing exercises, in order to select the most appropriate one allowing an improvement in performance and a decrease in soreness.

The specific aims of this doctoral thesis are:

- **Aim A:** To review describe, synthesize benefits, identify limitations, and provide a practical approach for active individuals, trainers, and clinicians regarding what type of active recovery could improve performance level after strenuous activities (Chapter 4.1.).

- **Aim B:** To examine the acute effect of a combination of massage and cold water immersion, on soreness, isometric and dynamic strength and gait kinematics (Chapter 4.2.).

- **Aim C:** To investigate the benefits of an uphill high-intensity running recovery protocol on soreness, muscular strength, sprint and jump compared with a control group with complete rest (Chapter 4.3.).

Objetivos

El objetivo general de la presente tesis doctoral es proporcionar un marco de conocimiento sobre los principales protocolos de recuperación que se llevan a cabo después de un ejercicio inductor de daño muscular, con la finalidad de poder seleccionar el más adecuado que permita una mejora del rendimiento y una disminución de la percepción del dolor.

Los objetivos específicos de esta tesis doctoral son:

- **Objetivo A:** Revisar, describir, sintetizar los beneficios, identificar las limitaciones y proporcionar un enfoque práctico para las personas activas, los entrenadores y los clínicos con respecto a qué tipo de recuperación activa podría mejorar el nivel de rendimiento después de actividades extenuantes (Capítulo 4.1.).

- **Objetivo B:** Examinar el efecto agudo de una combinación de masaje e inmersión en agua fría, sobre la percepción del dolor, la fuerza máxima isométrica y dinámica, y en la cinemática de la marcha (Capítulo 4.2.).

- **Objetivo C:** Analizar los beneficios de un protocolo de recuperación de carrera de alta intensidad en pendiente, sobre el dolor, la fuerza muscular, el sprint y la altura de vuelo en comparación con un grupo con descanso completo (Capítulo 4.3.).

Chapter 3: Materials and Methods

In this section the general methodology adopted in the thesis and leading to all results will be detailed. A systematic review of the literature and two different original research will be included. The general characteristics for both projects, the ethical considerations as well as the statistical treatment of the data will be explained in separate sections including details and information about the two projects.

Our aim in this chapter is to summarize the entire methodology adopted in the thesis as a compendium, this will allow the reader to have a global vision. The results of the thesis include the original articles as they have been published, the methodological aspects of each article are repeated in the following chapters, this chapter allows the reader a quicker and more integrated reading of those sections.

3.1. Ethical considerations

In both experimental designs, research followed the guidelines of the Declaration of Helsinki 1961 (revision of Fortaleza 2013) of the Ethical Principles for Medical Research on Human Beings[229] and complied with Spanish legislation and legal regulations (Ley 14/2007, of July 3, Biomedical Research). The study was also approved by the Research Ethics Committee of Principality of Asturias (292-19). Participants were notified about the details of the experiments in both studies, they have also completed and signed a written informed consent and filled a questionnaire about their health profile and medical history.

3.2. Sample characteristics and project design

The initial sample of the whole project comprised of a total of 77 healthy participants, who were recruited via social advertising at University. In accordance with chapters 4.2. and 4.3., the participants who did not commit to the whole experiment and did not meet the following inclusion criteria for both projects were excluded from the study: 1) physically active, 2) no musculoskeletal injuries, 3) do not take anti-inflammatories or performance enhancing substances prior to the study, 4) no history of cardio-respiratory condition, 5) no pregnancy for female participants, 6) not previously trained in plyometrics, 7) no training 72 h before the first physical assessment, and 8) no hypersensitivity to cold. The final sample of the whole project was 63 participants of which 41 males and 22 females and an average age of 21.95±1.4.

All samples related to each study separately are listed and summarized in the following chapters:

A. In chapter 4.1 a systematic review of the literature is performed is depth following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology[230].
B. In chapter 4.2, a quasi-experimental study with intra-subject comparison of both legs is conducted, with a sample of 35 participants (18 males and 17 females, and an average age: 21.6 ± 0.8).
C. In chapter 4.3, a crossover randomized controlled trial (RCT) is included with a sample of 31 participants (24 males and 7 females, and an average age: 22.3 ± 2.1).

3.3. Methodology of the systematic review in chapter 4.1.

We conducted in chapter 4.1. a systematic review of the existing literature up to January 2nd 2020, concerning active recovery protocols and their effect on delayed onset muscle soreness (DOMS) and other associated symptoms following EIMD. This review was conducted following the methodology described in the Cochrane Handbook of Systematic Reviews of Interventions[231], and is presented following the recommendations of the PRISMA Statement[230]. The review was registered with PROSPERO (CRD42018114679) at the University of York, United Kingdom. The methods used are described in detail in the review article in chapter 4.1.

3.4. Methodology of the experimental studies

3.4.1. Exercise-induced muscle damage (EIMD)

In order to induce sufficient amount of muscle damage and to evaluate the effectiveness of the investigated recovery methods, a protocol of EIMD was adopted in both projects (chapters 4.2. and 4.3.). Following a 10 min warm up on a cycloergometer, participants were instructed to stand on 50 cm height box, and without any prior take-off, to land on the floor in a squatting position, then to jump as high as possible with a self-selected range of motion and contraction time. This was performed in 10 sets of 10 repetitions in the first project, whereas, in the second project the original protocol was modified and the number of repetitions was increased to 20 in each set in order to induce higher level of soreness. Between each set, participants rested for one minute[232,233].

3.4.2. Tests and assessment

Different tests and assessments were performed in the present doctoral thesis in order to demonstrate the effectiveness of the recovery protocols investigated. The results of these outcome measures are detailed and discussed with their statistical analysis separately in each experimental project.

3.4.2.1. Pain

Muscle pain due to soreness was assessed using two methods: Visual Analogue Scale (VAS) and Pressure Point threshold (PPT).

- VAS:

Visual analogue scale is a numerical scale using a subjective evaluation to rate the level of pain resulting from soreness, it consists of a 10 cm line ranging from 0 (no pain) to 10 (maximal pain)[234]. VAS was recorded in both projects, on different times in order to monitor the modifications in pain level throughout the whole experiment.

- PPT:

In the first study, PPT was used in order to assess the pain threshold defined as the minimum force applied in a specific point of a muscle and corresponding to painful stimulus[235]. In order to obtain this value, a hand held electronic pressure algometry (Somedic Algometer Type II, Sweden) was applied perpendicular to the skin, on the middle of a vertical line between the greater trochanter to the base of the patella in both legs, with a 90° flexion of both hip and knee joints. In order to keep consistency, the spots were marked to apply the pressure on the same location along the study[236]. Participants were instructed to express their pain when a painful sensation is perceived, immediately then, the pressure is released and the value collected, corresponded to the reading on the device. The procedure was repeated twice and the mean value was taken into account.

3.4.2.2. Muscle performance

In the following two projects, muscle performance was assessed by measuring vertical jump using two techniques: a force platform and MyJump application on a mobile phone, and by determining the time for 20m sprint in the second project.

- Vertical jump using a force platform:

In the first study, participants performed a counter movement jump (CMJ) on a force plate (SG 9, Advanced Mechanical Technology Inc., Newton, MA) and low-pass filtered at 500 Hz to calculate maximum dynamic force. The procedure consisted in asking the participants to stand on the force plate with their hands on the hips, to jump vertically as high as possible and finally to land on the same spot of the starting position. Jump height was calculated by the vertical reaction force impulse of the jump during take-off, taking in consideration the participants' body mass, previously measured on the force plate. The procedure was repeated three times, with a 2-min rest between trials, and the best result was recorded for analysis (CV < 5%)[237].

- Vertical jump using Myjump2.0 application:

In the second study, CMJ was determined using an iPhone 6® mobile device to record every jump at 240 fps. Flight time was used to calculate the jump height. Participants were instructed to place their hands at their hips and to land with straight legs and flat feet to ensure the consistency of the results throughout the assessment process. Three trials were performed and seperated by two minutes of rest, with the best result taken for analysis[103].

- Sprint time:

In the aim of determining the performance of the sprint, the time needed for performing a 20-m sprint was evaluated in the second project. Participants started with a general warm-up, afterwards, three trials of 20-m maximal sprinting were performed and separated by three minutes of rest[237]. The best result was collected for analysis. Sprint time was assessed using four photocells (Bio-Medic, Barcelona, Spain)[237].

3.4.2.3. Muscular strength

Muscular strength was assessed by measuring either MVIC in the first study or 1RM in the second study

- MVIC

MVIC was also assessed in the first project using a platform as mentioned previously and low-pass filtered at 1050 Hz. Participants were asked to stand on the platform in a squat position with 90° knee flexion and 110° hip flexion with bar fixed on their shoulders and anchored by two cables to the ground. Participants were instructed to push by an extension of their knees against the bar for six seconds. Three trials were performed separated by 5-min of rest and the best result was collected for data analysis as the highest produced value (N) according to the body weight (per Kg)[238].

- 1RM

In order to assess maximal strength of the quadriceps in the second project, 1RM was evaluated using a leg extension machine (Lumex, Ronkonkoma, NY, USA). Participants were instructed to sit on the machine with the seat and back adjusted individually. The result was collected following a standardized protocol with a progressive increased resistance. Participants started with a bout of 10 repetitions with 50% of the perceived maximum load. Then 3 to 4 lifting attempts were performed until they were unable to perform a full range of motion. A rest of two minutes was set between each attempts to avoid the influence of fatigue[237].

3.4.2.4. Gait analysis

In the first project gait cycle was biomechanically analyzed by asking the participants to perform ten walking cycles, five at normal pace and five at fast pace, on a 10-m walkway. For the normal pace, participants were instructed to walk with a self-selected comfortable speed, whereas for the fast pace, they instructed to increase their speed just before starting running[239]. The analysis consisted in using movement markers placed on specific anatomical landmarks on the participants' legs, and capturing the movement at 100 Hz using an eight-camera Vicon system (Oxford Metrics Limited, Oxford, UK). Data related to the gait cycle events and cadence, step length, support time, push time, and ROM of hip, knee and ankle were all assessed and analyzed using the Vicon Workstation and Polygon software[239].

3.4.2.5. Fatigue

Following EIMD prior to the recovery method, RPE was used to assess the level of fatigue experienced by the participants in the second experiment. RPE consists of a numerical scale ranging from 6 (no exertion) to 20 (maximal exertion)[126]. A score for each participant was recorded in order to make sure that EIMD created enough fatigue.

3.4.2.6. Serum concentration of CK

The concentration of CK was assessed in the second project through blood samples taken from the antecubital vein of the participants. The samples consisted of 5 ml of blood collected by vacutainers and centrifuged at 3000 rpm for 15 min. As a result, serum was separated and collected in plastic tubes then stored at -18°C. For this matter, routine technique was used (Orthoclinical Diagnostics Vitros, 250 Chemistry Analyzer, Manufacturer USA)[148].

3.4.2.7. Thigh circumference

In order to assess the swelling resulting from muscle damage following EIMD, circumference of the thigh was assessed in the second project. Participants were standing equally on both legs, with no prior contraction, the mid-thigh circumference of the dominant leg was measured in the middle of a vertical line joining the greater trochanter and the base of the patella using a constant tensiontape (Lufkin, Cooper Industries, Houston Texas, USA). The measurement was repeated three times and the average value was collected[141].

3.5. Investigated recovery protocols

Although all the intervention protocols adopted in the present doctoral thesis are detailed and explained with all the corresponding characteristics in chapters 4.2. and 4.3., an overview of these protocols is presented in the following paragraphs.

3.5.1. Combination of Massage and CWI

In the first project, a passive recovery protocol including a combination of massage and CWI was applied in that order on one leg chosen by the physiotherapist for each participant. The treatment was alternated between legs for the following participants, (e.g., right leg for the first participant, left leg for the second one…) regardless of their individual characteristics. Consequently, the treatment was administered on 50% of the total legs of the participants.

Manual massage was performed for 20 min, according to the duration adopted in previous studies[202,240,241]. The protocol consisted in effleurage (2 min), petrissage (12 min), wringing (4 min) and tapotement (2 min) movements, and was performed on the quadriceps, hamstrings and triceps surae muscles. Participants were placed in a supine position for the massage of the quadriceps and then turned to a prone position for the massage of the hamstrings and triceps surae. In effleurage, rhythmical, centripetal and multidirectional light stroking movements were performed. In petrissage, rhythmical movements including kneading and squeezing are applied centripetally over the muscle. The wringing movement consists on mobilizing superficial tissues by grasping and twisting them in opposite directions. Finally, repeated light strikes to muscle mass are applied as tapotement[241]. The same physiotherapist always applied the protocol to control the rhythm and pressure of the maneuvers according to the perceived soreness of each participant. The duration of the treatment was set by a chronometer. Temperature of the surface of both rectus femoris (intervention and control limb) was measured using a Technoline WS 1006 thermometer at the end of the massage session

Following massage, participants were asked to sit in a mobile bath with 90º sitting angle between their back and legs, they were immerged up to their iliac crests and stayed for 15 min in a 12ºC temperature, according to previous studies[185,242]. A thermometer was used to monitor and maintain a low water temperature every five minutes, and if necessary, ice cubes were added to the water. At the end of the cryotherapy session, temperature of the surface of both rectus femoris was measured, same as following the massage session.

3.5.2. Uphill high-intensity interval exercise (u-HIIE)

In the second project, we examined the effect of an active protocol including an uphill high-intensity interval exercise (u-HIIE). The study was a crossover randomized controlled trial, performed during four consecutive days and consisted in two identical sessions separated by a three-week period. In each session, 31 participants (24 males and 7 females) were divided in two groups, a u-HIIE group, who performed the active protocol on the second day only, and a passive rest (PR) group throughout the whole experiment. The u-HIIE protocol started with a 5 min warm-up, starting at 6km/h in the first minute and increased by 1 km/h every minute. Following the warm-up, the treadmill was inclined at 15% and participants were asked to perform four bouts of high speed running for 30 sec followed by four minutes of active rest. The speed of running for each participant was previously set as their maximum velocity (MV), and they were encouraged constantly to achieve the whole duration of each running bout. Participants were refrained from exercising for the next 48 h until the experiment was completely accomplished.

The MV or maximal self-selected speed for each participant was calculated one week prior to the experiment. The test started by a warm-up with walking at 4 km/h on the treadmill for 10 min, from 1% to 15% of inclination. Following the warm-up, participants started running on a 15% inclined treadmill in intervals of 1 min each, starting at 5 km/h, speed was increased by 1 km/h for every interval, until reaching volitional exhaustion. Heart rate (HR) was monitored throughout the test using a polar monitoring system (Polar Electro®, Oy, Kempele, Finland). In order to assess the fatigue during and at the end of the test, RPE was monitored[126]. When participants reached 90% of their estimated HRmax (220-age), or when the RPE score reached 17 or “very hard” at the moment of volitional exhaustion, the test was considered maximal

3.6. Statistical analysis

The following section offers a brief description of the statistical tests implemented in order to obtain the results of the doctoral thesis. Nonetheless, in chapter 4, an in-depth description of the statistical analyses for each study will be elaborated separately. Depending on each study, data analysis was performed using SPSS 24.0 (Statistical Package for Social Sciences, Chicago, IL, USA). Analyzed variables are presented as mean values ± standard deviation and a p value to the main intervention and time effect was reported for all measurements with a statistical significance set at $P < 0.05$. Both studies used a one-sample Kolmogorov–Smirnov test to confirm the assumption of normal distribution for all the variables.

In the first study, 35 participants were investigated, in a within-subject strategy and a leg-to-leg comparison model. Each participant received a passive protocol on one leg and the other leg served as control, we analyzed 70 lower limbs in total. In order to determine intra-group differences and the effect of a combination of massage and CWI on the assessed outcome measures, a two way (group x time) repeated measures analysis of variance (ANOVA) was performed. A post hoc analysis with Bonferroni correction was conducted when significant main effect or interaction effect was reached.

In the second study, 31 participants were distributed in two groups, a u-HIIE group and a passive rest (PR) group in a crossover study design. A two way (group x time) repeated measures analysis of variance (ANOVA) was used to analyze the effect of active recovery protocol on different parameters between the two groups and at different time points. A post hoc analysis with Bonferroni correction was conducted in case of significant main effect or interaction effect.

Chapter 4: Results and Discussion

The following sub-chapters will develop in details all the results and discussion of the present doctoral thesis. Chapter 4.1 presents a systematic review of the literature concerning active recovery protocols and their effect on delayed onset muscle soreness (DOMS) and other associated symptoms following EIMD. In chapter 4.2 a passive protocol consisting of a combination of massage and CWI was investigated, where each participant received the treatment on one leg and the other leg received no treatment at all. Similarly, the results of this study showed no significant effect or advantage of this combination on soreness, muscle performance or gait parameters, when compared with no treatment. In chapter 4.3 we examined the effect of u-HIIE following EIMD in a randomized controlled trial with a crossover design. The main highlights of this study showed no significant difference between the examined active protocol and the control condition however, no adverse effects were significantly reported as well.

Chapter 4.1.: *Effect of active recovery protocol of management of symptoms related to exercise induced muscle damage (EIMD): A systematic review*

ABSTRACT

Active recovery offers an efficient method to relieve delayed onset muscle soreness (DOMS) and recover from exercise-induced muscle damage (EIMD). The main aim of this systematic review is to identify and compare different active recovery protocols following EIMD. Six databases were searched and seventeen eligible studies were selected. Results showed alleviation of soreness, prevention of muscle strength loss, improvement in flexibility, and a decrease in inflammation following one or more recovery protocols such as isolated muscle contractions, aqua exercise, yoga, and combined jogging and running. A better strategy should focus on prevention of symptoms following EIMD through a precise training periodization and adjustment of load used in exercises.

