

# Archivos de medicina del deporte

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Analysis of ventilatory equivalent responses for gases. Physiological significance





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# Sport-related concussion (SRC). Current challenges and implications for team doctors

## *La conmoción cerebral relacionada con el deporte (SRC). Problemática actual e implicaciones del médico deportivo*

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Sports-related concussion (SRC) is defined in the 6th international consensus statement on concussion in sport (Amsterdam, 2022<sup>1</sup>) as a traumatic brain injury caused by a direct blow to the head, neck or body resulting in an impulsive force being transmitted to the brain that occurs in sports and exercise-related activities. This initiates a neurotransmitter and metabolic cascade, with possible axonal injury, blood flow change and inflammation affecting the brain. Symptoms and signs may present immediately, or evolve over minutes or hours, and commonly resolve within days, but may be prolonged. These symptoms and signs may not involve loss of consciousness. No abnormality is seen on standard structural neuroimaging studies although abnormalities may be present on functional, blood flow or metabolic imaging studies<sup>1</sup>.

SRC occurs most often in such contact sports as boxing, football, ice hockey or rugby, reaching an incident rate in the latter of up to 17.1 concussions per 1,000 hours of play<sup>2</sup>.

SRC can have short-, medium- and long-term consequences on the athlete. In the acute stage, it has been associated with greater risk of muscle injuries stemming from reduced motor control after a concussion<sup>3</sup> and the risk of a fatal outcome can even increase were a second concussion to occur within a short time frame<sup>4</sup>. In the medium term, some athletes can continue to show symptoms over a period of time in excess of two weeks, with headaches being the main symptom, and can even present with post-concussion headaches for over three months<sup>5</sup>. In terms of the long-term effects of SRC, repeated concussions in the same person has been linked to chronic traumatic encephalopathy. However, this link has not been entirely demonstrated<sup>6</sup>.

Early diagnosis of SRC and proper management allows recovery time to be accelerated and the risk of complications or other brain and musculoskeletal injuries to be reduced<sup>7</sup>. The lack of objective image testing makes diagnosing this injury more complicated. The diagnostic criteria for mild traumatic brain injury were published recently<sup>8</sup>, not only

for traumas in the field of sport but also in civilian and military situations, establishing different criteria that would help to perform a differential diagnosis. These criteria include: 1) the mechanism of injury; 2) acute symptomatology; 3) clinical examination and laboratory findings; 4) neuroimaging tests; and 5) ruling out any symptomatology that could be better explained by other possible causes<sup>8</sup>.

Various complementary tests are being designed that could be applied for the diagnosis, prognosis, recovery markers and possible complications of SRC: analysis of biomarkers in bodily fluids (microRNAs, glial fibrillary acidic protein (GFAP), total Tau, microneurofilament light chains (NFL) etc.), advanced neuroimaging (functional MRI), EEG, pupillometrics, etc. All these tests might enable the detection of persistent biological abnormalities after clinically observed recovery. Nonetheless, these techniques are not included in regular clinical practice given that the majority of them are currently at the research stage and, moreover, it is unknown whether the possible abnormalities revealed are pathological, adaptive or benign. The data produced to date are also insufficient for linking the neurobiological change to the clinical indicators of recovery<sup>9</sup>. Hence, SRC continues to be a mainly clinical diagnosis at present. In light of this problem, various international expert consensus events continue to take place with a view to designing standardised tools capable of helping sports medicine physicians treat SRC. The *Sport concussion assessment tool - 6* (SCAT6)<sup>10</sup> was recently published, with a separate version for children (Child SCAT6). This tool enables a multi-modal assessment of athletes with suspected SRC to be conducted, including an immediate on-field assessment in several steps: establish alarm signals (red flags), the Glasgow coma scale, an assessment of the cervical spine, a coordination test, an oculomotor exam and a memory test. An off-field assessment is subsequently performed that includes a history of the athlete, the assessment of symptoms, the cognitive testing, the coordination and balance test and deferred memory in order

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to finally enable a decision to be reached. It is a tool designed for use in the acute stage, ideally within 72 hours and up to seven days after the injury. SCOT6<sup>11</sup> is recommended for an assessment several days later, which would include the assessment of neurological symptoms and signs, cognitive function, balance, orthostatic blood pressure and heart rate, cervical spine assessment, oculomotor function and sight, a standardised stress test for concussion and the psychological and neuropsychological study<sup>9</sup>.

In light of all the above, it is clear that the diagnosis and treatment of SRC is complex and occasionally requires multi-disciplinary teams. In practice, it represents an added problem for the sports medicine physician, who needs to perform a diagnosis on-field and in the shortest time possible. Various international federations have therefore designed action protocols in response to suspected SRC.

World Rugby — a pioneer in this field — uses a protocol for treating head injuries in rugby (HIA)<sup>12</sup>. This protocol is divided into four stages: HIA 1) Off-field assessment, which is performed via direct assessment and viewing the video. If a player meets the criteria for immediate removal, no further assessment methods would be necessary before removal (criteria 1). The doctor responsible for performing the assessment will have at least 12 minutes to complete this protocol, in which the player cannot return to the field (criteria 2). HIA 2) This is performed three hours after the match ends and the SCAT6 tool may be used. HIA 3) This is performed 36-48 hours after the event and the SCAT6 tool is recommended, as well as a computerised neurocognitive tool (chosen by each team). HIA 4) Full authorisation to return to play after completing rehabilitation, noting the recovery time in the medical history of the athlete.

FIFA also has a protocol for treating SRC in football<sup>13</sup>, which is divided into eight stages: 1) Observation and recognition; 2) Initial (on-pitch) examination, these stages are also performed via direct assessment and viewing the video; 3) and 4) Off-pitch/quiet-area examination; 5) to 7) Post-match examinations and observation, between 18 and 72 hours after the event; and 8) Graduated Return-to-Football Programme.

In all cases, the team doctor is responsible for treating and monitoring SRC, who, on most occasions, lacks the necessary resources to follow the diagnostic protocols (video assessments, among others). This increases the difficulty of treating SRC and its early on-field diagnosis. Although all tiers of sport agree that the doctor has authority to force the player to be removed from the field of play in the event of suspected SRC, it must be realised that the athlete often appears to be well and both he and the team specialists see no reasons for the player to be forced to retire. This only adds more pressure to the decision-making process. For these reasons, there is a certain degree of controversy at present regarding the on-field treatment of concussion. On the one hand, sports organisations defend temporary substitution to be allowed,

which would give the doctor time to perform a more complex examination. However, on the other hand, were the examination to produce a false negative, the risk to the player would be increased. This is why other organisations prefer permanent substitution without the option to return to play, even though the result could be negative.

As a result, the greatest limitation faced by the sports medicine physician, on-field, lies in not having objective markers for the immediate diagnosis of SRC. Hence, in any case, it is desirable for all the professionals involved in sport (experts, players, referees, the media, etc.) to work together in treating this issue. That would facilitate the work of healthcare staff and would be beneficial to minimising the possible consequences of SRC in the short, medium and long term.