Keywords: Eccentric exercise, fatigue, muscle soreness, pain, strength.

1. INTRODUCTION

Physical exercise offers numerous advantages and benefits for both general health status and performance level. For increased effectiveness of exercise, particular precautions and requirements are recommended to prevent the incidence of injuries and speed up the recovery process if an injury occurs. One of the most common and reported occurrences following unaccustomed exercise, known as exercise-induced muscle damage (EIMD), is a phenomenon called delayed onset muscle soreness (DOMS). DOMS is defined by a sensation of discomfort experienced in the skeletal muscle and is usually associated with a decrease in muscle force[167]. The intensity of this discomfort is characterized by an increase within the first 24 h after exercise, a peak between 24 and 72 h, a reduction, and finally disappearance by five to seven days post-exercise[243]. The mechanism underlying DOMS is still unclear, but many hypotheses and theories have been attributed to this phenomena: muscle spasm[244], connective tissue and muscle damage[245], enzyme efflux[222], hypoxia and ischemia[246], and inflammation[247].

From a physiological perspective, in the absence of muscle pathology, the injury caused by eccentric exercise leads to an intramuscular inflammation[248]. This reaction is a coordinated dynamic process that leads to adaptive remodeling and a return to homeostasis[249]. Blocking or reducing such a response interferes with muscle regeneration and faster recovery[250]. Particularly, changes in acute phase reactants such as serum C-reactive protein (CRP) and Creatine kinase (CK) as well as increases in circulating white blood cells are observed as a result of inflammation following most types of tissue damage[251]. As a result, prostaglandin and leukotriene synthesis take place; the former being responsible for sensation of pain, and the latter responsible for increasing vascular permeability and attracting neutrophils to the site of damage, generating free radicals, causing swelling in the muscle, and aggravating damage to the cell membrane[163,252].

The severity of DOMS is influenced by the duration and intensity of EIMD, with intensity being the primary determinant[253], although the type of muscle contraction (isometric, concentric, eccentric, or a combination of both) is another factor affecting soreness[254]. Results have shown that isometric and eccentric contractions have caused a higher perception of muscle soreness when compared to concentric contractions, with eccentric causing more soreness than isometric[255]. Moreover, eccentric contractions compared to rest or other types of contraction have elicited a 30-36% decrease in force[256], 5-7% decrease in range of motion (ROM)[257] and an increase in muscle stiffness persisting for several days without significant differences in values of CK plasma levels[255,258–260]. A comparison between the effect of running downhill, versus running on a level surface, on soreness and plasma CK was also investigated and showed that both parameters increased significantly following running downhill[261]. Moreover, according to a study examining different protocols of high intensity interval training (HIIT), short sprints, compared to longer intervals, showed higher muscle damage and muscle soreness[262].

In this review, different active recovery protocols were investigated in an attempt to address DOMS and other associated symptoms. Focus will exclusively be directed on active methods comprising movements or activities performed by the participants. Several studies have favored active over passive recoveries due to potential physiological benefits: better blood lactate removal and increased muscle performance[263], higher muscle voluntary isometric contraction[264], higher total quality recovery (TQR), and a decreased feeling of heavy legs[265]. The last two findings support the use of active recovery not just for the physiological benefits already mentioned but also for positive perceptual and psychological considerations[265]. Nonetheless, a number of active protocols have shown controversial findings regarding the choice of intensity, duration, and type of exercise[148,166,222,266–268]. To our present knowledge, there are no other reviews that have provided an exclusive and in-depth analysis of active recovery methods in order to improve performance following EIMD. This review aims at summarizing benefits, identifying limitations, and providing a practical approach for active individuals, coaches, and therapists regarding what type of active recovery could enhance performance level following strenuous activities. The main question to be asked is whether the investigated active protocols meet the demands of sports practitioners in terms of efficiency and offer athletes optimal improvement of their performance level.

2. METHODS

The methodology adopted in this literature search is implemented according to the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement[230]. The review was registered with PROSPERO (CRD42018114679) at the University of York, United Kingdom. The following sections detail how the review was conducted in order to address any bias in selection.

2.1. Search strategy

A detailed search of four major databases was conducted up to and including January 2nd 2020. Articles were collected from the following electronic databases: PubMed/MEDLINE, WEB OF SCIENCE, SPORTDiscus EMBASE, SCOPUS, and CENTRAL. Details of the search strategy for PubMed/MEDLINE are shown in Appendix 1. We also searched clinical trial registries on March 1st 2020 in ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP) to identify ongoing trials. Additional studies were identified by supplementing the electronic database search with manually screened references of the included articles and citation tracking of included studies in SCOPUS.

2.2. Eligibility criteria

Studies were included if they met the following criteria: trials including experimental and control groups, crossover designs, studies including at least one active recovery method, studies including outcome measures taken at different intervals up to a minimum of 48h, studies conducted on humans, and articles in English. Systematic reviews or meta-analyses were excluded**.** After examining the inclusion and exclusion criteria, a total of 17 references were selected for the present systematic review (Figure 1).

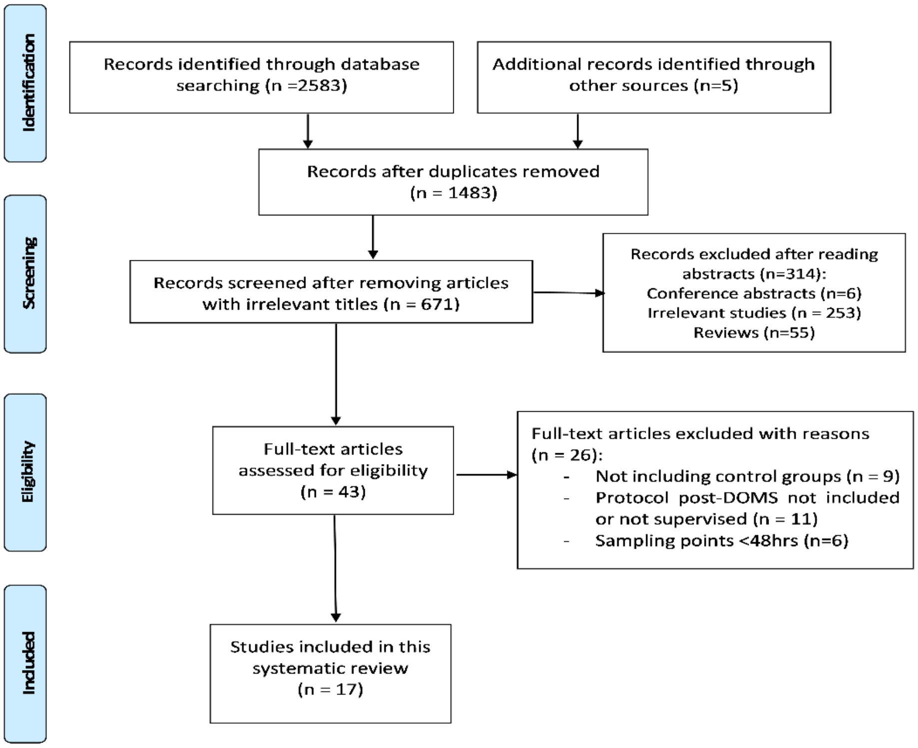

Figure 1: A flow chart of the study selection process

2.3. Study selection

Search strategy consisted of gathering all results from all databases and removing duplicates using Mendeley Reference Manager. Articles identified by the search strategy were screened independently by two reviewers (RF and HO) using the title and abstract first and then the full text. Disagreements over article inclusion were settled through discussion with a third reviewer until consensus was reached. Data were extracted in duplicate and independently by two reviewers (RF and HO) using an electronic data extraction form. The data extracted included the following: author and year, characteristics of participants (number, training status, sex, and age), and corresponding exercise-induced muscle damage and active recovery protocols.

2.4. Quality assessment

Selected studies were evaluated by two reviewers independently (RF and HO) using a checklist of 5 sub-categories and a total of 27 items for assessment of the methodological quality of randomized and non-randomized studies of health care intervention. The different sub-scales address respectively; 1) reporting, consisting of 10 items assessing if the information provided by the studies gives the reader an unbiased assessment of the findings, 2) external Validity, consisting of 3 items addressing to which extent the findings of the studies can be generalized to the population from which the sample size was taken, 3) internal Validity (bias), consisting of 7 items for biases in the measurements of the intervention and the outcomes, 4) internal Validity (confounding-selection bias), consisting of 6 items for biases in the selection of the subjects, and 5) power, to assess whether the negative results of the study are possibly due to chance. A score of 0 or 1 was given to each answer, except for one item in the reporting subscale, which scored 0 to 2 and the last sub-category with one question on power, which was scored 0 to 5. Therefore, the total maximum score was 31[269]. The average score of our selected studies was 17.7 (Table1).

Table 1: Checklist for the assessment of the methodological quality

	Reporting										External validity			Internal validity - Bias							Internal validity - Confounding						Power	Score
References	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	
Andersson et al. (2008)	1	1	1	1	0	1	1	0	1	0	0	0	1	0	0	1	1	1	1	1	1	1	1	0	0	1	0	17
Boyle et al. (2004)	1	1	1	1	0	1	1	0	1	1	0	0	1	0	0	1	1	1	1	1	1	1	0	0	0	1	0	17
Buroker et al. (1989)	1	1	1	1	0	1	1	0	1	0	1	1	1	0	0	1	1	1	1	1	1	1	1	0	0	1	0	19
Gulick et al. (1996)	1	1	1	1	0	1	1	0	1	0	1	1	0	0	0	1	1	1	0	1	1	1	1	0	0	1	0	17
Hasson et al. (1989)	1	1	1	1	0	1	1	0	1	0	1	1	0	0	0	1	1	1	1	1	1	1	1	0	0	1	0	18

Kawczynski et al. (2013)	1	1	1	1	0	1	1	0	1	1	0	0	1	0	1	1	1	1	0	1	1	1	1	0	0	1	0	18
Law et al. (2007)	1	1	1	1	0	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	23
Naugle et al. (2017)	1	1	1	1	0	1	1	0	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	0	0	1	0	19
Olsen et al. (2012)	1	1	1	1	0	1	1	0	1	1	0	0	1	0	0	1	1	1	0	1	1	1	1	0	0	1	0	17
Sakamoto et al. (2009)	1	1	1	1	0	1	1	0	1	1	0	0	0	0	0	1	1	1	0	1	1	1	1	0	0	1	0	16
Takahashi et al. (2006)	1	1	1	1	0	1	1	0	1	0	0	0	1	0	0	1	1	1	0	1	1	1	1	0	0	1	0	16
Tufano et al. (2012)	1	1	1	1	0	1	1	0	1	0	0	0	0	0	0	1	1	1	0	1	1	1	1	0	0	1	0	15
Wahl et al. (2017)	1	1	1	1	0	1	1	0	1	0	0	0	1	0	0	1	1	1	1	1	1	1	1	0	0	1	0	17

Weber et al. (1994)	1	1	1	1	0	1	1	0	1	0	0	0	0	0	0	1	1	1	0	1	1	1	1	0	0	1	0	15
Wessel et al. (1994)	1	1	1	1	0	1	1	0	1	0	1	1	1	0	0	1	1	1	0	1	1	1	1	0	0	1	0	18
Yanfei et al. (2018)	1	1	1	1	0	1	1	0	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	22
Zainuddin et al. (2006)	1	1	1	1	0	1	1	0	1	0	1	1	0	0	0	1	1	1	0	1	1	1	1	0	0	1	0	17

3. RESULTS

3.1. Studies included

The search strategy and filters were adapted and used for each database in order to maximize sensitivity and specificity. A total of 2588 references were researched, out of which 1105 duplicated articles were removed. Titles and abstracts of the remaining articles were analyzed, with irrelevant topics or studies, conferences papers and reviews removed, and the 43 remaining articles were screened for further investigation. Following the reading of full-texts copies, 26 articles were excluded and 17 studies meeting the eligibility criteria were included for qualitative analysis[141,144,268,270–275,145,146,148,157,164,166,221,222] (Figure 1).

3.2. Participants characteristics

The qualitative analysis included 481 participants, comprising 190 males and 291 females. Three studies assessed only males[145,148,268], and four assessed only females[164,166,270,276], the remaining 10 studies used mixed-sex samples. The number of participants in each study ranged from a minimum of 10[268,273], to a maximum of 70[222]. The average age of participants was 24.4 years old, the minimum was 18.7 years old[145] and the maximum was 38.0 years old[276].

Regarding the fitness level of participants, studies included participants from different types of sports: soccer players[145,270], long distance runners[268], students practicing different types of sports[148], yoga practitioners[276], regular recreational physical exercise[146], and also untrained healthy individuals[141,157,164,166,221,222,272,273,275,277,278].

3.3. Intervention characteristics

All studies investigated the effect of active recovery protocols following EIMD. Studies were categorized according to the type of recovery protocol and summarized in Table 2. The categories are as follows: isolated muscle contractions[157,273,275], cycling or arm cranking[146,164,166,222,270], stretching[141,221,272], general physical activity[145,277,278], exercise in water[148,268], and yoga[276]. All recovery protocols were performed on the same group of muscles which had induced damage. All studies measured soreness whether through scales, algometer, or questionnaire. Muscle performance parameters such as maximal voluntary contraction (MVC), counter movement jump (CMJ), peak torque (PT), total work (TW), angle of PT, muscle power, stretch-shortening cycle (SSC), sprint time, and dynamic fatigue were measured in 12 studies[141,146,148,157,164,166,222,268,270,272,273,275]. Seven studies assessed inflammatory markers: CK[145,148,157,268,270,272,275], myoglobin (Mb)[145,148], lactate dehydrogenase (LDH)[148], urea and uric acid[270]. Flexibility was evaluated in three studies[221,268,276], rating of physical exertion (RPE) was assessed in three studies[145,148,276], active and passive range ROM were measured in six studies[141,157,222,268,275,278], muscle circumference was evaluated in four studies[141,222,272,275], and other parameters related to body awareness, disabilities, reaction time, and perceived physical state were assessed in four studies[145,268,276,278].

Table 2: Different recovery protocols in the management of symptoms following exercise-induced muscle damage (EIMD)

Reference	Subjects (sex, age, groups)	Training status	DOMS inducing protocol	Active protocol post-EIMD	Outcome measures	Sampling points	Results
Isolated Muscle Contractions							
Hasson et al. (1989)	6♂ 4♀ (28.7±8.0) MCE (n=5) CG (n=5)	Not specified	10' bench stepping-15 steps/min	6 sets/20 reps knee F-E	MVC/PT/ TW/SPI	PRE, POST, P24H, P48H	Decrease of soreness and SPI, less decrease in muscle performance
Sakamoto et al. (2009)	7♂ 5♀ (25.9±3.7) MCE arm (n=12) Control arm (n=12)	Untrained active	5 sets/ 6 reps ECEF	5 sets arm curls until failure (70% MVC), repeated for 4 days	VAS/MC/ SJA/CK/ MVC/SSC	PRE, POST, P1D, P2D, P3D, P5D, P7D	Increase in static relaxed angle for MC. Increase of circumference, MVC, DEA for control and MC
Zainuddin et al. (2006)	10♂ 4♀ (24.4±2.4) LCE arm (n=14) Control arm (n=14)	Not specified	10 sets/ 6 reps ECEF	25' LCE: 10 sets/60 reps elbow F-E, repeated for 4 days	VAS/ tenderness/ MVC/CON-PT/ROM	PRE, POST, P1D, P2D, P3D, P4D, P7D	Decrease of soreness and tenderness immediately after LCE

					(difference between FANG and SANG)/RANG /MC/CK		
Cycling and Arm Cranking							
Andersson et al. (2008)	17♀ (22±3.4) AR (n=8) CG (n=9)	Elite soccer players	One soccer game	20' cycling (60% HR max), 30' RT (<50% 1RM) (UE+LE) - 10' cycling (60% HR max)	LIKERT scale/ CMJ/ST/PT /CK/ UA/U	PRE, POST, P5H, P21H, P27H, P45H, PH51, P69H	No effect
Olsen et al. (2012)	15♂ 21♀ (20-30) Warm-up (n=12) Cool-down (n=12) CG (n=12)	Recreationally active	5 sets/10 reps front lunges	Cool-down: 20' MIC, 65-75 rpm (60-70% HR max)	VAS/PPT/ MVC	PRE, P24H, P48H	Cool-down group: decrease of PPT from PRE to P24H
Tufano et al. (2012)	26♀ (22.1±2.49) MIC (n=10) LIC (n=10) CG (n=6)	Familiar with DOMS	6 sets/ 10 reps ECKE	MIC: 20' cycling, 80 rpm (70% HR max) LIC: 20' cycling, 80 rpm (30% HR max)	PS/MVC/PT	PRE, POST, P24H, P48H, P72H, P96H	MIC group:Increase in MVC at P72H and P96H from P24H and P72H from IP