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# Reference values for creatine kinase activity in a group of high-performance athletes

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## Summary

Physical activity integrates processes that are manifested in biochemical adaptations, such as the increase in the serum activity of the enzyme creatinquinasa (CK). People who participate in daily training have higher CK activity values, suggesting that those of an athlete cannot be compared with those established for healthy non athletic subjects. This study proposes possible reference intervals for male and female athletes, evaluated critical values, examine the dependence of gender on these results, and compare them with those established for healthy non athletic individuals. For this, 436 results of serum CK activity obtained from male and female athletes (age: 18-40 years) were analyzed.

Results: the medians of the mean athletes (325 U/L) present a high result ( $P < 0.0001$ ) compared to the median of the female athletes (156 U/L). 59% of the results obtained in men and 39 % in women exceed the reference value established for healthy subjects. (men: 32-294 U/L; women: 33-211 U/L). The 2.5% and 97.5% percentiles and their 90% confidence intervals were calculated (men: 88 (56-90) to 833 (781-973) U/L; women: 58 (44-63) to 448 (433-497) U/L). Comparing the results with the reference values used by the laboratory for healthy subjects, significant differences were observed, with higher values obtained for the groups of athletes. From the analysis carried out, specific reference intervals were obtained, whose limits are higher than those already established, and differ by sex, being higher in men than in women. The value of biochemical expertise in the health control within their training plan is relevant to organize the distribution of workloads, prevent injuries and ensure health care.

## Key words:

Adaptation. Enzymatic activity. Creatine kinase. Reference intervals.

## Valores de referencia de actividad de creatinquinasa en un grupo de deportistas de alto rendimiento

### Resumen

La actividad física integra procesos que se manifiestan en adaptaciones bioquímicas, como el incremento de la actividad sérica de la enzima creatinquinasa (CK). Quienes participan de entrenamientos diarios poseen valores de actividad de CK elevados, sugiriendo que los de un deportista no pueden compararse con los establecidos para sujetos sanos no atletas. Este trabajo propone intervalos de referencia posibles para atletas hombres y mujeres, evaluar valores críticos, examinar la dependencia del sexo en esos resultados, y compararlos con los establecidos para los individuos sanos no deportistas. Para ello se analizaron 436 resultados de actividad sérica de CK obtenidos de hombres y mujeres deportistas (edad: 18-40 años).

Resultados: La mediana de los deportistas varones (325 U/L) presenta un resultado mayor ( $p < 0,0001$ ) respecto a la mediana de las deportistas mujeres (156 U/L). El 59% de los resultados obtenidos en varones y el 38% en mujeres supera el valor de referencia establecido para sujetos sanos (varones: 32-294 U/L; mujeres: 33-211 U/L). Se calcularon los percentiles 2.5% y 97.5%, y sus intervalos de confianza 90% (varones: 88 (56-90) a 833 (781-973) U/L; mujeres: 58 (44-63) a 448 (433-497) U/L). Comparando los resultados con los valores de referencia utilizados por el laboratorio para sujetos sanos, se observaron diferencias significativas, con valores más altos para los grupos de deportistas. Del análisis realizado se obtuvieron intervalos de referencia específicos para esta población, cuyos límites son superiores a los ya establecidos, y difieren por sexo, siendo más altos en varones que en mujeres. El valor de la experticia bioquímica, en el control de salud a deportistas dentro de su plan de entrenamiento resulta relevante para organizar la distribución de cargas de trabajo, prevenir lesiones y asegurar el cuidado de su salud.

## Palabras clave:

Adaptación. Actividad enzimática. Creatinquinasa. Intervalos de referencia.

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## Introduction

Physical activity involves a series of mechanical, psychological, emotional and physiological processes that are expressed in biochemical changes and adaptations in order to get sufficient energy to perform the activity. One of these processes is the increase in serum activity of the creatine kinase enzyme (CK, EC 2.7.3.2.), which is released into the blood stream from muscular fibres, due to repeated intense contractions.

In these conditions, CK activity increases considerably, and although its validity as a biochemical marker of a real muscular lesion induced by exercise is still questioned by some authors, its use as such is accepted by most. Its highest serum values are attained between 12 and 24 hours after exercise and remain high for up to 96 hours or more, depending on the stopping of the stimulus<sup>1-5</sup>.

Individuals taking part in training programmes have higher CK activity values at rest than people who are not in a programme, although this response is individual and depends on the training model and the type of contraction performed. Furthermore, this condition is alleviated by adapting the repetition of exercises, which lowers the quantity and quality of muscular lesions. Determining the serum CK activity levels among athletes is a very useful biochemical marker to estimate the stress caused by the training on the muscle, suspect cases of over-training, prevent lesions from appearing and monitor the post-effort muscular recovery processes. In apparently healthy subjects, CK levels which exceed the reference value might be correlated with their physical condition; however, if these levels persist at rest, this might be a sign of subclinical muscular disease, demonstrated through the appearance of symptoms such as chronic fatigue<sup>4,6-9</sup>.

Within this situation, we should mention the need to get reference values from the actual groups of athletes. The reference value concept was proposed by the IFCC panel of experts and accepted with different nuances by the national commissions for the purposes of unifying concepts, methods, terminologies and conducts. A reference value is defined as a value obtained from a reference individual, a person within the community, who has a determined state of health. All individuals who meet the defined inclusion conditions constitute a reference population which makes it possible to set values for specific groups<sup>10-12</sup>.

It is intriguing to think that CK activity results for an individual doing their sport cannot be compared with the reference intervals determined for healthy non-athlete subjects. We might therefore ask which value would be reasonable to expect as a physiological response in athletes without considering an associated pathology. The answer to this question has great practical value, as if a CK result has increased over the reference value in an athlete within what is stipulated as an appropriate response, the training load might even be increased without risking an additional lesion, in search of greater physical and physiological responses. On the contrary, if the value was very high, it would be advisable to reduce loads to protect the athlete and prevent possible muscular lesions.

The goals of this paper were to propose possible reference intervals in male and female athletes between 12 and 24 hours after training, examine how much these results depend on gender, compare them to the results determined for healthy non-athletes and assess critical values that should raise the alarm among treating physicians.

## Material and method

A cross-sectional, descriptive and retrospective design was produced which analysed 436 results obtained over a period of 10 years (March 2009-November 2019), from male and female athletes aged between 18 and 40 years old, which were sent to the LACBA S.A. Laboratory at the TCBA Diagnostic Centre for routine biochemical control. They were all high-performance hockey players who went to training sessions lasting 60-120 minutes, six days a week with one rest day per week. On admission, they were asked to fill in a form asking if they considered that they met the criteria to be included in this study, alongside the form asking for informed consent to use the results for scientific purposes. Inclusion criteria were the absence of previous diseases, muscular lesions diagnosed by the sports medical team, admission to hospital in the last three months or for periods over 15 days during the year prior to the sample-taking, and use of medication.

### Obtaining results

The results analysed were obtained from serum samples using elbow fold venepuncture on the athletes 8-10 hours after 12 hours of fasting and sleep, with two days of prior training. The athletes abstained from training in the morning, to avoid changes in the plasma volume induced by exercise which might affect measurements. The blood sample was left to coagulate for 30 minutes at room temperature, it was centrifuged for 12 minutes at 3,500 rpm and then processed. CK serum activity was determined using the IFCC UV method in an Advia 1800 Siemens auto-analyser, and the results were expressed in U/L at 37°C. The reference values used were provided by the manufacturer (men: 32-294 U/L; women: 33-211 U/L) and verified by the laboratory. Institutional endorsement was provided to use the results obtained through the LACBA laboratory computer system, copied onto password-protected Excel sheets, saved on two pendrives which could only be accessed by the researchers.