Gulick et al. (1996)	35♂ 35♀ (21-40) NSAID UEE;IM; SS; OSP; CG	Untrained	15 sets/ 15 reps ECWE	10' UEE high velocity (360^{O}/s)	A+ P ROM/MC/ volume/VAS/PPT/MVC/ TW-PT-angle of PT CON/ECC	PRE, POST, P20', P24H, P48H, P72H	No effect
Weber et al. (1994)	40♀ (18-35) Massage (n=10) UEE (n=10) NMES (n=10) CG (n=10)	Untrained	10 reps or repeated until failure, ECEF, 5"/rep	8' UEE, 60 rpm, workload 400Kg-m/min	VAS/MVC/ PT	PRE, P24H, P48H	No effect
Stretching							
Buroker et al. (1989)	16♂ 7♀ (18-33) Stretch LKE (n=7) Stretch LKE+RPF (n=8) CG (n=8)	Moderate	20' bench stepping-15 steps/min	10 reps/30s SS, 10" rest between reps, left KE and right PF	VAS/PPT/ MC/MVC/CK	PRE, P24H, P48H, P72H	No effect
Wessedl et al. (1994)	13♂ 7♀ (25.2±3.36) Stretch pre-EIMD/	Sedentary	3 sets/ 20 reps CECKF	10x hamstrings static stretches, 60" holding,	VAS/PPT/ SLR	VAS*: P12H, P24H, P36H, P48H, P60H,	No effect

	control leg (n=10) Stretch post-EIMD/ control leg (n=10)					P72H/ PPT*+SLR*: PRE, P48H	
Yanfei et al. (2018)	20♂ 28♀ (21.7±1.4) DS (n=16) SS (n=16) CG (n=16)	Healthy individuals	3 sets heel raising against elastic band-120x/min	DS: 10x C-R S+G/5" IC-30" holding stretching. SS: 10x SS S+G/30" holding, 2x/day-5 days	VAS/PPT/ ROM/MC/ MIC	PRE, POST, P24H, P48H, P72H, P96H, P120H	No effect
General Physical Activity							
Kawczynski et al. (2013)	11♂ (18.7±1.2) S1; S2; S3	Professional football field players	3 soccer games	Standard recovery (No activity after the game, 30´jogging at 24h and ball control skills at 48h)/ control: No activity recovery/DOMS reduction training (20´ jogging after game, 20’ jogging,, 20’ running-eccentric	RPE/PPT/ CK/Mb	PRE, P24H, P48H	Increase in PPT for the "DOMS reduction" protocol and increase in CK* for "no activity" and "DOMS reduction session

				muscle action related with football and 20’ ball control skills at 24h and 48h)			
Law et al. (2007)	23♂ 29♀ (17-40) Warm-up + Cool down (n=13) Warm-up (n=13) Cool-down (n=13) CG (n=13)	Not specified	30' walking backwards downhill, 35 steps/min	Cool-down: 10' walking on inclined treadmill, 4,5-5kph	VAS/NRS/PPT	P10', P24H, P48H, P72H	Decrease of pain and tenderness in Warm-up grp. No significant effect for Cool-down on soreness or tenderness
Naugle et al. (2017)	4♂ 44♀ (20.0±1.9) WB (n=12) IT (n=12) LCE (n=12) CG (n=12)	Healthy adults	3 sets/ 10 reps ECEF	20' WB / 8 sets/60 reps EF	Active total ROM/Pain free ROM/ VAS/PPT/ Quick DASH	PRE, P24, post AR1, P48, post AR2	Increase in EF and pain free ROM, decrease in VAS and increase in PPT in WB from pre to post test. Higher Quick DASH scores for WB at day 2
Exercise in Water							
Takahashi et al. (2006)	10♂ (20±1) AE (n=5)	Long-distance runners	3 sets/5' downhill running	30' walking, jogging and jumping in the pool	Stiffness/MP/ SR/SL/ ROM/CK/	PRE, P24H, P48H, P72H	Better recovery of soreness in AC. No decline of whole body reaction time in AC

	CG (n=5)				WBRT		
Wahl et al. (2017)	20♂ (24.4±2.2) AC (n=10) CG (n=10)	Sports students	300 CMJ, one jump every 8"	30' LIC in a pool, cadence: 65-75 rpm	VAS/RPE/PEPS/MVC/dynamic fatigue test/Mb/CK/LDH	PRE-EIMD, POST-EIMD, PRE-recovery, POST-recovery, P1H, P2H, P4H, P24H, P48H, P72H	No effect
Yoga							
Boyle et al. (2004)	24 ♀ (37.8-38.3) YG (n=12) CG (n=12)	Yoga trained and no yoga experience	20' bench stepping (15.5 steps/min)	90' gentle or moderate yoga class, 24 and 72h after initial testing	BA/SR/VAS/RPE	PRE, P24H, P48H, P72H, P120H	Decrease in pain and increase in flexibility in YG

♂: male; ♀: female; MCE: muscle contraction exercise; CG: control group; WB: Wii boxing; IT: ice therapy; AR: active recovery; NMES: neuro-muscular electrical stimulation; UEE: upper extremity ergometry; LKE: left knee extensor; RPF: right plantar flexor; EA: endurance activity; AE: aqua exercise; AC: aqua cycling; S: session; IM: ice massage; SS: static stretching; OSP: ointment sublingual pellets; ECEF: eccentric contractions for elbow flexors; LE: lower extremities; ECKE: eccentric contractions of knee extensors; ECWE: eccentric contractions of wrist extensors, CECKF: concentric-eccentric contractions of knee flexors; F: flexion; E: extension; EF: elbow flexion; LCI: light concentric exercise; MIAE: moderate intensity aerobic exercise; RT: resistance training; MIC: moderate intensity cycling; LIC: light intensity cycling; HR: heart rate; KE: knee extensors; PF: plantar flexors; C-R: contract-relax; S+G: soleus and gastrocnemius; IC: isometric contraction; DEA: dynamic extension angle; NRS: numerical rating scale; VAS: visual analogue scale; A: active; P: passive; MC: muscle circumference; Quick DASH: quick disabilities of the arm, shoulder and hand; SJA: static joint angles; PPT: pressure point threshold; MVC: maximal voluntary contraction; PT: peak torque; TW: total work; CON: concentric; ECC: eccentric; WBRT: whole body reaction time; SPI: soreness perception index; SSC: stretch shortening cycle; PS: pain scale; ROM: range of motion; FANG: flexed joint angle; SANG: stretched joint angle; RANG: relaxed joint angle; ST: sprint time; CK: creatine-kinase, Mb: myoglobin, LDH: lactate dehydrogenase ; UA: uric acid; U: urea; SLR: straight leg raise; STAI: state-trait anxiety inventory; RPE: rate of perceived; CMJ: countermovement jump; PEPS: persons perceived physical state; MP: muscle power; SR: sit-and-reach; SL: stride length; BA: body awareness; MM: magnitude matching procedure; YG: yoga group

3.4. Results of recovery protocols

Following a recovery protocol of knee flexion-extension exercise, a significant decrease of pain and a more modest decrease of MVC, TW, and PT of knee extensors compared to a control group (8.3% vs. 33.4%, 2.3% vs. 13.8% and 3.8% vs. 12.1%, respectively) were both reported at 48 h[273]. Light concentric flexion-extension exercise of the elbow flexors resulted in a significant immediate decrease in soreness perception (43% on average); however, this effect was short-termed and not sustained[157].

Two types of dynamic recovery protocols were performed immediately, 24 h and 48 h following a soccer game: "DOMS reduction training" session (jogging, running, low intensity eccentric exercises and ball control skills) and "standard recovery training" session (jogging and ball control skills)[145]. Differences in results between before and 48 h following the game have shown a significant increase in pain threshold by 29% following "DOMS reduction training" whereas a decrease of 19% was noticed following "standard recovery training" session [145]. Plasma CK decreased significantly from 24 h to 48 h following the game by 36.6% when no recovery protocol was performed, and by 22.3% following a DOMS reduction training session[145].

Naugle et al. have investigated Wii sports boxing active game and a standardized elbow flexion-extension exercise (1lb, 8 sets x 60 reps), both compared to each other and to rest. A greater pain threshold was noticed following Wii boxing along with an increase in active total ROM on day 1 compared to light concentric exercise (150.67°±1.16° vs. 148.33°±1.16°)[278].

Exercise in water involving general dynamic exercise for three consecutive days[268] and cycling[148], was also investigated. The aqua exercise group showed a significant decrease in calf muscle soreness and stiffness and a significant result on muscle power, where a more pronounced decline was noticed in the control group at day 2 following EIMD[268]. All blood markers showed a greater increase in the aqua cycling group compared to the control group[148].

Yoga exercise results showed a lower peak muscle soreness and an improved flexibility at 24 h and 48 h following EIMD when compared to control group[276].

Finally, there were no significant results reported in any of the outcome measures assessed following cycling and arm cranking[146,164,166,222], combined cycling and low-intensity resistance training[270], and stretching in both forms, static and dynamic[141,221,272].

All outcome measures assessed in the papers are also summarized in Table 3.

Table 3: Different outcome measures used to assess symptoms following exercise-induced muscle damage (EIMD)

	Outcome measures						
References	**Soreness**	**Muscle performance**	**Inflammatory markers**	**Flexibility**	**Fatigue**	**ROM**	**Other**
Andersson et al. (2008)	LIKERT scale	PT, CMJ, ST	CK, UA, U				
Boyle et al. (2004)	VAS			SR	RPE		BA
Buroker et al. (1989)	VAS, PPT	MVC	CK				MC
Gulick et al. (1996)	VAS, PPT	MVC, TW, PT, angle PT				Active & passive ROM	MC/volume

Hasson et al. (1989)	SPI	MVC, TW, PT					
Kawczynski et al. (2013)	PPT		CK, Mb		RPE		
Law et al. (2007)	VAS, NRS, PPT						
Naugle et al. (2017)	VAS*, PPT*					Active total ROM, Pain free ROM	QuickDASH
Olsen et al. (2012)	VAS*, PPT*	MVC					
Sakamoto et al. (2009)	VAS*	MVC, SSC	CK			RANG, FANG	MC

Takahashi et al. (2006)	Stiffness by a questionnaire	MP	CK	SR, SL		Total active ROM	WBRT
Tufano et al. (2012)	PS	MVC, PT					
Wahl et al. (2017)	VAS	MVC, dynamic fatigue	CK, Mb, LDH		RPE		PEPS
Weber et al. (1994)	VAS	MVC/PT					
Wessel et al. (1994)	VAS, PPT			SLR			
Yanfei et al. (2018)	VAS, PPT	MVC				Active total ROM	MC

Zainuddin et al. (2006)	VAS, tenderness by pressure	MVC, CON-PT	CK			ROM (difference between FANG and SANG), RANG	

♂: male; ♀: female; MCE: muscle contraction exercise; CG: control group; WB: Wii boxing; IT: ice therapy; AR: active recovery; NMES: neuro-muscular electrical stimulation; UEE: upper extremity ergometry; LKE: left knee extensor; RPF: right plantar flexor; EA: endurance activity; AE: aqua exercise; AC: aqua cycling; S: session; IM: ice massage; SS: static stretching; OSP: ointment sublingual pellets; ECEF: eccentric contractions for elbow flexors; LE: lower extremities; ECKE: eccentric contractions of knee extensors; ECWE: eccentric contractions of wrist extensors, CECKF: concentric-eccentric contractions of knee flexors; F: flexion; E: extension; EF: elbow flexion; LCI: light concentric exercise; MIAE: moderate intensity aerobic exercise; RT: resistance training; MIC: moderate intensity cycling; LIC: light intensity cycling; HR: heart rate; KE: knee extensors; PF: plantar flexors; C-R: contract-relax; S+G: soleus and gastrocnemius; IC: isometric contraction; DEA: dynamic extension angle; NRS: numerical rating scale; VAS: visual analogue scale; A: active; P: passive; MC: muscle circumference; Quick DASH: quick disabilities of the arm, shoulder and hand; SJA: static joint angles; PPT: pressure point threshold; MVC: maximal voluntary contraction; PT: peak torque; TW: total work; CON: concentric; ECC: eccentric; WBRT: whole body reaction time; SPI: soreness perception index; SSC: stretch shortening cycle; PS: pain scale; ROM: range of motion; FANG: flexed joint angle; SANG: stretched joint angle; RANG: relaxed joint angle; ST: sprint time; CK: creatine-kinase, Mb: myoglobin, LDH: lactate dehydrogenase ; UA: uric acid; U: urea; SLR: straight leg raise; STAI: state-trait anxiety inventory; RPE: rate of perceived; CMJ: countermovement jump; PEPS: persons perceived physical state; MP: muscle power; SR: sit-and-reach; SL: stride length; BA: body awareness; MM: magnitude matching procedure; YG: yoga group

DISCUSSION

The main objective of this systematic review was to examine and assess different active recovery protocols and show potential benefits on the recovery of DOMS and other related symptoms following EIMD. Positive effects on muscle soreness have been shown with isolated muscles contractions but less on muscle performance and ROM. Studies examining cycling for lower and upper extremities as well as static and dynamic stretching did not show significant results on recovery parameters following EIMD. Jogging/running activities showed satisfying results concerning soreness perception and a decrease in inflammatory markers in the blood starting immediately after an intensive activity. Walking uphill seems more efficient when used as a warm-up rather than a recovery protocol with positive effects on the reduction of DOMS. In the same direction, aqua exercise facilitated the recovery of leg muscles and showed faster improvements on muscle soreness, stiffness and power. Finally, the practice of yoga appears to relieve DOMS and improve flexibility.

Accordingly, strong evidence supports the effect of muscle contractions on soreness. Adding motivation and fun to exercise in order to maximize its effects compared to other active methods has also been revealed to be very important[278]. Similarly, the choice of the intensity of exercise might have an influence on the present results, hence Wii boxing involving light to moderate intensity might lead to higher muscle activation and can potentially be required to optimize the effectiveness of exercise in the days following the intervention protocol[278]. Conversely, the use of light concentric exercise (LCE) involving repetitions of flexion-extension without weight, performed in the days following an intensive training session have shown a positive result on soreness only immediately after the recovery protocol[157]. This finding correlates with the "exercise-induced analgesia" hypothesis which showed that light to moderate intensity seems to contribute in alleviating soreness, although the effect is temporary and not sustainable[279]. Therefore, from a practical perspective, LCE seems to be recommended to help relieving soreness immediately after an intensive training session.

A possible explanation for the lower decrease in muscle performance following knee flexion-extension is the potential effect that high-speed maximal contractions (300º/sec) or shorter time under muscle tension have on inflammatory markers[273]. During eccentric and high-speed contractions, predominantly fast-twitch units are recruited[50], thus stimulating type II muscle fibers that potentially are more often injured than type I[280]. The selective recruitment of these affected type II fibers reduces the fluid accumulation and swelling and delays the upregulation of pro-inflammatory cytokines such as nerve growth factor, histamine, and prostaglandins which are responsible for nociceptor activation[260]. Therefore, participants showed a better muscle performance in the exercised leg because of the reported decrease in perceived pain compared with the control leg. However, upper extremities were studied[157,275,278], and no significant difference was found in all muscle performance-related parameters between the exercising and control groups. The aforementioned studies using upper extremities stated no significant positive result on muscle recovery after a damaging exercise and fatigue. The reason behind that might be related to the muscle mass involved in the recovery as the lower extremity has a greater muscle mass than the upper extremity, as a result, the exerted muscle contraction is more accentuated and might lead to significant positive findings.

The contradictory results between the two recoveries on ROM could be attributed to the difference in LCE protocols performed[157,278]. For example, 10 sets of 60 reps (2 sec/flexion-extension) using an isokinetic dynamometer at 240º/sec, were performed for 20 min in one study[157], whereas, 8 sets of 60 repetitions of flexion-extension with a free weight of 1 lb. were included in another study[278].

This difference in the mode of exercise could be translated into a modification in muscle tension occurring between isotonic and isokinetic exercise in terms of speed velocities and load intensities. Recently, some authors have highlighted the importance of speed in order to quantify the intensity of an exercise, leading to differences in performance[256,267].

Neither the upper or lower extremity showed a significant change on pain or on isometric or dynamic strength after application of a low or moderate intensity protocol[145,146,166,222,270], however an increase in isometric strength at 72 and 92 h compared with 24 h post EIMD was found in one study following moderate cycling with no effect on dynamic strength[166]. The result is in contrast to previous findings of previously mentioned studies stating the positive effect of isolated muscle contractions on soreness perception[157,273,275]. The reason behind this dissimilarity might be attributed to the choice of intensity in the examined recovery protocols. Acute endurance exercise is related to higher blood flow and an increase in muscle perfusion helping in removing noxious waste products following a high intensity exercise causing contractile elements disruption[281]. It was suggested that in order to increase this muscle perfusion and thus decrease soreness, heart rate should be elevated before each exercise in order to enhance tissue repair[252]. Consequently, the light endurance intensity (between 30 and 60%HRmax) used in cycling and arm cranking[166,270] and the submaximal contractions in upper ergometry (360/sec)[222] might not have been effective in obtaining a considerable decrease in muscle pain. Whereas, higher intensities (between 60 and 70% HRmax) have shown better results on muscle performance[166].

Additionally, no significant difference was detected after a stretching protocol on pain and soreness perception. This is consistent with all the studies involved in this review[141,221,272]. The soreness outcomes are reported to reflect the process of muscle nociception in response to the accumulation of endogenous analgesic agents[282]. The fact that participants cannot be blinded during their recovery protocol is an important factor to be mentioned since subjective positive perception was expected in the groups that performed stretching, which leads to greater expectation of relief after their session[221]. Although dynamic stretching was suggested for its reported analgesic effect caused by isometric contraction and thus interrupting the transmission of pain[283,284], the results did not support this idea. Also, there was no positive effect observed on muscle performance and inflammatory markers, which might be due to the low level of muscle damage reported after a combination of concentric and eccentric contractions instead of pure eccentric bouts to induce muscle deficits soreness[141].

General physical activity involving warm-ups and cool-downs showed potential benefits including increased temperature and muscle compliance, reduced muscle strain injuries[285] and decreased DOMS[286]. In the reviewed study, only warm-up showed a significant effect at 48h post eccentric exercise on reducing soreness and muscle tenderness[277]. This finding justifies the use of dynamic exercise before the main activity to alleviate soreness through the removal of waste products by stimulating blood flow and increasing endorphins[253].

Consequently, the main difference with all of the previously covered studies is the inclusion of a high volume exercise protocol performed 24 and 48 h after an intensive activity such as a soccer game. This extra stimulation to the main muscle affected by DOMS may lead to a higher level of interference in the pain sensation mediated by mechanoreceptor fibers[169].

Regarding the positive effect on plasma CK activity, an immediate active recovery protocol seems to help decrease blood markers following an activity while also increasing the blood circulation and removing metabolic waste products, such as carbon dioxide, urea, and uric acid. This, in fact, may explain the decrease in CK seen after implementing an immediate active protocol with a bigger volume[145].

Exercising in water has also been found as an effective method for dealing with soreness[268]. A possible explanation for this could be the decrease of load over the legs when immersed into water, causing a massage effect which, therefore, could increase peripheral blood flow, facilitate the elimination of edema and reduce local muscle stiffness. Consequently, muscles appear to be less swollen and less painful. This massage effect could be lower when performing cycling in water[148], which may explain the similarity of results on pain intensity following that modality and in the control group.

Nevertheless, the increase in blood markers following the aqua cycling group might be due to the effect of a localized exercise (cycling) performed on the anterior thigh muscle in water, after a highly fatiguing activity (300 jumps), which might have potentially accentuated the muscle damage[148]. The positive effect of aqua exercise on muscle performance was also supported in previous studies showing the benefit of water jets in preventing any potential loss of muscle power[281].

Finally, results on yoga practice showed positive results on muscle soreness. This could be related to originally existing differences in muscle condition for yoga practitioners in comparison with untrained participants[276]. Flexibility was also improved and could explain the improvement in pain intensity following the bouts of yoga since flexibility has always been linked with a decreased perception of muscle soreness in yoga practice[287].

CONCLUSION

Active recovery protocols showed several advantages and benefits over rest with the main improvements observed on the magnitude of soreness. Muscle isolated contractions, jogging, running, aqua exercise, and yoga, all seem to offer a limited management of DOMS following

EIMD. Aqua exercise prevented to some extent a loss in muscle power, jogging and running decreased inflammatory markers, and the practice of yoga improved flexibility. On the other hand, arm cranking, cycling, and stretching did not seem to help soreness or any other symptom. Furthermore, the impact of active recovery was less obvious on outcomes related to functional capacity and performance. It is also important to note that none of the tested methods have shown an adverse effect on soreness. Consequently, the attempt of decreasing the recovery period without affecting an athlete’s overall performance is still a critical challenge and requires further investigations in order to optimize training benefits and outcomes.

PRACTICAL IMPLCATIONS

Our present review offers a few practical implications for sports practitioners. Although no particular active recovery was found to be efficient in helping the improvement of performance level following an intensive training session. It is essential to highlight the benefits on different aspects related to performance. Exercise under water might be a good option to limit the decrease in muscular strength following an intensive training session. Additionally, pain due to soreness can be relieved by a number of recovery protocols ranging from isolated muscle contractions to general physical activity.

Chapter 4.2.: *Combined effect of Massage and Cold Water Immersion (CWI) on the treatment of symptoms related to exercise Induced Muscle Damage (EIMD)*

ABSTRACT

OBJECTIVES: To examine the potential benefit of combining massage and cold water immersion (CWI) as a single recovery protocol on delayed onset muscle soreness (DOMS), muscle performance and other related symptoms, 24h following an intensive exercise.

METHODS: 35 participants whose one leg was randomly assigned to receive a combination of a 20-minute massage and a 15-minute CWI at 12ºC temperature, 24 h following an exercise-induced muscle damage (EIMD); the other leg served as control. Outcome measures included pain at rest, pressure point threshold (PPT), maximum voluntary isometric contraction (MVIC), counter-movement jump (CMJ) and gait analysis. All variables were taken on day 1 (PRE) and day 3 (POST), except for pain which was also evaluated at day 4. Day 2 consisted only in EIMD.

RESULTS: The combination of massage and CWI did not show any significant result on hip, knee and ankle range of motion (ROM), heel height, MVIC, CMJ or soreness on the treated leg in comparison with the control leg.

CONCLUSION: The combination of massage and CWI did not offer any superior advantage on soreness and other symptoms related to EIMD, when compared to each protocol applied separately. More controversy is added on the advantage of massage and cryotherapy in relieving soreness, accelerating recovery and maintaining muscle performance.

Key words: cold water immersion, massage, DOMS, EIMD, recovery.

INTRODUCTION

Exercise-induced muscle damage (EIMD) consists of a number of symptoms resulting from the damaging exercise and tearing of the contractile muscular tissue[288]. EIMD is often followed by delayed onset muscle soreness (DOMS), muscle stiffness, swelling in the belly of the muscle and altered biomechanics to the adjacent joints[289], with a decreased range of motion (ROM)[290] and an impaired muscle strength[291]. These symptoms can progress typically following an eccentric exercise or any other intensive unaccustomed workout[32], peaking up to 72 h post exercise[250] and lasting up to two weeks. Their extent and repercussion on performance depends both on the intensity and duration and the individual susceptibility to intensive workouts[48]. To date, no therapeutic approach has been elicited as the gold standard in order to alleviate EIMD[292], therefore, the choice for the optimal recovery protocol in terms of perceived pain and muscle performance is necessary. Active recovery appears to be an efficient alternative following unaccustomed efforts, and even vigorous intensities are well tolerated[293,294].

Massage has been traditionally used to combat EIMD but the lack of a strong scientific basis makes it controversial. Muscle soreness has been reported to decrease after applying 15-20 min of massage following EIMD[295,296], even restoring muscle strength in comparison with a control group[295]. A meta-analysis including 1012 participants concluded significant improvements from massage in terms of DOMS relief, although no benefits were found on performance[241]. The underlying mechanism by which massage mitigates muscle soreness could be related to a decrease in tissue adhesion and muscle stiffness and an increase in temperature. This situation may result in decreased inflammatory markers, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)[297]. It is worth mentioning that other studies have shown no effect of 8-10 min of massage neither on DOMS[298] nor in muscle function[299] following EIMD.

Despite massage has been found to be the most effective technique for reducing DOMS and perceived fatigue[132], there are other methods that have been used for this purpose. For instance, cryotherapy is commonly applied following intense efforts. Similar to massage, the effectiveness of this method on athletic recovery remains inconclusive, with several studies obtaining positive results[300,301] and being challenged by others[302,303]. A one-week whole-body cryotherapy protocol consisted of three-minute exposures induced a positive effect on DOMS relief up to six hours following the intensive exercise, although this was not sustained till 24 h or later[304]. Additionally, when cryotherapy has been applied as cold water immersion (CWI) positive results has been noted in performance[305] and muscle soreness reduction[306].

According to the existing literature, massage and cryotherapy are usually applied individually and separately following EIMD. To date, no studies have examined the effects of combining both techniques on muscle soreness recovery and sports performance. This is striking, bearing in mind that professional and recreational athletes commonly used massage coupled with cryotherapy in their recovery processes. Therefore, there is a lack of evidence on this topic that needs to be resolved. The main objective of the present study was to investigate the effects of a combined protocol including massage and subsequent CWI in an intra-subject, leg-to-leg comparison model regarding pain relief, muscle performance and gait patterns following EIMD.

METHODS

Participants

A power analysis was performed with a total sample size of 31 subjects required to satisfy a significance level of 0.05 with power of 0.90 (G-power software 3.1.2; Franz Faul, University of Kiel, Kiel, Germany)[307]. Taking into consideration possible dropout, the minimal number of subjects was increased by 10%, and the adjusted sample size was 34.

Thirty-seven young active individuals recruited among university students volunteered to participate, of which two were excluded later due to the inability to register post-test data. Overall, 35 individuals (18 males and 17 females; mean age: 21.6 ± 0.8 years) completed the entire protocol. The participants' characteristics are shown in table 1. All participants were previously informed of the study purpose and procedures, including risks and benefits, and completed a health questionnaire. The inclusion criteria consisted of being physically active adults, according to the physical activity guidelines for Americans[308]. Participants were excluded if they trained in plyometric, presented musculoskeletal injuries, had or were at risk of cardiovascular disease, suffered intolerance or hypersensitivity to cold, or took anti-inflammatory medication during the study. Individuals were requested to refrain from any strenuous exercise 48 h prior to the first test.

Design and procedures

This study consisted of a prospective controlled trial aimed to assess the effects of a combined protocol of massage and cold water immersion on muscle recovery and performance. All research was in compliance with the ethical guidelines of the Declaration of Helsinki 1961 (revision of Fortaleza 2013)[229] and approved by the Research Ethics Committee of Principality of Asturias (292-19).

Following EIMD, the legs of each participant were randomly assigned to massage and CWI or control. The physiotherapist that performed massage, who was not involved in the study, was responsible for random allocation and evaluators were blinded to the treatment procedure. We choose a within-subject strategy, in which each participant acted as their own control, in order to minimize between-group variability[147].

Subjects were called to the laboratory four consecutive days (24 h apart) along the same week. On day 1, participants were interviewed and were subjected to a preliminary assessment. This consisted of anthropometric and pain measurements, kinematic gait analysis, counter movement jump (CMJ) and maximal voluntary isometric contraction (MVIC) testing. On day 2, all participants performed an EIMD protocol followed by a treatment session with massage and cold water immersion on one lower limb. This procedure was carried out by a physiotherapist. On day 3, individuals repeated the same tests that had performed on the first day, except the anthropometric measurements. Pain was the unique outcome assessed on day 4. Figure 2 represents a scheme of the study design.

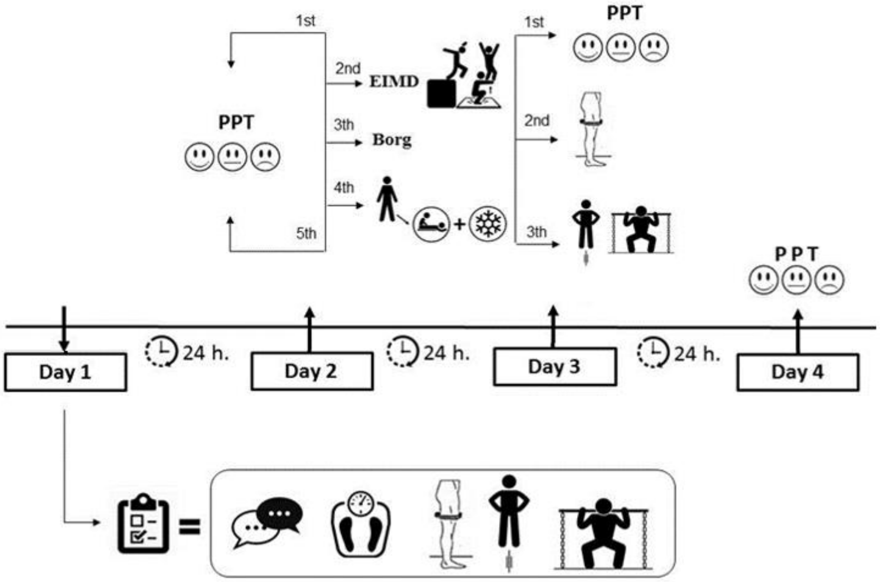

Figure 2: Graphic representation of the study protocol (massage/CWI)

Day 1: Preliminary assessments

An interview was conducted with participants to collect information about their dominant leg, the sport(s)/physical activity that they used to do, their sports experience and the treatments that they had applied in the past for DOMS recovery.

Anthropometric measurements

Weight was measured in underwear and without shoes with an electronic scale (Type SECA 861), while height was assessed barefoot (Type SECA 225). To estimate the percentage of body fat Evans' equation and anthropometry data was used[309] following the International Society for the Advancement of Kinanthropometry (ISAK) standards[310], with a caliper, anthropometric tape, and anthropometer (Holtain, Crymych, UK).

Muscle circumference

Swelling of the thigh muscle was assessed by measuring muscle circumference. Mid-thigh girth of the dominant leg was taken at the middle of a vertical line between the greater trochanter and the base of the patella. The measurement was performed by a constant tensiontape (Lufkin, Cooper Industries, Houston, Texas, USA)[294].

Visual analogue scale (VAS)

In order, to assess the severity of pain, a numerical scale was used consisting of a 10 cm line, starting with "no pain" (0 cm) to "worst pain" (10 cm)[234]. Participants were instructed to assess their subjective sensation of pain on both legs from day 1 to day 4 of the experiment.

Pressure pain threshold (PPT)

PPT is defined as the minimum force applied that generates a painful stimulus in a determined point of a muscle[235]. PPT was measured with a hand held electronic pressure algometry (Somedic Algometer Type II, Sweden) on the middle of a vertical line joining the greater trochanter to the base of the patella in both legs. These spots were marked in order to apply the pressure on the same location along the different assessments. Prior to applying the pressure, the algometer was positioned perpendicular to the skin[236], while participants were seated with a 90° flexion of both hip and knee joints. They were instructed to inform whenever a painful sensation was perceived; thus, the pressure was released immediately and the reading on the device corresponded to the measurement taken. This assessment was repeated twice and the mean value was registered.

Gait analysis

The gait assessments consisted of ten walking cycles, five at normal pace and five at fast pace, on a 10-m walkway. Normal pace corresponded to a self-selected comfortable speed, whereas fast pace was considered as the maximum speed for safe walking just before starting running[239]. Movement markers were placed on specific anatomical landmarks on the legs of the subjects, and were captured at 100 Hz using an eight-camera Vicon system (Oxford Metrics

Limited, Oxford, UK). Data was then analyzed using the Vicon Workstation and Polygon software, which allowed defining gait cycle events and assessed the following spatiotemporal parameters: cadence, step length, support time, push time, and ROM of hip, knee and ankle[239].

Maximum dynamic force

Maximum dynamic force was calculated by performing a CMJ on a force plate (SG 9, Advanced Mechanical Technology Inc., Newton, MA) and low-pass filtered at 500 Hz. Participants were instructed to stand on the force plate with their hands fixed on the hips and to jump as high as possible before landing on the same spot of the starting position.

The vertical reaction force impulse of the jump during take-off helped determine jump height. All subjects were required to perform three trials interspersed by two minutes of rest, the best result was used for analysis (CV < 5%). Participants' body mass, which was previously measured on the force plate, was used to calculate jump height[237].

MVIC

MVIC of knee extensors muscles was also assessed as described previously on the aforementioned force plate and low-pass filtered at 1050 Hz. Subjects were standing in a squat position with a 90º knee flexion and a 110º hip flexion and a bar at their shoulders anchored to the ground by two cables. Subjects were encouraged to exert a 6-sec maximum force of knee extension by pushing powerfully against the fixed bar. Three attempts were made with a 5-min break between each one, recording the best result. This was determined as the highest value of force produced (N), according to body weight (per Kg)[238].

Day 2: Experimental protocol

EIMD protocol

Subjects arrived 24h after the preliminary measurements to perform an EIMD protocol. The protocol was adapted from previous studies[232,233] and consisted of 10 sets of 10 repetitions of drop jumps, with a one-minute break between each set. EIMD was preceded by a 10-min warm-up on a treadmill. Participants stood on a box of 50 cm height, without any prior take-off. They dropped on the floor in a squatting position with a self-selected contraction time and range of motion of knees and hips, and then jumped upwards as high as possible.

Application of massage and CWI

Following the jumping protocol, massage and cold water immersion were performed in that order to each participant on a single lower limb, which was chosen by the physiotherapist. Once the first participant was treated, the lower limb subjected to the combined protocol was alternated for the rest of subjects (e.g., left – right – left, etc.), regardless of the individual characteristics. Thus, treatment protocol was accomplished on 50% of the total lower limbs of the participants.

Manual massage was performed for 20 min, in accordance with the duration chosen by previous studies[202,240,241]. Massage protocol comprised effleurage (2 min), petrissage (12 min), wringing (4 min) and tapotement (2 min) movements, and was applied on quadriceps, hamstrings and triceps surae muscles. Effleurage consists of light stroking movements applied rhythmical, centripetal and multidirectional. In petrissage, rhythmical kneading and squeezing movements are applied centripetally over the muscle. The wringing movement is based on grasping superficial tissues and twisting them in opposite directions. Finally, tapotement applies repeated light strikes to muscle mass[241]. Subjects were requested to lie in supine position to applied massage on quadriceps, and then they received this therapy lying in prone position to treat hamstrings and triceps surae. Massage was always applied by the same physiotherapist, who controlled the rhythm and pressure of the maneuvers according to the perceived soreness of each participant. A chronometer was used in order to control the exact duration of the massage. Immediately after massage completion, temperature of the surface of both rectus femoris (intervention and control limb) was measured using a Technoline WS 1006 thermometer.

Immediately after massage, participants were sat in a mobile ice water bath with legs at 90º to the torso and were immersed up to their superior iliac crests. The duration and the temperature were 15 min and 12ºC, based on previous studies with successful results[185,242]. The temperature was monitored each five minutes using a thermometer and, if necessary, ice cubes were added in order to maintain it strictly. Similar to post-massage, temperature of the surface of both rectus femoris was measured at the end of the CWI protocol.

Day 3: Post-protocol measurements

Participants were called 24 h following the intervention protocol in order to repeat the assessments. The VAS and the circumference of both thighs were measured for each subject. Gait analysis, CMJ and MVIC were all reevaluated in the same way as the preliminary measurements.