### Statistical analysis

The CK variable distributions in the groups being analysed were significantly different ( $p < 0.05$  for the Kolmogórov-Smirnov test)<sup>10,13</sup>. Medians were compared using the Mann Whitney test between the male and female groups; and between the reference values obtained and those used by our laboratory (2.5 and 97.5 percentiles and 90% confidence interval) with the Wilcoxon test. In all cases, a  $< 0.05$  level of significance was considered. The Rout method was used to define outliers. The statistics programs used were SPSS 25.0 and GraphPad 8.

## Results

The CK activity distribution in the athletes being studied, differentiated by gender (male and female), presented non-parametric behaviour, as shown in the histograms in Figures 1 and 2.

The outlier values were determined, and the descriptive statistics and 2.5% and 97.5% percentiles were calculated, and then used to calculate the respective reference values with their confidence intervals (CI 90%) (Table 1). The reference values for healthy subjects used by the laboratory were provided by the equipment and reagent manufacturer.

Figure 1. Distribution of the CK serum activity levels in male athletes.

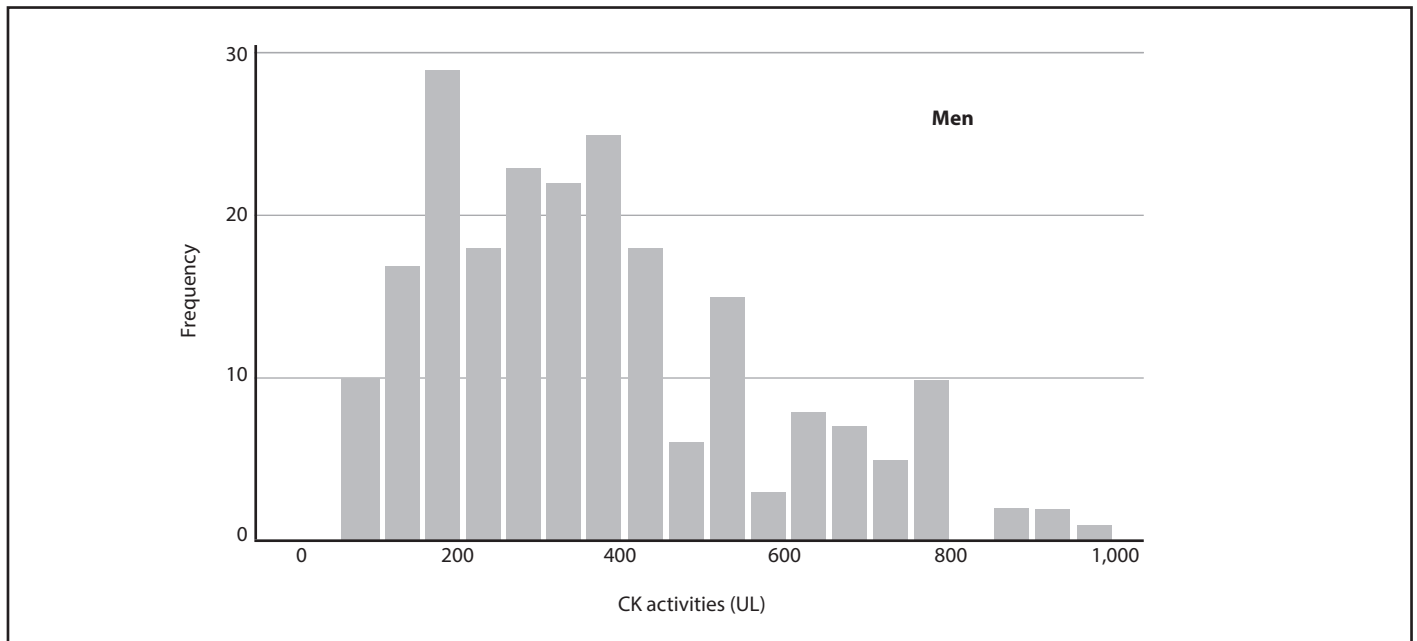
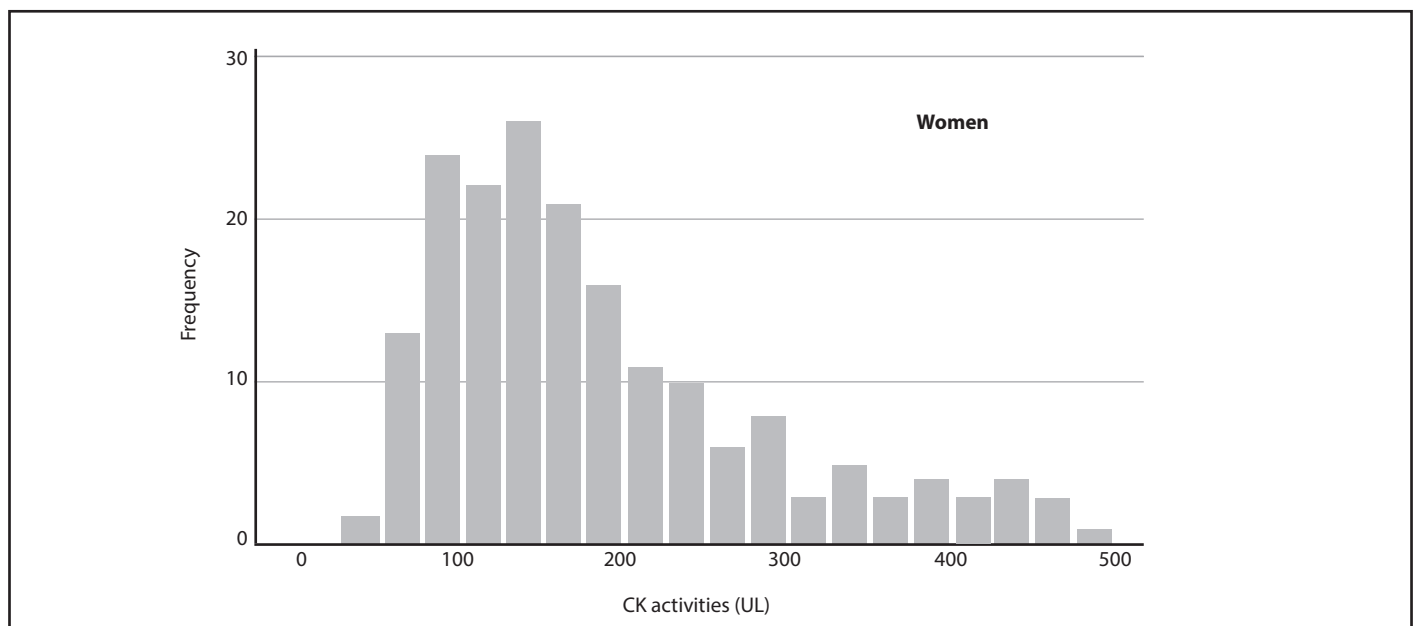


Figure 2. Distribution of the CK serum activity levels in female athletes.



The transferability was verified for these reference values from a sample population of 160 individuals (84 men and 76 women), considering that 95% of these values fall within the manufacturer's reference limits<sup>14-16</sup>. The comparison of the laboratory reference values with those obtained from the group of athletes was significantly different ( $p < 0.001$ ). It was observed that 59% of CK results obtained among men and 38% in women exceed the reference value set for healthy subjects. From the analysis of the gender-differentiated CK activity results, a statistically significant difference ( $p < 0.0001$ ) was observed when comparing the medians. The median of male athletes presents a higher result (325 U/L) than the median of female athletes (156 U/L).

Figure 3 shows the comparison of the CK activity results by gender, detailing the boundaries of the upper reference value used by the laboratory.

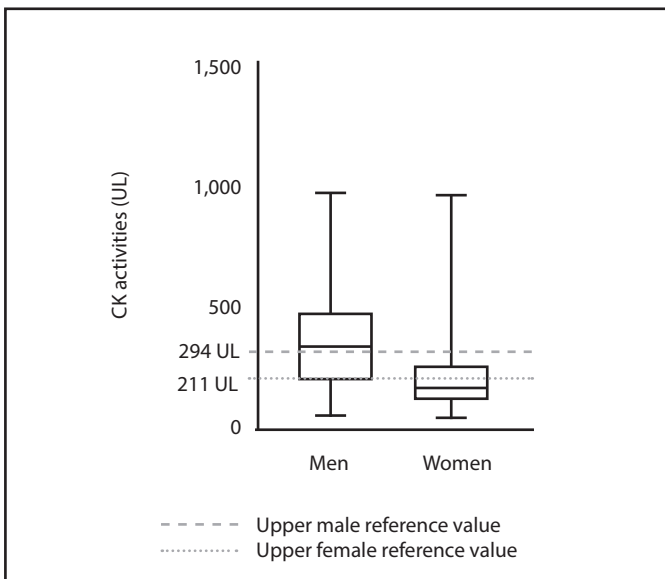
**Table 1. Medians and lower and upper reference values with their respective CI 90% for male and female athletes.**

	Men	Women
Median U/L	325	156
<b>Reference intervals</b>		
Lower limit U/L	88 (CI 90%: 56-90) *	58 (CI 90%: 44-63)*
Upper limit U/L	833 (CI 90%: 781-973) *	448 (CI 90%: 433-497)*

CI 90%: confidence interval 90%

\*  $p < 0.001$ .

**Figure 3. Comparison of CK activity values by gender. The diagram shows the upper limits of the reference value used in the laboratory with broken lines.**



## Discussion

CK serum activity is an important indicator of the extent of muscular effort and adaptation to the training. It has become an exceedingly interesting option to assess athletes and a very useful tool for the medical team looking after them, although it is not easy to interpret.

This paper demonstrates that CK activity values are higher in athletes, both men and women, which can help to explain the meaning of this data by providing specific reference values for a group of athletes that can be used in sports medicine during daily practice<sup>17,18</sup>.

It should be considered that the values obtained depend on the type of training (intensity, duration, type of muscular contraction performed), so different groups of athletes might refer to slightly different results. This study assessed male and female high-performance grass hockey players. This sport has undergone radical changes in its technical, tactical and physiological requirements, above all in elite athletes, particularly associated with the playing surfaces and the greater intensity of the game. There are few publications in the literature on muscular damage among elite grass-hockey players<sup>19</sup>.

Given that CK activity remains high a few days after the stimulus and that the athletes studied carry out successive training sessions, the results obtained reflect the accumulative effect of the loads and the degree of adaptation to the training. In this particular case, the hockey players carry out high-intensity intermittent activities and these results might suggest that they could be extrapolated to sports with similar characteristics (such as football)<sup>20-22</sup>.

However, we suggest that it is reasonable to assess specific reference intervals per sport. The athletes' reference limits were 2 to 3 times higher than those used by the laboratory for healthy subjects. It should be emphasised that the values generally used in the laboratory concur with the bibliography in general and with the data reported by the reagent suppliers for healthy subjects who do not do any physical activity, and that require physical activity to be stopped for 72 hours prior to the extraction as a preanalytical rigour condition.

The CK activity reference intervals in athletes demonstrated differences by gender, greater in men than in women, in concordance with what was reported by the studied bibliography and in line with the existence of specific reference values per gender in the general population<sup>23,24</sup>. The upper limit of the reference value obtained for the group of men demonstrated higher results than for the group of women, 1.8 times higher. These differences can be explained by different reasons, such as higher CK content in men's muscles, their greater muscle mass, the protective effect of oestrogen in women, and muscle factors such as stabilisation in the permeability of the membrane due to the hormonal influence, the rate of CK elimination and the lymphatic activity<sup>25,26</sup>.

When comparing both groups against the reference values used for healthy subjects by the laboratory, significant differences were seen, with higher values for the groups of athletes whose upper reference limits were 2.8 times higher for men and 2.1 times for women.

There are many factors that determine the increase in enzyme activity during and after exercise. The greatest values are obtained after exercises with predominantly eccentric contractions, after very lengthy or high intensity exercises<sup>27</sup>.

The medical team must be aware of borderline situations where these increases might be associated with the possibility of muscular lesions or with pathological situations. Beyond the reference values, the concept of alarm values then appears, understanding this to be results which must be immediately reported to the doctor so that corresponding actions can be taken to keep the athlete healthy. These values must be determined by each laboratory according to the respective medical teams, in concordance with their acquired experience. The bibliography presents the approved lists of critical values, that place the CK activity value above 1,000 U/L in this alarm point. Given that the reference values obtained in this paper do not exceed the upper limit of this value, this study group considers that it should not be modified<sup>28-30</sup>.

## Conclusions

From the analysis carried out on CK serum activity results among male and female elite athletes, specific reference intervals were obtained that differ from those generally used in the laboratory for healthy subjects without the stimulus of physical activity. The limits of the intervals obtained are higher and differ by gender, higher in men than women.

These differences suggest the need to review the reference intervals used for athletes, and each laboratory has its own values, to be able to interpret them correctly. We suggest setting alarm values, to improve assessment of results, from which other diagnostic alternatives should be considered that might influence them. The value of the biochemical expertise, in the knowledge and interpretation of the studies performed on athletes within their training and health control plan is relevant when organising the distribution of workloads, preventing lesions and ensuring their healthcare.

## Conflicts of interest

The authors declare that there were no conflicts of interest.

## Acknowledgments

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# Performance of young female ballet dancers' dominant and non-dominant lower limbs during hop and Y-balance testing

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## Summary

**Introduction:** Ballet requires coordination and integration of movement, proper body alignment, cardiovascular and muscular endurance, muscular strength, flexibility, static and dynamic balance. Epidemiological studies indicate that most injuries that affect ballet dancers are related to the lower limb, especially the ankle, foot, knee, and hip due to the implications of these joints in specific movements. These injuries can result in significant lost time in rehearsals, high costs, and may cause long-term dysfunction. In this context, preventive strategies should be considered to decrease the risk of injury, and to provide insight to help to create prevention programs or rehab plans. For this are widely used the functional tests.