Day 4: Pain assessment

VAS and PPT were evaluated 72 h after completion of the entire intervention protocol.

Statistical analysis

A one-sample Kolmogorov–Smirnov test confirmed the assumption of normal distribution for all the variables. Overall, 70 lower limbs were analyzed. This was due to our study design, including 35 subjects of which one lower limb received the treatment and the opposite served as control. A two way (group x time) repeated measures analysis of variance (ANOVA) using SPSS 24.0 (Statistical Package for Social Sciences, Chicago, IL, USA) was performed to determine intra-group differences and the effect of the combined treatment (massage + CWI) on the outcomes evaluated. A post hoc analysis with Bonferroni correction was conducted when significant main effect or interaction effect was reached. The descriptive analysis included the calculation of the mean and standard deviation.

For each outcome measure, a p value was reported corresponding to the main intervention effect and time effect. Statistical significance was set at $P < 0.05$.

RESULTS

Mean data of physical characteristics of the included participants are shown in Table 4. Both groups were comparable in age, height, weight and fat percentage.

Table 4: Physical characteristics of the participants

Age (years)	**Height (cm)**	**Weight (Kg)**	**Fat percentage (%)**
21.6 ± 0.8	170.7 ± 9.4	64.4 ± 12.1	20.6 ± 5.7

Data are presented as mean ± standard deviation (SD)

No significant time x group interactions were found in any of the variables of the hip, knee and ankle ROM ($p = 0.349$, $p = 0.448$ and $p = 0.256$, respectively). The p value of ankle ROM was adjusted by the method of Bonferroni.

The intervention produced significant improvements in hip, knee and ankle ROM ($p = 0.037$; $p = 0.031$ and $p = 0.024$, respectively). No significant time x group x sex interaction was found ($p = 0.511$, $p = 0.898$ and $p = 0.493$ respectively).

Data for ROM measurements are displayed in Table 5.

Table 5: Data of joint ROM for intervention (I) and control (CTR) lower limbs at baseline (PRE) and following the protocol (POST)

		PRE	**POST**
Hip	I	36.44 ± 9.94	40.42 ± 4.94
	CTR	42.78 ± 8.31	44.12 ± 7.26
Knee	I	54.57 ± 5.63	56.63 ± 4.90
	CTR	57.95 ± 5.31	58.73 ± 5.22
Ankle	I	18.04 ± 3.66	20.60 ± 4.10

	CTR	19.83 ± 2.72	19.30 ± 2.85

Data are presented as mean ± standard deviation (SD)

Regarding heel height, there was no significant variation ($p = 0.324$), and no significant differences in time x group ($p = 0.064$), time x sex ($p = 0.270$) and time x group x sex interaction ($p = 0.363$) were noticed.

Furthermore, no significant interactions were found in maximum dynamic force ($p = 0.80$) and maximum isometric force [maximum force ($p = 0.88$); average force ($p = 0.82$)]. The complete data of maximum dynamic and isometric forces are detailed in Table 6.

Table 6: Data of maximum dynamic force and maximum isometric force for intervention (I) and control (CTR) lower limbs at baseline (PRE) and following the protocol (POST)

			PRE	**POST**
Maximum dynamic force		I	2009.35 ± 982.44	2043.10 ± 868.81
		CTR	2069.80 ± 1170.34	2053.05 ± 1090.89
Maximum isometric force	**Maximum force**	I	688.37 ± 213.68	680.85 ± 273.34
		CTR	699.70 ± 192.40	698.31 ± 215.30
	Average force	I	543.60 ± 175.47	548.37 ± 229.51
		CTR	573.42 ± 134.12	568.94 ± 140.51

Data are presented as mean ± standard deviation (SD)

Finally, no significant differences were found in VAS scale following the plyometric protocol and up to day 4 for both the intervention and the control lower limb ($P = 0.57$). Moreover, a significant increase in pain perception was found following the plyometric protocol in both treatment and control legs ($p < 0.001$). Following the EIMD protocol, pain perception increased up to day 3 and decreased on day 4 in the intervention lower limb but no significant differences were established in comparison with the control limb (*p* = 1.00 and *p* = 0.34, respectively).

DISCUSSION

This is the first study to evaluate the effects of a combined protocol including massage and cryotherapy on soreness, muscle recovery and performance after an EIMD protocol using an intra-subject, leg-to-leg comparison model. We found no statistically significant differences between treated and untreated lower limbs. These results suggest that massage therapy coupled with subsequent cryotherapy does not induce superior benefits on recovery and performance in comparison with untreated control.

Our study adds even more controversy to the existing literature on the effectiveness of massage and cryotherapy in relieving soreness, accelerating recovery and preserving muscle performance. Some studies support the application of massage as a means to favor recovery[176,201,202,240,311]. Hilbert et al. observed a reduction of soreness intensity at 48 h post-EIMD in the healthy individuals subjected to a 20-min massage, in comparison with an untreated control group[202]. A similar pattern emerges in the study from Kargarfard et al., who reported a significant decreased in DOMS up to 72 h post an strenuous exercise bout in the group that received massage[176]. Other studies have concluded small benefits on muscle recovery from the application of massage. Dawson et al applied a 30-min massage on a single leg on days 1, 4, 8 and 11 following a half marathon, and they did not show significant differences in soreness and swelling with respect to the untreated control leg[312]. Their results are particularly interesting, since we have performed the same design in regards to treat one lower limb and used the opposite as a control. Massage contributes to the reabsorption of muscle edema by increasing blood flow, and it may reduce neural excitability and induce a relaxation response[313]. This method has been proposed to induce changes along the inflammatory process that finally derive in pain reduction[314], favoring a faster recovery[132]. It is worth noting that practically all the aforementioned studies concluded no significant improvements on performance from massage therapy, independently of the effects on recovery. Thus, massage did not show positive results in muscle strength[202,312], vertical jump height[176,201,240] and sprint time[240]. Only Farr et al. reported a massage-induced improvement in strength recovery[201].

Besides massage, CWI might be an interesting alternative for improving recovery and performance following EIMD. Delextrat et al. concluded similar positive results between massage and CWI in recovery in young basketball players following a competitive match[315]. Interestingly, these authors also noted a significant improvement in jump performance only in the group subjected to CWI. Although this could be associated with a powerful effect from cryotherapy on performance, none of the techniques had an effect on repeated-sprint measures. Our primary rationale for coupling massage with subsequent cryotherapy was to investigate a possible booster effect, given that CWI also contributes to the reabsorption of muscle edema and induces a nociceptive stimulus[316]. However, the overall lack of significant positive results from the combined protocol suggests the ineffectiveness of adding CWI to a previous massage. We are not able to explain why these techniques did not facilitate recovery and enhance performance, since we have not established comparisons with the single application of each technique. CWI resulted effective in improving next-day run performance when was applied after an EIMD protocol consisted of running[305]. Despite superior benefits were observed when cryotherapy was performed immediately following EIMD, positive results were also shown when it was administered three hours post-EIMD. The test used in our study to assess performance, CMJ, may be a key variable to consider when interpreting the results obtained. Kositsky and Avela concluded no superior effects of CWI on jump performance than passive recovery following an EIMD protocol in young soccer players[317]. Although no between-group differences were established, they found that the passive rest condition experienced increases in ankle stiffness from post-intervention to 48 h, whereas CWI did not[317]. This circumstance could be related with a lesser efficiency in jump performance in those participants subjected to CWI. Nonetheless, in a similar research using a leg-to-leg comparison model (one leg received CWI and the opposite acted as control) concluded no differences in maximal isometric voluntary contraction and muscle stiffness between conditions[318]. Sánchez-Ureña et al. investigated the effects of two 12-min protocols of CWI, continuous and intermittent, at 12 ºC on the neuromuscular function recovery following EIMD. These authors found no positive effects from CWI on CMJ performance and muscle properties measured by tensiomyography[319]. However, the suitability of applying chronic CWI after strength training remains in doubt when it comes to improve sports performance. A recent study observed a detrimental effect of an 8-week leg training protocol with a 10-min subsequent whole-body CWI on strength and CMJ performance[320]. Despite non-significant differences were established in comparison with passive protocols, current trends suggest that CWI could be a useful tool for highly-trained athletes for recovering neuromuscular performance in cases of successive efforts and accumulated levels of fatigue[321,322].

Our study may be interpreted in the context of its limitations. Owing to the small number of participants we have performed a within-subject protocol comparing a treated leg vs. a control leg. The application of a between-subject design would possibly registered more pronounced differences between groups and, consequently, greater effect sizes[312]. Furthermore, as well as unilateral resistance training has been proved to induce strength gains in the contralateral untrained limb, known as *cross-education* phenomenon[323], recovery therapies could cause a similar "interlimb transference". Jay et al. have reported a cross over effect by which perception of soreness in the control leg was reduced following massage therapy on the opposite treated leg[324]. Hence, we cannot discard changes in the control leg from the application of massage and CWI in the treated lower limb. By last, as we have not compared the combined condition (massage and cryotherapy) with i) only massage and ii) only cryotherapy, we are unable to determine its possible superior effects. The inclusion of these comparator groups would allow drawing firm conclusions about the potential benefits of combining both techniques in terms of muscle recovery and performance, so further studies are needed to clarify this issue.

CONCLUSION

The findings of our study suggest minimal effects of coupling massage and CWI on muscle recovery and performance following EIMD, adding more controversy to the literature on the effectiveness of these techniques.

Chapter 4.3.: *Effects of uphill high-intensity interval exercise (u-HIIE) on muscle damage and exercise performance during recovery*

ABSTRACT

BACKGROUND: Active recovery is believed to offer positive benefits related to exercise by improving recovery and potentially managing several symptoms following intensive exercise. The current study aimed to verify the effects of a session of low-volume and uphill high-intensity interval exercise on muscle soreness and exercise performance within the recovery period after an exercise-induced muscle damage protocol.

METHODS: 31 young physically active subjects completed two identical test sessions following an exercise-induced muscle damage protocol, separated by a three-week period, in which they performed uphill high-intensity interval exercise or a passive recovery. The uphill high-intensity interval exercise consisted of four bouts of 30 sec at maximum velocity, interspersed by 4 minutes of passive rest on an uphill treadmill. Rating of perceived exertion, muscle soreness, serum concentration of Creatine Kinase, muscle circumference, countermovement jump, sprint time, and one repetition maximum strength of quadriceps femoris were measured. The assessments were made for 4 consecutive days, before the exercise-induced muscle damage protocol and 24, 48, and 72 h afterwards.

RESULTS: A significant effect of time was found for all the outcome measures, but there were no significant differences between groups either in pain perception, muscle damage variables, nor in performance outcome measures at any point of time ($p>0.05$).

CONCLUSION: Uphill high-intensity interval exercise performed after an exercise-induced muscle damage protocol does not exacerbate muscle soreness or worsens exercise performance in comparison with passive recovery.

Key words: recovery; high-intensity interval exercise; performance; delayed onset muscle soreness; muscle damage.

Introduction

When active adults are generally involved in sports activities, an optimal balance between efficient training, recovery, and safe practice is highly recommended[325]. Safety is a major concern, since the risk of injuries and overtraining becomes highly significant when excessive training load occurs, reducing an athlete's overall performance[326]. Muscle damage is observed in the musculature unaccustomed to repetitive and intensive workout load, most commonly eccentric contractions, and it is often characterized by delayed onset muscle soreness (DOMS)[32]. Muscle pain and discomfort commonly start 24 h after exercise, peak up to 72 h, and subside within five to seven days post-exercise[250]. This process involves both histological and clinical modifications associated with delayed recovery and reduced performance, such as muscle weakness, muscle stiffness, muscle swelling, and an increase in inflammatory markers including creatine kinase (CK) and myoglobin[289].

Exercise-induced inflammation has recently been considered that upregulates muscle repair and regeneration by stimulating various satellite and inflammatory cells of skeletal muscle[32]. Nonetheless, these alterations might compromise improvement, delay normal recovery, and finally decrease performance[326]. Active methods have been hypothesized to offer physiological benefits related to exercise in comparison with passive recovery. They could improve recovery and tissue remodeling by creating an analgesic effect, increasing blood flow and enhancing CK clearance[145,327]. Additionally, active recovery methods might be challenging among young, encouraging athletes to exercise rather than receive a passive treatment[328]. Thus, isolated muscle contractions, walking, jogging, running, cycling, exercise in water or yoga practice have been concluded to decrease pain perception[145,151,157,268,276].

The type of exercise by itself does not only explain the above results, and the different intensity levels might be a crucial factor in determining the effectiveness of recovery, since high speed contractions cause a decrease in muscle soreness and facilities the return of normal muscular performance[329]. A recent study also concluded that a session of high-intensity interval exercise [90% of maximal velocity (MV)] has similar effects as a continuous protocol (60% MV) on DOMS at 24 h[330]. Moreover, light and moderate exercise intensities following EIMD did not show great improvements on recovery and muscle performance[146,151,166,274,327]. Therefore, the choice of appropriate intensity appears to be inconclusive, and a particular threshold for higher intensities could offer potential advantages for better recovery and an optimal response in tissue remodeling.

To date, no studies have considered the incorporation of highly demanding and challenging activities within the scope of recovery methods. We hypothesized that an active protocol consisting of uphill high-intensity interval exercise (u-HIIE) is beneficial on muscle damage and muscle performance during recovery following an intensive exercise. Consequently, our primary aim was to evaluate the effectiveness of a protocol of acute high-intensity bouts on pain perception, damage, muscle performance, and recovery time following an EIMD.

Materials and methods

This was a randomized controlled trial (RCT) aimed to investigate the effects of an acute u-HIIE on recovery from DOMS. Participants were submitted to two identical test sessions following an EIMD program: one consisted of the u-HIIE, while the other was based on a passive rest (PR). Overall, the performance of 31 assessment runs with u-HIIE was contrasted with that of the PR (Figure 3). All research was in compliance with the ethical guidelines of the Declaration of

Helsinki 1961 (revision of Fortaleza 2013)[229] and approved by the Research Ethics Committee of Principality of Asturias (292-19).

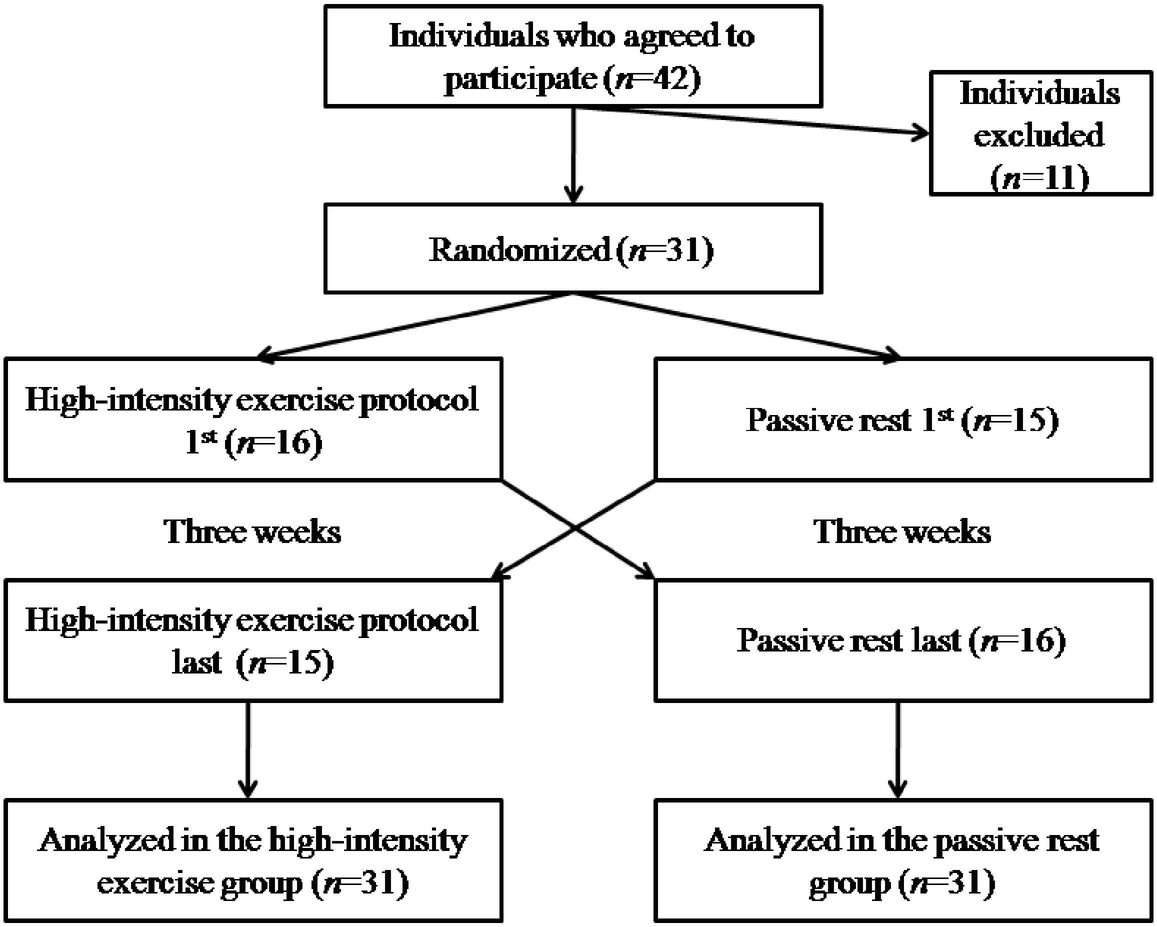

Figure 3: A flow chart representing the structure of study

Participants

A power analysis was performed with a total sample size of 30 subjects required to satisfy a significance level of 0.05 with power of 0.90 and effect size of 0.75 (G-power software 3.1.2; Franz Faul, University of Kiel, Kiel, Germany). To find the final adjusted sample size, allowing non-response rate of 10% in the above example, the adjusted sample size will be 33[331]. 42 young active individuals (32 males and 10 females), recruited from the department of physical education in Notre Dame university following an announcement of the experiment, volunteered to participate in the study. All of them were primarily informed of the experimental protocol and completed a written informed consent and also filled a questionnaire regarding their medical conditions. The inclusion criterion was being a physically active young adult. Participants with existing musculoskeletal injuries, taking anti-inflammatory medication or any performance enhancing substances, pregnant women, those who cannot tolerate high level of fatigue, and those who present any cardio-respiratory related condition were excluded from the study.