**Objective:** This study investigated the functional performance of lower limbs in young ballet dancers.

**Material and method:** Thirteen healthy female ballet dancers between 14 and 17 years who participated in dance Regional Festivals performed the Y-balance test (YBT) and four hop tests (single, triple, crossover, and timed hop tests). For both hop tests and YBT, ballet dancers completed three trials in each lower limb and the average of the three values was used to calculate the symmetry index between the limbs.

**Results:** There were no differences between the limbs in hop tests or YBT. However, it was observed the composite score of the YBT was below 94%, an average value lower than suggested by the literature.

**Conclusions:** Thus, the results demonstrated that young female ballet dancers have symmetry between the limbs in both functional tests, suggesting that dance training leads to greater skill in controlling the neuromusculoskeletal coordination between the limbs. However, they have a poor dynamic balance suggesting an increased risk of lower limb injuries. This research can contribute to the development of preventive programs and improve ballet dancers' performance and productivity.

## Key words:

Ballet. Young female dancers. Hop tests. Y-balance test.

## Rendimiento de las extremidades inferiores dominantes y no dominantes de jóvenes bailarinas de ballet durante hop test y Y-balance testing

### Resumen

**Introducción:** El ballet requiere coordinación e integración del movimiento, alineamiento corporal adecuado, resistencia cardiovascular y muscular, fuerza muscular, flexibilidad, equilibrio estático y dinámico. Los estudios epidemiológicos indican que la mayoría de las lesiones que afectan a los bailarines están relacionadas con el miembro inferior, especialmente el tobillo, el pie, la rodilla y la cadera, debido a las implicaciones de estas articulaciones en movimientos específicos. Estas lesiones pueden resultar en una pérdida significativa de tiempo en los ensayos, altos costos y pueden causar disfunción a largo plazo. En este contexto, se deben considerar estrategias preventivas para disminuir el riesgo de lesiones y para proporcionar información que ayude a un proveedor a crear programas de prevención o planes de rehabilitación. Para eso las pruebas funcionales son muy utilizadas.

**Objetivo:** Este estudio investigó el rendimiento funcional de las extremidades inferiores en jóvenes bailarinas de ballet.

**Material y método:** Trece bailarinas sanas de ballet entre 14 y 17 años que participaron en presentaciones regionales realizaron lo Y-balance test (YBT) y cuatro hop tests (single, triple, crossover, y timed hop tests). Tanto para las pruebas de salto como para YBT, las bailarinas completaron tres pruebas en cada miembro inferior y se utilizó el promedio de los tres valores para calcular el índice de simetría entre los miembros.

**Resultados:** No hubo diferencias entre las extremidades en los hop tests y YBT. Sin embargo, se observó un puntaje compuesto del YBT por debajo del 94%, valor promedio inferior al sugerido por la literatura.

**Conclusiones:** Así, los resultados demostraron que las jóvenes bailarinas de ballet tienen simetría entre las extremidades en ambas pruebas funcionales, lo que sugiere que el entrenamiento en danza conduce a una mayor habilidad en el control de la coordinación neuromusculoesquelética entre las extremidades. Sin embargo, tienen un equilibrio dinámico deficiente, lo que sugiere un mayor riesgo de lesiones en las extremidades inferiores. Esta investigación puede contribuir al desarrollo de programas preventivos y mejorar el rendimiento y la productividad de los bailarines de ballet.

## Palabras clave:

Ballet. Jóvenes bailarinas. Hop tests. Y-balance test.

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## Introduction

Ballet dance requires coordination and integration of movement, proper body alignment, cardiovascular and muscular endurance, muscular strength, flexibility, static and dynamic balance. These neuromuscular skills are essential for dancers to obtain a perfect and technically precise performance of functional movements important in ballet that requires grace and delicacy<sup>1</sup>. The ballet has been characterized as an intermittent type of exercise, in which lower limb explosive bursts such as jumps, and turns are followed by movements requiring precision and skill with adequate interaction of upper and lower limb movements<sup>2</sup>. Ballet dancers usually have complex and physically demanding routines with long training periods that may lead to physical exhaustion<sup>3</sup>.

Epidemiological studies indicate that most injuries that affect ballet dancers are related to the lower limb<sup>4,5</sup>. The most injured areas are the ankle, foot, knee, and hip due to the implications of these joints in specific movements<sup>3</sup>. The main triggering factors of injuries usually are micro-trauma repetition and muscle fatigue caused by overtraining<sup>6</sup>. Also, ballet dancers present incidence values around 1.09 injuries/1000 hours of exposure. Furthermore, there is a positive correlation between injury risk and age, and it was shown that ballet dancers at ten years have an injury incidence of 0.3 injuries/1000 hours; dancers 11 to 14 years have 0.7 injuries/1000 hours, while ages 15 to 21 years have 0.9 injuries/1000 hours<sup>7</sup>. Musculoskeletal injuries can result in significant lost time in rehearsals, high costs, and may cause long-term dysfunction<sup>6</sup>. In this context, preventive strategies should be considered to decrease the risk of injury, and to provide insight to help a provider create preventable programs or rehabilitation plans the functional tests are widely used<sup>8</sup>.

Functional tests are used to assess joint stability, balance, kinesthesia, agility, muscular control, and muscular strength<sup>9,10</sup>. Two types of functional tests, including the Y-balance test (YBT) and hop tests, are the most often used to assess the lower limbs function<sup>10</sup>. Hop tests are used to evaluate dynamic stability, lower limb strength, and neuromuscular control in pre-season or pre-competition and during a rehabilitation session to track progress with an intervention<sup>11</sup>. The YBT is used to verify the lower limb dynamic balance, identify the risk of injury, evaluate muscle imbalance, and assess rehabilitation progress<sup>12</sup>. Hop tests and YBT have as main advantages: low cost, easy application, not time-consuming, not require a great deal of expertise, not require expensive equipment, and they are considered open field tests that can be performed in several locations<sup>13</sup>. In different sports, the hop tests and the YBT are used as screening tools to identify inter-limb asymmetries that have been associated with an increase in injury risk by several authors<sup>14-17</sup>. Considering that the functional tests are excellent tools to detect the risk of injury and they can help to create programs to improve performance<sup>2</sup>, that few studies explore the YBT and the hop tests in ballet dancers; the main purpose of this study was to investigate the lower limbs functional performance of young female ballet dancers.

## Material and method

### Experimental approach to the problem

This study used a cross-sectional design to assess functional performance in dominant limb (DL) and non-dominant limb (NDL) lower extremities. This study was carried out in three different ballet schools in Garibaldi, Rio Grande do Sul, Brazil. The study was approved (protocol number 3.361.817) by the Ethical Committee at the University of Caxias do Sul. The study was in accordance with the Helsinki Declaration and 2012 Law N° 466 of the National Health Council, which approves the guidelines and rules for research involving humans.

### Participants

Thirteen pre-professional young female ballet dancers (mean age  $15.0 \pm 0.91$ ) who participated in dance Regional Festivals were recruited to participate in this research. The inclusion criteria to be eligible were: if they trained at least two days per week for at least two years and if they signed the Written Informed Consent by themselves and by their parents or legal keepers. The exclusions criteria were: acute illness on the day selected for evaluation, acute musculoskeletal injury, lower limb acute injury in the previous 30 days of assessment, use of medications such as analgesic, anti-inflammatory, and/or antihistaminic 48 hours before testing, and cognitive deficits that could interfere with the Written Informed Consent or study instructions. The anthropometric characteristics of the ballet dancers are summarized in Table 1.

### Sample size

The sample size was determined by convenience conforming to the number of ballet dancers and their availability for participation in the research. Therefore, the sample was determined intentionally and not probabilistically<sup>18</sup>.

### Procedures

Prior to the tests assessments, aiming to assess the general health and wellness variables (e.g., the previous history of musculoskeletal injury, amount of training per week, number of rehearsals per week, number of performances per week/year, years of experience in the dance, leg dominance, and warm-up practices) each participant completed a health history questionnaire.

To define which test (YBT or hop tests) the ballet dancers would execute first, we performed a randomly draw (e.g., if first the ballet dancer

**Table 1. Means  $\pm$  standard deviations of anthropometric characteristics of young female ballet dancers.**

Variable	M $\pm$ SD
Age (years)	15.0 $\pm$ 0.91
Body weight (kg)	52.59 $\pm$ 6.80
Height (m)	1.63 $\pm$ 0.05
Body mass index (kg/m <sup>2</sup> )	19.69 $\pm$ 2.41

M: Mean; m: meters; kgmm<sup>2</sup>: kilograms per square meter.

was drawn to execute the hop tests, after the hop test the ballet dancer executed the YBT, or vice-versa). The tests were performed in a specific room of assessment on a single day. The assessments were executed before the regional presentations and the tests were conducted from 2:00 to 5:00 p.m.

Prior to the tests, the ballet dancers received some recommendations such as do not consume stimulant substances (e.g., caffeine) 24 hours before testing, sleep at their usual time the day before testing, do not have any analgesic and/or anti-inflammatory medicine within 48 hours before testing, and do not perform high-intensity physical activities in the 48 hours prior to the tests.

### Musculoskeletal injury questionnaire

Intending to verify if the ballet dancers could have some injury that could interfere with the YBT and hop tests performance, the ballet dancers answered a questionnaire containing the following questions: (1) personal data such as name, age, weight, height, and BMI; (2) if the ballet dancers have been submitted to some surgery on lower limbs; (3) if the ballet dancers suffered some injury; (4) type of injury and anatomic region; (5) if the injury was contact injury or noncontact injury; (6) pain intensity after injury; (7) if the ballet dancers did physiotherapy for the injury.

### Functional performance tests

To investigate if the ballet dancers could have inter-limb asymmetries, the ballet dancers performed the hop tests that show inter-limb

asymmetries relating to muscle power, and the YBT that indicates inter-limb asymmetries corresponding to dynamic balance.

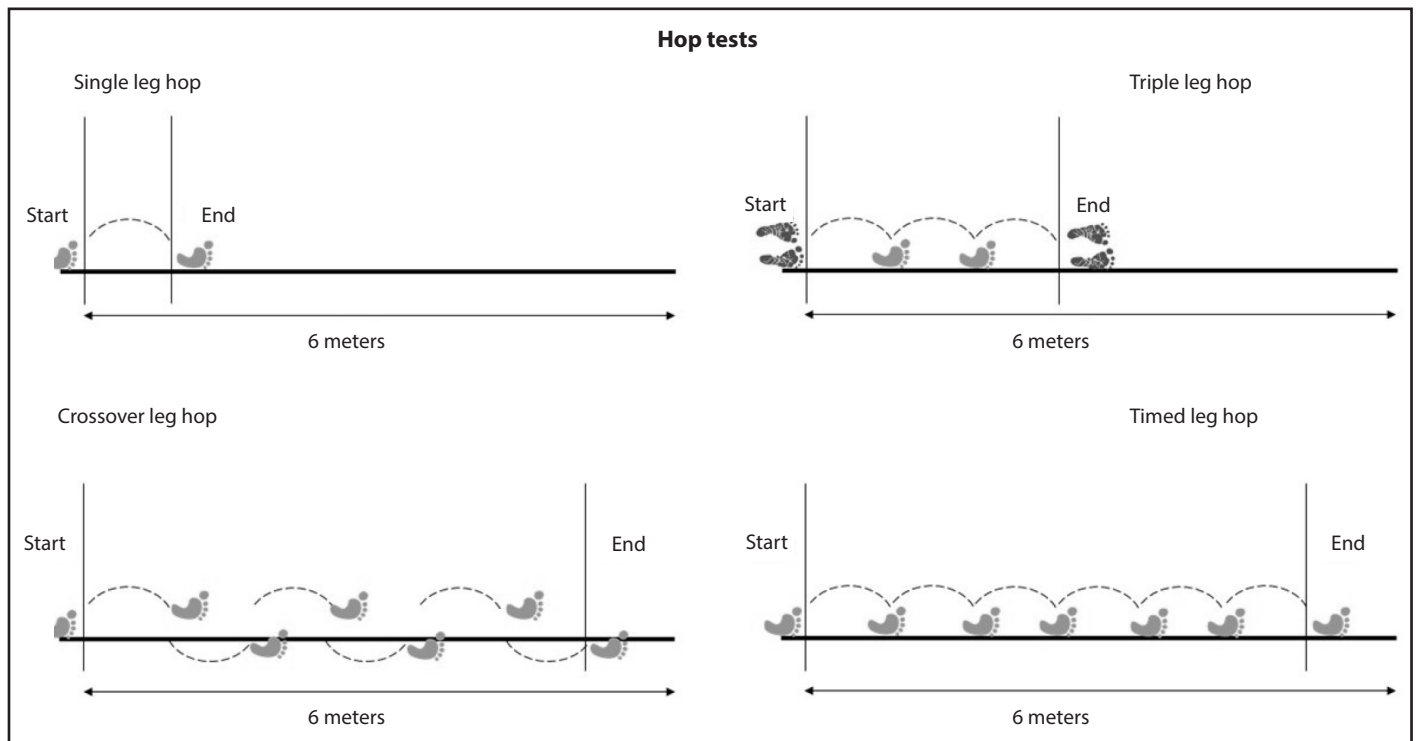
**Hop tests.** Hop tests are unilateral functional performance tests used to evaluate lower limb power and neuromuscular control in preseason or pre-participation in competition, to monitor progress in rehabilitation, and identify dynamic knee stability<sup>11,19</sup>. Hop tests provide an index of the ratio of limb symmetry known as LSI that expresses the distance or time recorded from the test as a percentage<sup>11,20</sup>. Four hop tests were selected to assess the dancers: single hop for distance, triple hop for distance, crossover hop, and timed hop<sup>21,22</sup>.

The tests were executed as described previously by Wiprich *et al.* (2022)<sup>23</sup>. Firstly, the ballet dancers received the instructions about the test and then they performed three practice trials for each hop test in each lower limb. The trials were executed with 30 seconds of resting period between each test to reduce the errors associated with learning and fatigue such as landing with the assistance of the opposite lower extremity, lost imbalance, or took an extra step after landing. If some ballet dancer made an error the hop test was repeated. In all hop tests the dancers performed the tests with the NDL and next with the DL, and the upper limbs were free<sup>23</sup>.