Overall, 11 subjects were excluded throughout the study because of absences during the experiment; hence, 31 remaining subjects accomplished the whole study protocol. Data of physical characteristics of the included participants are shown in Table 7.

Table 7: Physical characteristics of the subjects participating in the study

	Male (n=24)	**Female (n=7)**	**Overall (n=31)**
Age (years)	22.3±2.1	22.1±2.5	22.3±2.1
Height (cm)	177.3±6.2	166.3±4.0	175.0±7.4
Weight (kg)	79.1±11.5	59.9±7.0	74.7±13.3

Data are presented as mean ± standard deviation (SD)

Design and procedures

A RCT was established to prove the effectiveness of a u-HIIE protocol on DOMS. The study consisted of a crossover experiment performed during four consecutive days with two groups of participants, the u-HIIE and the PR.

The two sessions were separated by a three-week period, and the order in which these were performed was previously randomly decided (u-HIIE vs. PR or vice versa). The assessments were performed before and immediately after the EIMD protocol (day 1), after the u-HIIE or under PR (day 2), and similarly for both groups on days 3 and 4. Muscle soreness, serum concentration of CK and thigh circumference were evaluated along with specific performance measures, such as vertical jump height, sprint completion time and the maximum strength of the quadriceps femoris (Figure 4).

Subjects were asked to avoid smoking, alcohol, and caffeine in the 24 h preceding each visit. They were requested to have a light meal at least 3h before reporting to the laboratory and not to modify their diet habits throughout the study. They were also instructed to refrain from any physical exercise 72 h prior to the experiment. During the experiment, subjects were not allowed to stretch, apply ice, receive a massage, take anti-inflammatory drugs, or perform any other recovery modality. All visits were scheduled at the same time of the day, with temperature between 20-22ºC, and humidity between 35-45%.

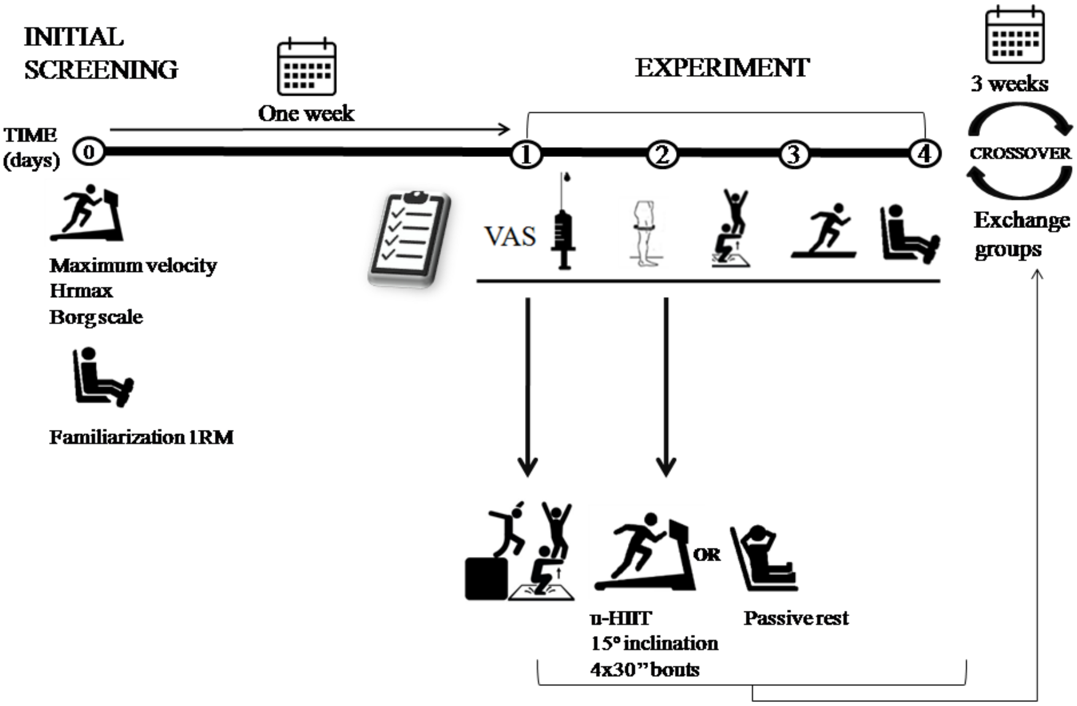

Figure 4: Graphic representation of the study protocol (u-HIIE)

Determination of participant maximal velocity (MV)

One week prior to the experiment, subjects went to the laboratory to determine their maximal self-selected speed on the treadmill, which would be used later in the intervention group. The warm-up consisted of walking at 4 km/h for 10 min from 1 to 15% inclination. Following the warm-up, the test was performed with an inclination grade of 15% and intervals of one-minute each starting at 5 km/h, which were increasing by 1 km/h for each interval until volitional exhaustion. The velocity reached during the last full stage before volitional exhaustion was defined as the MV. A Polar Monitoring System (Polar Electro®, Oy, Kempele, Finland) was used to record continuously the heart rate (HR) throughout the test. Fatigue was assessed during each stage of the test and at the end of the screening using Borg's rating of perceived exertion (RPE) scale[332]. The test was considered maximal if participant's HR reached or exceeded 90% of their estimated

HRmax (220–age) and if RPE score exceeded 17 “very hard” at the moment of volitional exhaustion. In addition, they were submitted to a familiarization session with the leg extension machine.

EIMD protocol

On the first day of the experiment, subjects were called to the laboratory to perform an EIMD protocol. This protocol was based from a previous study[233] and consisted of 20 sets of 10 repetitions of drop jumps with a one-minute rest between each set, accomplished after a 10 min warm-up on a treadmill. Participants were instructed to stand on a 50 cm high box, and landing on the floor without any prior take-off from the box. Once they reached the floor, they were asked to squat down, with a self-determined range of motion and contraction time and then jumps vertically as high as possible.

u-HIIE recovery protocol

On the second day of the experiment, participants belonging to u-HIIE group underwent an intervention protocol consisting of running on a 15° inclined treadmill at their previously calculated maximum speed.

The u-HIIE protocol started with a 5-min warm-up from fast walking to light jogging on the treadmill with 15° inclination. The speed was set at 6 km/h in the first minute and was increased by 1 km/h every minute. Following the warm-up, participants performed four bouts of high-speed running; each bout lasted 30 sec, with a period of active rest (4 min) between them. Bouts were performed at previously calculated MV, and subjects were encouraged to achieve the total duration for each bout.

Outcome measures

Rating of perceived exertion (RPE)

Once the EIMD protocol was completed, participants were asked about their perceived exertion using a numerical scale from 6 (no exertion) to 20 (maximal exertion)[332]. A score for each participant was recorded, and observations were also made to confirm that the assigned exercise induced sufficient fatigue. This index was also used during and after the initial screening on the treadmill.

Muscle soreness

Muscle soreness was evaluated at rest using a visual analogue scale (VAS)[234]. This scale consists of a 10 cm line and polar descriptors at its two extremes, and allows participants to subjectively quantify the intensity of their pain using values ranging from 0 (no pain) to 10 (unbearable pain). In order to follow-up closely the changes in soreness, VAS was monitored immediately after EIMD, and then again every 12 h until the last day of the experiment.

Serum concentration of CK

Venous blood samples were collected from an antecubital vein of the participants. In total, 5 ml of blood were extracted using vacutainers for blood withdrawal. Samples were centrifuged at 3000 rpm for 15 min. Resulting serum was then separated and pipetted into plastic tubes and stored at -18°C[148]. Analyses of CK concentrations used routine techniques (Orthoclinical Diagnostics Vitros, 250 Chemistry Analyzer, Manufacturer US).

Thigh circumference

Circumference was measured to assess the swelling of the thigh muscles. Subjects were asked to stand equally on both legs without any active muscle contraction. Mid-thigh girth of the dominant leg was taken at the middle of a vertical line between the greater trochanter and the base of the patella. The measurement was repeated three times and the average value was taken in consideration, a constant tensiontape (Lufkin, Cooper Industries, Houston, Texas, USA) was used in this assessment[141].

Vertical jump

Vertical jump height was assessed by measuring the counter-movement jump (CMJ). Three trials were performed, each separated by two minutes of rest; the best attempt was then recorded as the baseline reference. The CMJ was measured using the mobile application MyJump 2.0©, which uses the flight time to calculate the jump height[103]. An iPhone 6® mobile device served to record every jump at 240 fps. To ensure a correct execution of the jumps throughout the assessment process, participants were asked to place their hands at their hips during each jump and to land with straight legs and flat feet on the ground.

Sprint time

Sprint performance was assessed by calculating the time needed for each participant to perform a 20-m sprint[237]. Following a warm-up, the participants were asked to perform three maximal 20-m sprints interspersed by three minutes of passive recovery; the best attempt was recorded for data analysis. Four photocells were placed in order to measure sprint time (Bio-Medic, Barcelona, Spain).

Maximum repetition (1RM)

Maximal strength was assessed during the first test session using one repetition maximum (1RM) leg extension of the quadriceps[237]. Subjects were seated on a leg extension machine (Lumex, Ronkonkoma, NY, USA) with the seat and the back adjusted individually. The resistance was progressively increased after each successful performance until participants were unable to extend their legs to reach full extension. To minimize fatigue, the rest between maximal attempts was always three minutes.

All measurements were repeated at similar time points except for VAS and RPE. On day 1, measurements were repeated twice, before (pre) and after (post) EIMD. 24 h after EIMD, both groups had their measurements taken but the experimental group was assessed following the u-HIIE protocol. Similarly, outcome measures were assessed for groups after 48 h and 72 h post-EIMD.

Statistical Analyses

A one-sample Kolmogorov–Smirnov test confirmed the assumption of normal distribution for all the variables. The effect of active recovery protocol on different parameters measured between the two groups and at different time points was analyzed by a two way (group x time) repeated measures analysis of variance (ANOVA) using SPSS 24.0 (Statistical Package for Social Sciences, Chicago, IL, USA). In case of significant main effect or interaction effect, a post hoc analysis with Bonferroni correction was conducted. For each outcome measure, a p value was reported corresponding to the main intervention effect and time effect. Statistical significance was set at $P < 0.05$.

Data availability

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

Results

The values for the analyzed variables (Mean, SD, and the statistically significant differences between all conditions for performance and outcome measures) are shown in Table 8. Since further analysis did not show any sex-specific results, these data were analyzed together.

Table 8: Changes in counter-movement jump (CMJ), 20-m sprint, 1RM, muscle circumference and visual analogue scale (VAS) at baseline level (PRE), immediately after (POST), at 24, 48 and 72 h following the exercise-induced muscle soreness (EIMD) for running group (u-HIIE) and control group (PR)

		PRE	**POST**	**24h**	**48h**	**72h**
CMJ (cm)	u-HIIE	36.1 ± 7.8	32.6 ± 7.7*	29.1 ± 8.0*	32.7 ± 7.2*	34.7 ± 8.3*
	PR	35.3 ± 7.8	32.9 ± 8.4*	32.9 ± 8.0*	33.5 ± 8.0*	34.5 ± 8.1*
20m sprint (s)	u-HIIE	4.7 ± 0.5	4.9 ± 0.6*	4.9 ± 0.5*	4.9 ± 0.5*	4.9 ± 0.6*
	PR	4.7 ± 0.5	4.9 ± 0.6*	5.0 ± 0.7*	4.9 ± 0.6*	4.8 ± 0.5*
1RM (kg)	u-HIIE	122.9 ± 27.8	105.8 ± 25.4*	101.3 ± 29.8*	116.8 ± 31.9*	124.5 ± 30.3*
	PR	124.5 ± 30.3	105.6 ± 27.4*	109.4 ± 32.7*	113.7 ± 34.0*	119.2 ± 30.6*
Muscle circumference (cm)	u-HIIE	54.3±4.8	55.1±4.8*	55.5±4.7*	55.4±4.6*	55.2±4.7*
	PR	54.3±4.3	55±4.4*	55.2±4.4*	55.3±4.4*	55±4.3*

VAS (cm)	u-HIIE	1.4±0.6	3.9±2.4*	4.6±2.3*	5.6±1.7*	2.5±1.3*
	PR	1.4±0.6	3.5±2.3*	4.5±2.7*	4.8±2.6*	3.1±2.1*

*Values are presented as mean ± SD, *significant time effect: p values ≤ 0.05, (CMJ group effect: p=0.687; 20m sprint group effect: p=0.966; 1RM group effect: p=0.975; muscle circumference group effect: p=0.886; VAS group effect: p=0.449)*

Overall ANOVA showed a significant time effect for all the outcome measures: VAS [F(4,120)=51.83, $p<0.01$, $n^2=0.63$], concentration of CK [F(4,116)=11.38, $p<0.01$,$\eta^2=0.28$], muscle circumference [F(4,120)=37.77, $p<0.01$, $\eta^2=0.55$], vertical jump height [F(4,57)=26.892, $p<0.01$, $\eta^2=0.654$], sprint time [F(4,120)=27.97, $p<0.01$, $\eta^2=0.48$] and quadriceps femoris 1RM [F(4,120)=28.01, $p<0.01$, $\eta^2=0.483$]. Comparisons between u-HIIE and PR did not indicate differences in either damage muscle variables or in performance outcome measures at any point of time. Both groups showed similar changes in pain level, with an immediate increase after EIMD and a peak level at 36 h (u-HIIE: 404.7%, PR: 315.1%; $p>0.05$). Pain was gradually reduced between 36 and 72 h for both groups, with a greater decrease in u-HIIE (u-HIIE:-61.1%; PR: -34.7%; $p>0.05$). Pain remained increased for both groups at 72 h compared with baseline values (u-HIIE: 90.6%; PR: 152.2%; $p<0.05$). Overall ANOVA showed significant interaction effect (intervention x time) for CMJ [F (4,120) = 4.03, $p < 0.01$, $\eta^2 = 0.12$] and quadriceps femoris 1RM [F (4,120) = 4.39, $p= 0.05$, $\eta^2 = 0.12$].

Regarding thigh circumference, both groups showed an immediate increase following EIMD. After that, the u-HIIE group on average showed an apparently greater amount of swelling on the next day following the running protocol compared with PR (2.1% vs. 1.6%), though this difference was not statistically significant ($p=0.886$). Both groups followed the same pattern of decrease for 48 to 72 h, with a remaining swelling compared to the baseline level (u-HIIE: 1.7%; PR: 1.3%; $p<0.05$). Figure 5 represents variations of serum concentrations of CK.

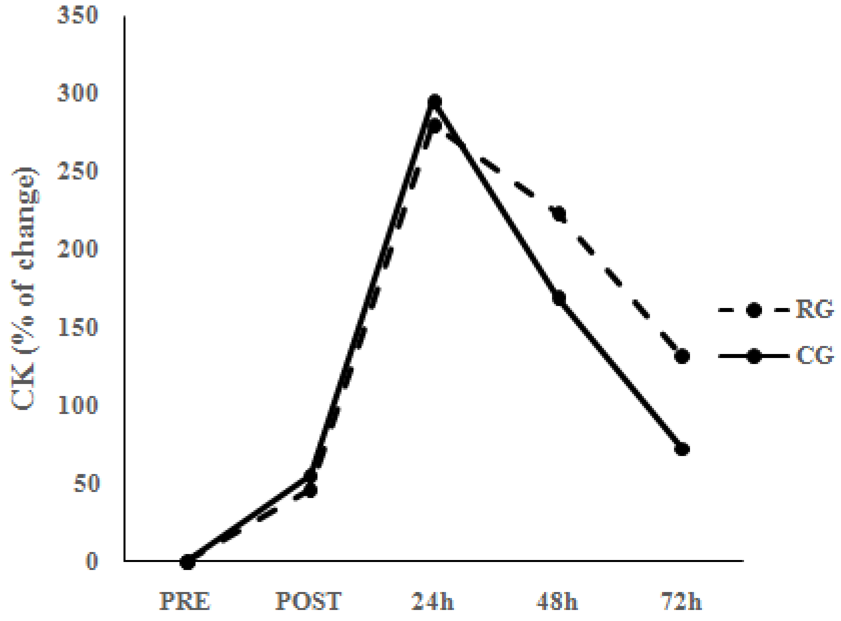

Figure 5: Variations of serum concentration *CK* along the experiment

Discussion

This is the first study to assess the effectiveness of an uphill high-intensity interval exercise protocol on DOMS recovery after a single bout of strenuous exercise. The main findings were the following: (i) all the outcomes measures exhibited a significant time effect in both u-HIIE and PR groups; (ii) there were no u-HIIE and PR group interactions for any variable at any time of the follow-up. Therefore, the results from our study do not support our hypothesis that a u-HIIE may favor the recovery process by accelerating the tissue remodeling response, although they do not discard it either.