Distance (single hop, triple hop, and crossover hop) and time (timed hop) were measured in each one of the three trials. The distance was measured from the toe in the starting position to the heel where the subject landed (Figure 1).

The average of the three values was used to the comparison between NDL and DL and to calculate the hop symmetry index given by the formulas:

**Figure 1. The course for the four hop tests.**





For the single hop, triple hop, and crossover hop: Hop symmetry index = (NDL hop mean distance / DL hop mean distance) X 100<sup>21,22</sup>.

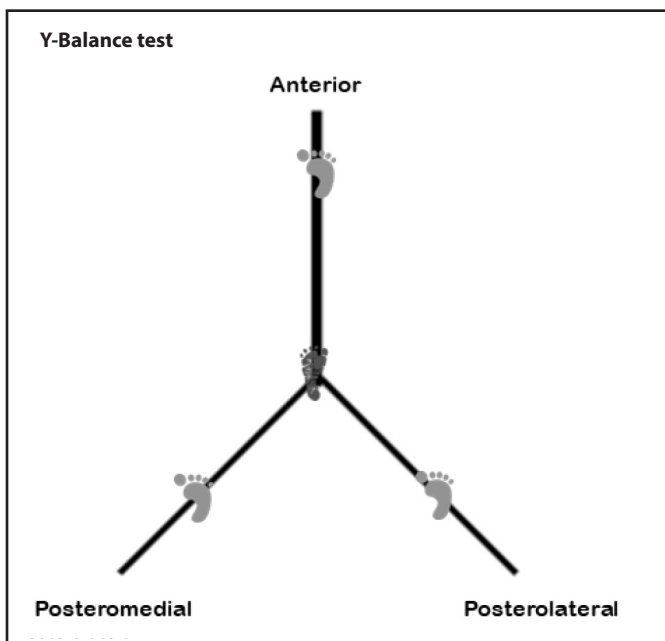
For the timed hop: Hop symmetry index (NDL hop mean time / DL hop mean time) X 100<sup>21,22</sup>.

**YBT.** The test was executed based on Wiprich *et al.* (2022)<sup>23</sup> and Plisky *et al.* (2009)<sup>24</sup>. The ballet dancers received the instructions about the test and subsequently, they performed three warm-ups in each lower limb. Then, they executed the trials. In both warm-ups and trials, three metric tapes were placed on the floor and separated by an angle of 135°. One metric tape was placed in the anterior (ANT) direction, and the two other metric tapes, one in the posterolateral (PL) direction and the other in the posteromedial (PM) direction divided by an angle at 90°<sup>24</sup>. The ballet dancers were positioned centrally to three metric tapes with single-leg support in the lower limb to be tested with the hands-on waist. The dancers stood on one leg on the center foot tape with the most distal aspect of the foot at the starting line. While maintaining a single leg stance, the dancer was asked to reach with the free limb in the ANT, PM, and PL directions in relation to the stance foot<sup>23,24</sup>.

Three practice trials were performed in each reach direction before the formal testing. From the fourth to the sixth trial, the examiner recorded the maximal reach distance (centimeters). In both warm-ups and trials, the ballet dancers first executed on the NDL, and next, on the DL, and the hands remained on the waist<sup>23,24</sup>. The maximal reach distance was measured by a tape measure, at the point where the most distal part of the foot reached (Figure 2)<sup>24</sup>.

The trial was discarded and repeated if the subject: failed to maintain a unilateral stance, failed to maintain reach foot contact with the reach indicator on the target area while it was in motion, and failed to return the reaching foot to the starting position under control<sup>24</sup>.

**Figure 2. The directions of Y-Balance test\*.**



\*The figure illustrates that the left foot is being tested in all directions of the YBT.

Three measures were calculated to quantify the dynamic balance: normal reach distance, total performance given by composite score, and limb symmetry index. For each limb, the reach distance was normalized by NDL and expressed as percent (%) (e.g., Normalized distance = distance reached (centimeters) X 100/ lower limb length). The total performance was determined by calculating the composite score, given by the formula:

Composite score = sum of three (ANT, PL, and PM) directions/ 3 X lower limb length) X 100.

For the lower limb length, the dancers were placed lying on a table in the supine position with the lower limbs extended, then the lower limb length was measured from the anterior superior iliac spine to the most distal portion of the medial malleolus with a tape measure<sup>24</sup>. The values used in the formulas were the means of each limb in each of the three directions<sup>24</sup>.

To calculate the symmetry index for each direction and the composite score were used the formula:

Symmetry index = (NDL mean distance / DL mean distance) X 100<sup>21,22</sup>.

## Statistical analysis

Initially, the Shapiro-Wilk test determined whether data were normally distributed. Data from DL and NDL were analyzed by a two-tailed Student's t-test, while data from YBT composite score was evaluated by a one-tailed Student's t-test. All data were recorded as mean  $\pm$  standard deviation (M  $\pm$  SD). For all comparisons, the significance level was set at P<0.05. Data were analyzed by GraphPad Prism 8.0 (GraphPad, Inc., San Diego, California).

## Results

**Hop tests.** There were no statistically significant differences between the limbs in all hop tests (Table 2). Moreover, the LSI presented a value above 90% in all hop tests (Table 2).

**YBT.** In YBT, the bilateral comparison did not show statistically significant differences between DL and NDL in all directions (Table 3). Nevertheless, the composite score in both DL and NDL limbs showed values significantly below 94% (P<0.001).

**Musculoskeletal injury questionnaire.** Two (15.3%) of the 13 ballet dancers reported injury (one in the lower limb and the other in the lumbar) the last three months before the tests, while eleven (84.7%) ballet dancers reported no injury (Table 4).

Further, Table 5 shows the overall activity level (amount of training per week, number of rehearsals per week, number of performances per week/year, years of experience in the dance, leg dominance, and warm-up practices) of ballet dancers.

## Discussion

The purpose of this study was to investigate if young female ballet dancers could have inter-limbs asymmetries. For this reason, we used the hop tests and YBT which are tests that evaluate the lower limbs functional performance. No significant differences were seen between the DL and NDL in either hop tests (single, triple, crossover, and timed hop tests) or YBT three distances reached (ANT, PL, and PM). Also, the

**Table 2. Means ± standard deviations of hop-tests scores in dominant limb and non-dominant limb of young female ballet dancers.**

Variable	DL (M ± SD)	NDL (M ± SD)	P-value	Bilateral asymmetry (%)/ Symmetry Index ≥ 90%
Single Hop (m)	1.13 ± 0.25	1.09 ± 0.23	0.15	96.41 ± 5.38
Triple Hop (m)	3.08 ± 0.74	3.01 ± 0.72	0.15	97.72 ± 5.89
Crossover Hop (m)	2.58 ± 0.41	2.55 ± 0.49	0.33	98.84 ± 4.04
Timed Hop (s)	3.93 ± 1.01	4.18 ± 1.15	0.21	106.31 ± 14.25

M: Mean; m: meters; DL: Dominant limb; NDL: Non-dominant limb; S: Seconds; SD: Standard deviations.