It is widely accepted that active recovery provides superior performance improvements than passive recovery[156,328]. Hence, this controversy could be related to our u-HIIE protocol, since the vast majority of studies that have examined active recovery modes on performance applied light to moderate intensities[148,166,333].

Regarding pain level, our results are similar to other previous studies which included endurance exercise at lower intensities as a recovery tool. Olsen et al did not find significant differences neither in VAS nor in pressure pain threshold (PPT) following 20 min of moderate-intensity (60-70% HRmax) cycling exercise, in comparison with a passive-recovery group[146]. Likewise, Tufano et al did not observe statistically significant interactions on a pain scale when applied a similar recovery protocol (20-min cycling) after a EIMD of the knee extensors, independently of exercise intensity (30% vs. 70% HRmax vs. sitting)[166]. However, Hasson et al found a significant reduction in soreness at 48h after performing a recovery protocol consisting of knee flexion-extension voluntary contractions at high-speed (~300º/s)[329]. The speed of execution could be the key factor in muscle recovery, suggesting that higher intensities may lead to accelerate it, since it has been described a directly proportional relationship between movement velocity and exercise intensity. High-intensity exercise provokes an increase in lower limb blood flow, favouring the removal of waste products in sore muscles and relieving pain sensation[167]. Nevertheless, our results do not support this hypothesis, and we have not appreciated significant fast improvements in pain relief in u-HIIE. These divergences do not seem to be related with the EIMD protocol, since bench stepping and drop jumping activate predominantly the same musculature. Hence, the differences could reside in a series of arguments. First, Hasson et al. measured soreness objectively using a strain gauge and evaluated only quadriceps musculature[273], while we did not focus on any lower-limb muscle region and assessed pain subjectively through the VAS. However, the subjective perception of the subjects seems to be unaltered although they could have specifically lower pain at a specific point. Second, their recovery protocol consisted of repeated maximum knee flexion-extension contractions, which specifically increases the activation of that muscles with a higher prior demand during the EIMD protocol[334]. In contrast, we performed an uphill running, in which knee extensors may decrease their cycle activity with increased slope, to the detriment of gluteus major and biceps femoris[335,336]. In view of these inconclusive results, further research is expected to find the relationship between high-speed contractile activities on the sore muscles.

The increase of CK concentrations were elevated after our EIMD. Other studies reported similar findings when jogging[145] or a combined cycling and resistance training protocol[333] at moderate intensities were compared with passive recovery. Wahl et al[148] performed 30 min of moderate-intensity aqua-cycling recovery protocol and observed higher levels of CK and lactate dehydrogenase up to 72 h after recovery compared to passive group, although no statistical significance was concluded. These results should be viewed cautiously, since the slight increases in these blood markers were not linked to a higher ratings of perceived soreness. In addition, the great inter-individual variability in serum CK[337,338] avoids drawing a solid interplay between higher serum levels of these markers and muscle soreness. The circumference of the quadriceps femoris remained slightly increased from the conclusion of the strenuous exercise up to the 72 h assessment. Our results are similar to Sakamoto et al, who observed that limb circumference continued increasing after a resistance recovery protocol performed until failure (70% MVC) up to the seventh day, while it was reduced in the control group from the fifth day[275]. These findings may be related to the long duration of their recovery protocol (four days vs. ours only one session). It had no direct relationship to soreness or serum CK levels, and might be due to the increase in blood flow caused by muscle contractions, which make the muscle more swollen in the successive days following an intensive exercise bout.

In terms of sport performance, our study did not conclude statistically significant differences between the groups in any outcome (i.e. vertical jump height, sprint time, and maximum strength of the quadriceps muscle), beyond the expected time-effect for all variables. We have found that jump height values did not return to baseline, being the deterioration of CMJ performance influenced principally by fatigue in knee extensor muscles[339]. However, the study by Andersson et al observed impaired performance in vertical jump, even when the strength level of knee extensors and flexors, had returned to its previous state[333]. This circumstance suggests the existence of additional factors involved in CMJ, such as muscle stiffness induced by reductions in stretch-reflex sensitivity[340]. In line with these findings, sprint time did not present significant variations between conditions. Both groups expressed an increase in sprint time the days following the exhausting exercise, with a peak at 24 h (u-HIIE: 5.7%; PR: 6.2%, $p<0.01$) and a progressive reduction up to 72 h, although without reaching their previous scores. This impairment may be related to losses in force-generating capacity derived from exercise-induced structural disruptions in myofibers following the drop jumps protocol. Hence, muscle strength seems to be a key indicator of the status of muscle recovery. We observed a similar reduction in 1RM after the step jumps protocol in both groups, following by a non-significant continued decline in the experimental group (-4.8%) and an increase in the control group (3.2%) at 24 h. This higher impairment in muscle strength in the experimental group was similarly described in other studies that compared active recovery protocols with passive rest[146,164]. The subsequent assessments (48 and 72 h) reflected increases in both conditions, with a positive trend in the group submitted to active recovery (which exceeded the previous values) in comparison with controls (17.7% vs. 4.3% at 48 h, and 26.5% vs. 12.3% at 72 h). Although there are no significant results between groups, we can assume that a recovery protocol based on u-HIIE could accelerate the return of muscle strength to baseline values, even increasing it. In this regard, the aforementioned study by Sakamoto et al observed increases in strength without any differences between the resistance protocol and the control group[275] while Tufano et al reported larger isometric strength recovery with higher cycling intensities, even when no group recovered baseline values[166]. Additionally, an aqua-cycling protocol has shown to prevent decreases in muscle power in comparison with a passive rest group in the days following an intensive exercise[268]. All these previous findings might guide us towards an approach using active recovery and higher intensities in particular to prevent loss in muscle strength. This could be related to the accelerated blood flow caused by moderate and high-intensity activities, increasing the circulating concentrations of satellite cells, responsible for muscle repair[341]. The main difference state in our study is the increase in 1RM beyond the baseline values following the active protocol. The reason behind that could be attributed to greater concentrations of growth hormone, testosterone and testosterone/cortisol ratio have been found after a sprints-based protocol at 80% of maximal speed, which may suggest the importance of exercise intensity in muscle strength recovery adaptations[342]. However, this hypothesis remains unclear, since we did not take any hormonal measurements.

Strength and limitations

Despite the interesting findings of our study, some limitations need to be considered. First, the study involved physical education university students. Hence, the results may not be directly extrapolated to highly-trained or middle-age athletes, or participants with sedentary behaviors. Second, we have included a running-uphill protocol, which could be more suitable for runners or sports activities where this biomechanics pattern is involved. However, cyclists or swimmers could benefit from this model, since the eccentric load supported through the running would be minimize. Lastly, we did not include specific assessments of plantar flexors, which are crucial muscles in running and are also widely demanded and fatigued during drop jumping. The strength of our study lies in the crossover design model, and the relative high sample size, since most of the studies performed in active recovery methods involve a lower number of participants.

Implications for future research

U-HIIE could be performed as a feasibility protocol during recovery period after an EIMD. Multiple benefits can be obtained through this model, as reductions in the eccentric load supported through the uphill running, lower time per training session compared to a traditional "regeneration training", similar response in neuromuscular performance and do not exacerbate muscle damage more than rest or moderate continuous exercise[330]. Thus, active recovery has been seen to promote hormonal responses different from those of passive recovery following a high-intensity exercise,[343] so better training adaptations could be induced when active recovery is executed through low volume sprint bouts, although this fact needs to be confirmed in future trials. Lastly, it is worth mentioning the psychological benefits of continuing to train rather than remain inactive during the recovery period[344], which in turn can favor the regeneration process.

Conclusion

In this study, a single bout of u-HIIE performed 24 h after a DOMS-induction exercise protocol elicited similar results in terms of recovery than a passive rest condition. Thereby, both muscle soreness and performance indicators showed similar patterns in both groups from the end of the strenuous exercise to the next 72 h, although, curiously, strength resulted in a final increase in those performing the u-HIIE protocol.

In view of all the above, we encourage further studies assessing the effects of short high-intensity exercise within recovery protocols for athletes.

Chapter 5: Main limitations and Strengths of the thesis

Main limitations

I. The heterogeneity of the studies did not allow for a consistent meta-analysis. Completing our systematic review (Chapter 4.1.) with a meta-analysis would undoubtedly have allowed us to carry out a quantitative and not only a qualitative analysis, which would facilitate the understanding of the effect of an intervention on both the whole data set of participants as well as subsets of participants. Additionally, it would increase the precision by detecting and showing clinically relevant effects, as well as other sources of disagreement between these results.

II. In our first study (Chapter 4.2.), the participants are aware of the protocol that has been carried out on each leg. An experimental design in which participants are blinded, or the inclusion of a third group that did not receive any treatment, would have limited any subjective outcome and reduced this main bias.

III. The comparison of different running intensities in our second study (Chapter 4.3.) would have provided a better understanding on the appropriate or optimal intensity to be used for significant outcomes. Therefore, new research is proposed to address this issue.

IV. A four-day follow-up study carried out in our second paper (Chapter 4.3.) has resulted in a greater loss of subjects due to commitment and time management problems from the side of the participants.

Limitaciones principales

I. La heterogeneidad de los estudios no permitió realizar una meta-análisis consistente. Completar con un meta-análisis nuestra revisión sistemática (Capítulo 4.1.), indudablemente habría permitido realizar un análisis cuantitativo y no sólo cualitativo, el cual facilitaría la comprensión acerca del efecto de una intervención, tanto de manera global como en subgrupos de participantes. Además, permitiría aumentar la precisión al detectar y mostrar efectos clínicamente relevantes, así como otras fuentes de desacuerdo entre esos resultados.

II. En nuestro primer estudio (Capítulo 4.2.), los participantes conocen el protocolo que se ha llevado a cabo en cada pierna. Un diseño experimental en el que los participantes están cegados, o la inclusión de un tercer grupo que no recibió ningún tratamiento, habría limitado cualquier resultado subjetivo y reducido este sesgo.

III. La comparación de diferentes intensidades de carrera en nuestro segundo estudio (Capitulo 4.3.) habría ofrecido una mejor comprensión sobre la intensidad apropiada u óptima que se utilizará para obtener resultados significativos. Por lo que se proponen nuevas investigaciones que aborden este tema.

IV. El estudio de seguimiento de cuatro días realizado en nuestro segundo experimento (capítulo 4.3.), ha provocado una mayor pérdida de sujetos debido a problemas de compromiso y gestión del tiempo por parte de los participantes.

Strengths of the thesis

I. All previous systematic reviews in the literature have studied active recovery in general and compared it to other methods without discussing every single active protocol, however, in our systematic review in chapter 4.1., we have focused on each previously examined active recovery protocol and compared the benefits and limitations in a more in-depth approach.

II. In chapter 4.2. our results included gait analysis, all previous studies have focused primarily on variables related to muscle performance. Gait assessment is a crucial tool for studying the influence of recovery protocols on the gait cycle at a normal and fast pace. This highlights the importance of daily activities, not just sports, when adapting a recovery protocol to our exercise routine.

III. In our randomized controlled trial in chapter 4.3. we performed a crossover design in an attempt to limit bias from individual factors related to each subject. Therefore, participants underwent both, the recovery protocol and the control condition, so that each subject is being compared to himself. In addition, this design requires a smaller sample size.

Fortalezas de la tesis doctoral

I. Todas las revisiones sistemáticas anteriores en la literatura han estudiado la recuperación activa en general y la han comparado con otros métodos sin discutir cada protocolo activo de forma individualizada; sin embargo, en nuestra revisión sistemática en el capítulo 4.1., nos hemos centrado en cada protocolo de recuperación activa previamente estudiado y comparando los beneficios y las limitaciones en un enfoque más profundo.

II. En el capítulo 4.2., nuestros resultados incluyeron el análisis de la marcha, todos los estudios anteriores se han centrado principalmente en variables relacionadas con el rendimiento muscular. La evaluación de la marcha es una herramienta crucial para estudiar la influencia de los protocolos de recuperación en el ciclo de marcha a un ritmo normal y rápido. Esto destaca la importancia de las actividades diarias, no solo deportivas, a la hora de adaptar un protocolo de recuperación a nuestra rutina de ejercicio.

III. En nuestro ensayo controlado aleatorio en el capítulo 4.3., realizamos un diseño cruzado en un intento de limitar el sesgo que supone los factores individuales relacionados con cada sujeto. Por lo tanto, los participantes reciben ambas intervenciones, por lo que se someten tanto al protocolo de recuperación como a la condición de control, de modo de que cada sujeto es su propio comparador. Además, este diseño, requiere de un tamaño de muestra menor.

Chapter 6: Conclusions and Main contributions

Conclusions

- **Aim A**: The systematic review in chapter 4.1. identified various investigated active recovery protocols with partial benefits in managing DOMS without any detrimental effect following any of the examined methods. The main advantage reported on active recovery was the improvement in pain perception following various exercise models: isolated muscle contractions, jogging, running, aqua exercises and yoga. The loss of muscle power was less noticeable following aqua exercises, inflammation was decreased following jogging and running and flexibility improved after yoga.

- **Aim B:** A passive recovery protocol in chapter 4.2. combining massage and CWI did not show any significant benefit on soreness, muscle performance and spatiotemporal parameters of the gait cycle.

- **Aim C:** An active recovery protocol in chapter 4.3. consisting of a single running bout of uphill high intensity interval exercise 24 h following EIMD does not appear to offer advantages over passive recovery. Except for muscle strength which showed an increase at 48 and 72 h.

Therefore, in general we can affirm that a several active recovery protocols have shown limited advantages following intensive activities. Additionally, passive recovery protocols such as CWI and massage, have separately shown benefits in the literature; however, combining them does not seem to offer a particular asset in the recovery process. Moreover, high intensity running is not detrimental and potentially beneficial for the recovery of maximal strength. Nevertheless, the appropriate running intensity and duration still need further considerations. Finally, to date, no specific recovery protocol has been found efficient in increasing athletes’ performance; although most of the methods helped partially in managing soreness and limiting inflammation and strength loss.

Conclusiones

- **Objetivo A:** La revisión sistemática el capítulo 4.1. ha permitido identificar diversos protocolos de recuperación activa que muestran beneficios parciales en el manejo del dolor muscular de aparición tardía sin ningún efecto perjudicial. La principal ventaja observada fue la mejora en la percepción del dolor después de la realización de diversos modelos de ejercicio: contracciones musculares aisladas, trotar, correr, ejercicios acuáticos y yoga. La pérdida de potencia muscular se notó menos después del ejercicio acuático; la inflamación disminuyó después de trotar o correr; y la flexibilidad mejoró después del yoga.

- **Objetivo B:** Un protocolo de recuperación pasiva el capítulo 4.2. combinando masaje e inmersión en agua fría no mostró ningún beneficio significativo sobre el dolor, el rendimiento muscular y los parámetros espacio-temporales de la marcha.

- **Objetivo C:** Un protocolo de recuperación activa el capítulo 4.3. que consistió en una sola sesión de ejercicio de carrera en intervalos de alta intensidad cuesta arriba 24 h después de un ejercicio inductor de daño muscular, no parece ofrecer ventajas frente a la recuperación pasiva. Excepto para la fuerza muscular que mostró un aumento a las 48 y 72 horas.

Por lo tanto, en general podemos afirmar que varios protocolos de recuperación activa han mostrado limitadas ventajas después de realizar actividades intensas, adicionalmente, algunos protocolos de recuperación pasiva como CWI y masaje, han mostrado beneficios por separado en la literatura, sin embargo, combinarlos no parece ofrecer un beneficio extra en el proceso de recuperación. Además, la carrera de alta intensidad no es perjudicial y si, potencialmente beneficiosa para la recuperación de la fuerza máxima. Sin embargo, la correcta intensidad y duración de la carrera aún necesitan más estudio para determinarlas con precisión. Finalmente, hasta la fecha, no se ha encontrado ningún protocolo de recuperación específico eficaz para aumentar el rendimiento de los deportistas; aunque la mayoría de los métodos ayudaron a controlar parcialmente el dolor, limitar la inflamación y la pérdida de fuerza.

Main contributions

I. In the systematic review we collected all results investigating active recovery protocols and comparing them to control groups. We performed thoroughly an in-depth description and comparison of the results of all the collected papers. This has revealed inconclusive findings concerning the appropriate method to adopt following unaccustomed activities. Therefore, intensities and duration of these protocols require further investigation.

II. Massage and CWI are two widely used passive recovery methods, both techniques have shown a strong correlation between their use and pain management, however, we showed that their combination does not offer an additional benefit in managing other parameters related to muscle performance and gait patterns.

III. Acknowledging the importance of active recovery, we investigated an intensive running protocol 24 h after a fatigue-inducing exercise. Contrary to common belief and practice, DOMS was not exacerbated and other symptoms related to EIMD were not worsen.

IV. We have highlighted throughout this thesis the validity of some objective parameters that allow us to measure physical performance using force platform, gait analysis using movement markers, inflammation through collecting blood samples as well as other functional tests.

Aportaciones principales

I. En la revisión sistemática, recopilamos todos los resultados que han investigado los protocolos de recuperación activa, comparándolos con los grupos de control, realizamos una descripción detallada y una comparación de los resultados de todos los artículos recopilados. Esto ha revelado hallazgos no concluyentes sobre cuál podría ser el método apropiado a adoptar después de actividades intensas a las que el deportista no está acostumbrado. Por tanto, las intensidades y la duración de estos protocolos requieren más investigación.

II. El masaje y el CWI son dos métodos de recuperación pasiva ampliamente utilizados, ambas técnicas han mostrado una fuerte asociación entre su uso y el manejo del dolor, sin embargo, hemos demostrado que su combinación no ofrece un beneficio adicional en el manejo de otros parámetros relacionados con el rendimiento muscular y patrones de la marcha.

III. Reconociendo la importancia de la recuperación activa, hemos investigado un protocolo de carrera intenso, realizado 24h después de un ejercicio inductor de fatiga y, a la inversa de la creencia y práctica comunes, este estudio mostró que el dolor muscular tardío no se incrementó y que otros síntomas relacionados con el ejercicio que induce daño muscular no empeoraron.

IV. Hemos destacado a lo largo de esta tesis la validez de algunos parámetros objetivos que nos permiten medir el rendimiento físico mediante una plataforma de fuerza, análisis de la marcha mediante marcadores de movimiento, inflamación mediante recogida de muestras de sangre así como otras pruebas funcionales.

Chapter 7: *Prospects for future research in this area*

Prospects for future research

I. Conducting a systematic review and meta-analysis investigating a broader range of recovery protocols, active and passive, will be efficient in identifying all the benefits and limitations from a larger scope and more extensive manner.

II. Performing more randomized controlled trials that include and compare different active and passive recovery protocols will greatly improve the precision and validity of the results, showing the advantages of some recovery protocols not only over control groups but also over other protocols.

III. Investigating different intensities and durations of active recovery protocols in future studies will likely contribute to more conclusive findings regarding the appropriate parameters for recovery following intensive trainings.

IV. Selecting participants with different fitness levels, from beginners to professionals, can be a factor to take in consideration in the future, as the perception of intensive training and the management of resulting symptoms are potentially different among these groups.

Perspectivas para futuras investigaciones

I. La ejecución de una revisión sistemática y una meta-análisis que investigue una gama más amplia de protocolos de recuperación, activos y pasivos, será eficiente para identificar todos los beneficios y limitaciones desde un alcance más amplio y de una manera más extensa.

II. La realización de más ensayos controlados y aleatorizados que incluyan y comparen diferentes protocolos de recuperación activos y pasivos mejorará enormemente la precisión y validez de los resultados, mostrando las ventajas de algunos protocolos de recuperación no solo sobre los grupos de control, sino también sobre otros protocolos.

III. La investigación de diferentes intensidades y duraciones de los protocolos de recuperación activa en estudios futuros probablemente contribuirá a hallazgos más concluyentes con respecto a los parámetros apropiados para la recuperación después de entrenamientos intensos.

IV. La selección de participantes con diferentes niveles de condición física, desde deportistas principiantes hasta profesionales, puede ser un factor a tener en cuenta, dado que el nivel de percepción y asimilación de entrenamientos intensos resulta diferente entre estos colectivos, por lo que es posible que también los síntomas los controlen de forma diferente.

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Appendix

Appendix 1: PubMed/Medline search strategy (last literature search performed on January 2nd, 2020)

	PubMed/MEDLINE
#1	"physiotherapy"[MeSH Term] OR "exercise"[MeSH Term]
#2	physiotherapy[tiab] OR exercise[tiab] OR treatment[tiab] OR recovery[tiab] OR ac
#3	#1 OR #2
#4	"Muscle Soreness"[MeSH Terms]
#5	"Muscle Soreness"[tiab] OR "Delayed Onset Muscle Soreness"[tiab] OR DOMS[tiab]
#6	#4 OR #5
#7	#3 AND #6

Appendix 2: Impact factor and ranking of each journal in "ISI Web of Knowledge – Journal Citation Reports" within their subject categories.

Chapters included in the thesis	**Journal**	**Impact factor**
Chapter 4.1.	**Strength and Conditioning Journal** *Ranking in 2021 ISI-JCR: 70/116 (Sport Sciences) – Q4*	2.143
Chapter 4.3.	**The Journal of Sports medicine and Physical Fitness** *Ranking in 2020 ISI-JCR: 67/85 (Sport Sciences) – Q4*	1.432

Acknowledgements

"In all your ways acknowledge Him, and He shall direct your paths." *– Proverbs 3:6*

When I first decided to pursue my education and obtain my PhD degree, it happened nine years after my master's degree, and I was busy building up my career in my clinic and teaching part time courses at many universities. Finding the right circumstances to do this was definitely not an easy task and the challenge between becoming a student all over again, travelling abroad, and assuming my daily professional responsibilities was very tough and overwhelming. I wish I can say I had an easy start, it was beyond my expectations and at moments I felt I wanted to give up and come back home without any degree. The presence of **Dr. German Vicente-Rodriguez** and **Dr. Hugo Olmedillas** by my side has definitely had the greatest impact on my academic path and has helped me realize that giving up is not an option. They both provided me with all the necessary support, morally and academically, and they guided me all the way through my journey and made sure I was heading in the right destination.

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Dr. Olmedillas, you have travelled several times to my country Lebanon to closely follow-up my experiments in the lab and to help me improve the quality of my work. You have hosted me in your hometown and helped me side by side to get through all the readings and publish my own papers. You were tough, strict, and demanding, and this is something for which I will forever be thankful as you made me a better academic and provided me with the right tools. We also shared amazing moments and made wonderful lifetime memories, for that, I consider you my brother not

only my professor. Thank you!

During the passing years, many incidents and circumstances have marked and influenced my journey. My father was diagnosed twice with cancer, and both times the news came as a striking and choking shock. Dealing with this never became easier, but my father beat cancer both times and came out stronger than ever. **DAD**, you are a true fighter and a real survivor. Your strong will and your love for life taught me the meaning of holding on and never abandoning my dreams. You will always be my hero and the person I wish I could become like him one day. Thank you for making me the man I am today. This is for you!

With my father's illness, the situation also took a toll on my mother. She was very anxious, confused and depressed most of the time, but she never lost her faith and high spirit. Whatever positivity I might possess in my character, it is because of you, **MOM**. You have always been a strong, independent and ambitious woman who loves life. You infused me with encouraging vibes, you are my comfort and whenever I felt down, looking into your eyes and seeing you smile always made things easier. Thank you for believing in me; this is also for you!

To my sisters, **Dareen** and **Dima**, you have always been an essential support in my life, I remember how proud you were when I published my first paper. You both turned out to be powerful, determined women and wonderful mothers, and yet, a part of me still see us all gathered around **Teta Em Fares** in **Aishieh**. We have shared the best and the worst, and though life might physically separate us, our love and care for each other will keep our bond forever. Also, to your four angels, **Kenz, Ivy, Liesse** and **Raphael,** you were my sweet, comforting escape in moments of stress, Khallouli loves you!

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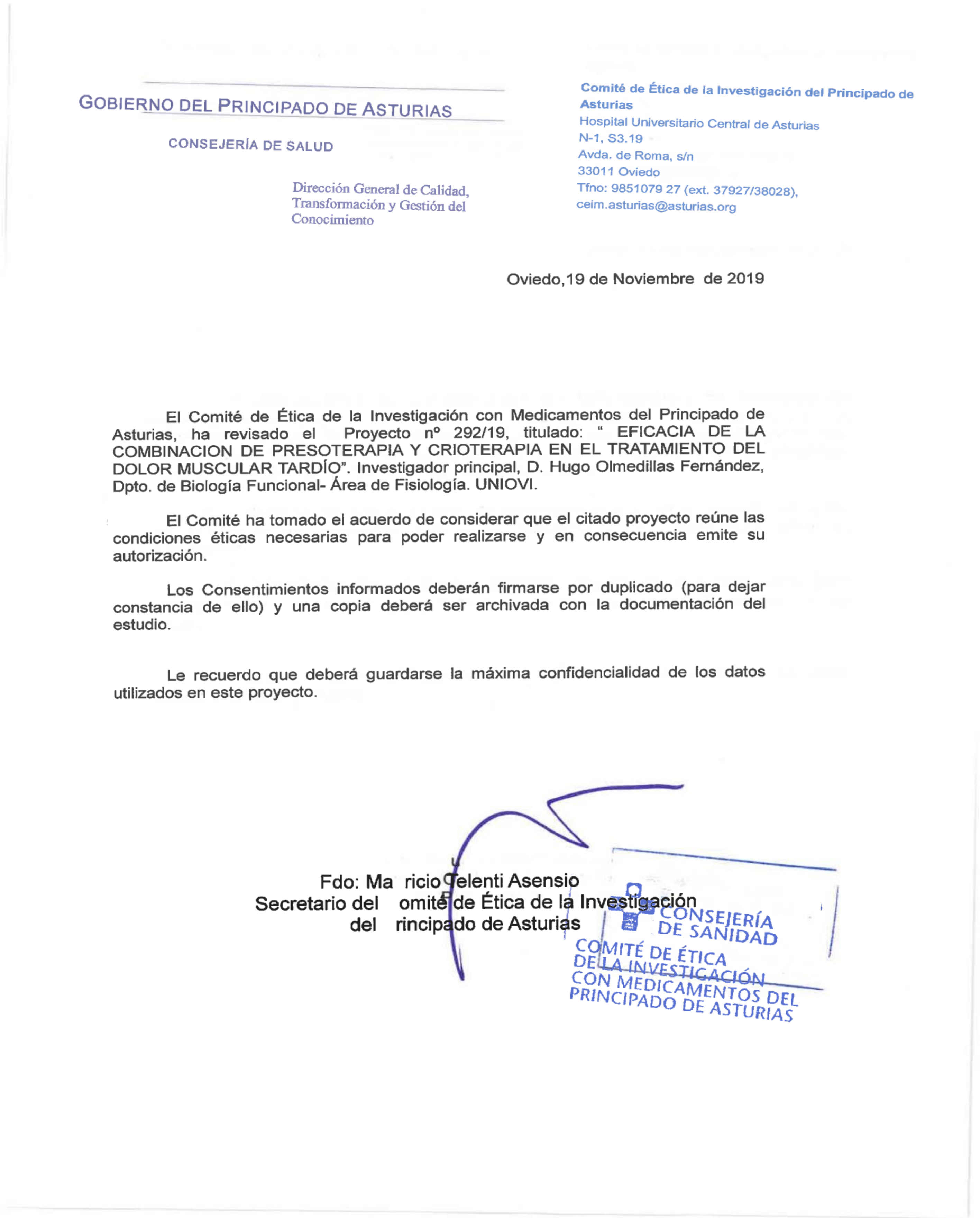
Finally, I would like to dedicate my work to my country **Lebanon.** In 2019, my country witnessed the beginning of a social revolution, which escalated later to become one of the worst economic crises of the century. This happened at the same time with the emergence of COVID-19 and its negative repercussions all over the world. Moreover, on August 4, 2020, my capital Beirut was hit by the third strongest explosion in human history, leaving hundreds dead and many more injured and homeless. This was one of the saddest days of my life. Surrounded by despair, destruction, and anger, finishing my work in the midst of all this chaos became less and less certain. Prayers and thoughts of our beloved people all over the world were very empowering. We were destined to rise up and start building again hoping for a better future. Wounds and scars are still here, but my faith in Jesus, my Lord, made me realize that no matter how hard and dark our days might turn, good things will happen again, and holding my thesis after five years of hard work is one of the good things I was longing for.

Annexes

Annex 1: Ethics committee approval



GOBIERNO DEL PRINCIPADO DE ASTURIAS

CONSEJERÍA DE SALUD

Dirección General de Calidad,
Transformación y Gestión del
Conocimiento

Comité de Ética de la Investigación del Principado de Asturias
Hospital Universitario Central de Asturias
N-1, S3.19
Avda. de Roma, s/n
33011 Oviedo
Tfno: 9851079 27 (ext. 37927/38028),
ceim.asturias@asturias.org

Oviedo,19 de Noviembre de 2019

El Comité de Ética de la Investigación con Medicamentos del Principado de Asturias, ha revisado el Proyecto nº 292/19, titulado: " EFICACIA DE LA COMBINACION DE PRESOTERAPIA Y CRIOTERAPIA EN EL TRATAMIENTO DEL DOLOR MUSCULAR TARDÍO". Investigador principal, D. Hugo Olmedillas Fernández, Dpto. de Biología Funcional- Área de Fisiología. UNIOVI.

El Comité ha tomado el acuerdo de considerar que el citado proyecto reúne las condiciones éticas necesarias para poder realizarse y en consecuencia emite su autorización.

Los Consentimientos informados deberán firmarse por duplicado (para dejar constancia de ello) y una copia deberá ser archivada con la documentación del estudio.

Le recuerdo que deberá guardarse la máxima confidencialidad de los datos utilizados en este proyecto.

Fdo: Mauricio Telenti Asensio
Secretario del Comité de Ética de la Investigación
del Principado de Asturias

CONSEJERÍA DE SANIDAD
COMITÉ DE ÉTICA DE LA INVESTIGACIÓN CON MEDICAMENTOS DEL PRINCIPADO DE ASTURIAS

GOBIERNO DEL PRINCIPADO DE ASTURIAS

CONSEJERÍA DE SALUD

Dirección General de Calidad,
Transformación y Gestión del
Conocimiento

Comité de Ética de la Investigación del Principado de Asturias
Hospital Universitario Central de Asturias
N-1, S3.19
Avda. de Roma, s/n
33011 Oviedo
Tfno: 9851079 27 (ext. 37927/38028),
ceim.asturias@asturias.org

proyecto 292 19 hugo olmedillas PRESOTERAPIA Y CRIOTERAPIA EN DOLOR.docx

Cod CEIm P Ast: proyecto 292/19
Cod protocolo: nd
Título: Eficacia de la combinación de presoterapia y crioterapia en el tratamiento del dolor muscular tardío
Inv. Principal: Hugo Olmedillas Fernández
Tutor:
Centro: UNIOVI

Cons. Informado: **SI**
Tipo de estudio:
Promotor:
Financiación:

CHECKLIST:

nota para el informe: "INFORME FAVORABLE. Deberán actualizar en la HIP/CI la normativa referente a la protección de datos (Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales (BOE-A-2018-16673)"

1. Título: se aporta, correcto.
2. Investigador Principal: se aporta
3. **Aceptación del Jefe de Servicio o Unidad:**
   - **COMENTARIO: en próximos proyectos deberán aportar la aceptación del jefe de Servicio o Unidad… (en su caso el Dr Miguel del Valle) con nombre, FECHA Y FIMA**
4. Copia de Dictamen de un CEI, si lo hubiera: CEImPA
5. Código del Promotor: nd
6. Copia de Informe de autorización / clasificación por la AEMPS, si se precisa: no aplica
7. Servicios Colaboradores: se aportan
8. Protocolo y Cuaderno de recogida de datos: se aporta, correcto

- **<u>COMENTARIO</u>: El estudio que proponen es correcto. De todas formas, convendría evitar determinados conceptos, aunque puedan ser correctos desde un punto de vista técnico:**
    - Metodología y plan de trabajo / Ámbito del estudio: se define como un **ensayo clínico aleatorio simple**.
        - El término de Ensayo Clínico es un procedimiento de estudio experimental que, en general, es necesario para evaluar fármacos y dispositivos (productos sanitarios, tales como los marcapasos); este concepto de *experimental* es el que hay que evitar, dado que, en general, implica que se esté trabajando fuera de la Lex Artis, por lo que los requerimientos éticos son mucho mayores que para uno observacional. Por ello, hay que intentar realizar estudios de corte "observacional" y "pseudoexpermiental"
        - El término de EC aleatorio simple es un poco confuso para su estudio. El propio concepto de EC hace que deba haber un componente experimental, en el que se compara un brazo "experimental" con un brazo "control"; en la aleatorización, los casos son distribuidos al azar en cada brazo del estudio. Es posible que Uds apliquen el concepto de "aleatorización" a diferentes procedimientos realizados en diferentes zonas del cuerpo o en diferentes momentos…
        - En resumen, si es posible debería irse hacia modelos tipo "estudio prospectivo y pseudoaleatorizado"

9. Promotor: los investigadores
10. Tipo de estudio: definir el tipo de estudio: prospectivo, minimamente intervencionista
11. Memoria económica: no
12. Justificante de pago de tasas (si precisa): no aplica
13. Seguro: no aplica.
14. Hoja de Información al Paciente / Consentimiento Informado: se aporta

Es obligación del CEI vigilar tanto los aspectos científicos de los estudios como revisar aspectos tales como la financiación, las cargas que puede suponer un proyecto de investigación para las unidades asistenciales o la seguridad jurídica tanto del paciente (Consentimiento, Seguro) como de los Investigadores y del Centro, dado que durante la investigación se trabaja fuera de la clínica médica asistencial.

M Telenti – Secretario CEIm del Principado de Asturias - 19/11/2019

Annex 2: Declaration of consent for participation in the clinical trial

Departamento de Morfología y
Biología Celular

Universidad de Oviedo
Universidá d´Uviéu
University of Oviedo

Departamentu de Morfoloxía y Bioloxía Celular
Department of Cellular Morphology and Biology

Yo
…………………………………………………………………………………………
…………………
…………………………… (Nombre y apellidos manuscritos por el participante)
He leído esta hoja de información y he tenido tiempo suficiente para considerar mi decisión.
Me han dado la oportunidad de formular preguntas y todas ellas se han respondido satisfactoriamente.
Comprendo que mi participación es voluntaria.
Comprendo que puedo retirarme del estudio.

1. Cuando quiera.
2. Sin tener que dar explicaciones.
3. Sin que esto repercuta en mis cuidados médicos.

Presto libremente mi conformidad para participar en el estudio y doy mi consentimiento para el acceso y utilización de mis datos en las condiciones detalladas en la hoja de información.
He recibido una copia de este documento.

Firma del participante Fecha (manuscrito por el participante)

Firma del investigador Fecha (manuscrito por el investigador)

Campus del Cristo
C/ Julián Clavería, 6

+34 985 10 36 14
dpto.morfologia@uniovi.es