**Table 3. Means ± standard deviations of Y-balance test scores in dominant limb and non-dominant limb of young female ballet dancers.**

Variable	DL (M ± SD)	NDL (M ± SD)	P-value	Bilateral asymmetry (%)/ Symmetry Index ≥ 90%
Composite score (%)	72.47 ± 9.13	71.74 ± 7.68	0.54	90.99 ± 5.21
Ant (m)	0.64 ± 0.05	0.66 ± 0.09	0.49	103.12 ± 3.44
PM (m)	0.86 ± 0.10	0.83 ± 0.11	0.41	92.52 ± 5.32
PL (m)	0.88 ± 0.14	0.86 ± 0.11	0.57	97.73 ± 5.67

Ant: Anterior; M: Mean; m: meters; DL: Dominant limb; NDL: Non-dominant limb; PL: Posterolateral; PM: Posteromedial; SD: Standard deviations.

**Table 4. Musculoskeletal injury of young female ballet dancers.**

Variable	%
Previous Injury Lower limb (n=1) Lumbar (n=1)	15.3%
No Previous Injury	87.7%

n: number of dancers.

**Table 5. Means ± standard deviations of activity level and injury of young female ballet dancers.**

Variable	M ± SD
Years of experience in the dance	10.12 ± 3.94
Leg dominance	
Right	12
Left	1

M: Mean; SD: standard deviations.

results did not present significant differences between the DL and NDL in the composite score. However, it was seen in the composite score in YBT in both DL and the NDL a mean score lower than the normal score (94%) suggested in the literature<sup>24</sup>.

In ballet, the dancers use one leg as the gesture leg, while the other leg as the supporting leg. Besides, they perform tasks more complex requiring solicitation of the two sides of the body alternately on jump behaviors which is the major contributing factor to develop inter-limbs asymmetries<sup>25,26</sup>. Therefore, the understanding of lower limb asymmetries in artistic modalities that demands a high performance is essential to identifying the functional and muscular imbalance, and consequently is a tool that can help to create strategies to prevent injuries, since larger asymmetry scores inter-limbs could induce decreased in physical

performance compromising the task technical efficiency, and thus can increase the risk of musculoskeletal injuries<sup>27,28</sup>.

Asymmetries are defined as unevenness or mechanical imbalance in corresponding body parts (e.g., contralateral upper or lower limbs)<sup>29</sup>. Studies have demonstrated that both athletes and non-athletes who exhibit inter-limb asymmetries between >10%<sup>30</sup> and >15% are more susceptible to injury<sup>31,32</sup>; while asymmetries <10% have been proposed when athletes are returning to sport after an injury<sup>33</sup>. In this sense, the hop tests are included as tests that prove valid and reliable in quantifying inter-limbs asymmetries because it provides a quantifiable number that helps identify if they are more susceptible to injury<sup>34</sup>.

We showed that no significant differences were found in the comparison between the limbs (DL and NDL) in hop tests. Another research studied ten professional female ballet dancers in a unilateral experimental task, and there were no differences between the impulsion (for the jump task) and gesture leg<sup>25</sup>. Moreover, the single leg hop performance in female collegiate dancers, around 18 years also did not show significant differences between left and right lower limbs<sup>35</sup>. In addition, an interesting study measured the effect of core stabilization training on lower limb performance in ballet and modern dancers<sup>36</sup>. The results showed that for the vertical jump performance before the training program, the dancers did not have significant differences between the DL and NDL, while after the training program, the dancers had a significant increase in the DL and NDL<sup>36</sup>. On the other hand, another study investigated the influence of structural muscle factors on vertical jump in female ballet dancers (around 17 years)<sup>37</sup>. It demonstrated significant differences between the DL and NDL during the first trial on a vertical jump that was not linked to muscle mass<sup>37</sup>. However, for the last trial, no differences were observed between the two limb sides, although the DL height of the jump was linked to its muscle mass<sup>37</sup>. Thus, the findings in the present study agree with the literature, suggesting that female ballet dancers do not have inter-limbs asymmetries in tasks requiring muscle power such as jumps.

The findings of YBT also showed no significant differences between the limbs in any of the three directions reached (ANT, PL, and PM) and the composite score. In addition, previous studies demonstrated that the differences between the limbs in the three directions range between two and three centimeters, and differences bigger than 4 cm in the anterior<sup>38,39</sup> and posterior directions<sup>9</sup> are associated with an increased risk of injury. In contrast, the dancers of the present study had a composite score of 72.47% in DL and 71.74% in NDL; statistically, less than 94% suggested by the literature, indicating more chance to have a lower limb extremity injury<sup>38</sup>.

The YBT is an excellent, quick, and inexpensive method to measure dynamic balance and requires neuromuscular characteristics, such as coordination, flexibility, strength range of movement, proprioception, and balance, activating different muscle groups in each reach direction<sup>39</sup>. A recent study used the YBT and athletic single leg stability to assess ballet dancers between 10 to 17 years, and the results did not identify significant differences between the limbs in the reached directions<sup>40</sup>. Similar results were found in female ballet dancers between 19 to 22 years old<sup>2,40</sup>. Furthermore, studies reported that female dancers from 18 to 24 years also did not demonstrate a significant difference between the limbs in all three (ANT, PL, and PM) reached directions in the modified star excursion balance test, also known as YBT<sup>35,36</sup>. Likewise, another study evaluated the YBT performance in female ballet dancers compared with female non-dancing athletes, aged from 22 to 23 years<sup>41</sup>. The authors observed that the ballet dancers had a value of 71.5% in the ANT direction, 113.5% in the PM direction, and 112.8% in the PL direction, whereas the non-dancer athletes had in all direction values lower (61.3% in the ANT direction, 97% in PM direction and 94.1% in PL direction) than ballet dancers<sup>41</sup>. On the contrary, another study analyzing the YBT in female dancers around 17 years old, showed that the dancers presented asymmetry between the limbs in all directions<sup>42</sup>.

Related to the composite score, previous reports showed that female ballet dancers at a mean age of 20 years have composite score values of around 90.8%<sup>43,44</sup>. Also, full-time preprofessional ballet dancers at a median age of 15 years obtained a composite score of 85.3% in the right and 85.4% in the left limbs<sup>45</sup>. The same study group also demonstrated that male and female ballet dancers at a mean age of 17.9 years had a similar composite score to the previous study (right limb 85.4%, and left limb 87.5%)<sup>9</sup>. Another research group found similar results in dancers aged 19 years old<sup>1</sup>. However, studies showed a composite score higher than 94% in ballet dancers from 18 to 22 years<sup>41</sup>. Therefore, our results are consistent with the literature, suggesting that in all reached directions (ANT, PM, and PL) the female ballet dancers do not present inter-limbs asymmetry, although presenting a composite score lower than the literature indicating a deficit in dynamic balance. Specifically, regarding the composite score found in our study that is lower than the previous studies mentioned above, we hypothesized that could be due to the age of ballet dancers once the neuromusculoskeletal system is not fully matured.

The major strengths of this study are (1) the use of two screening tools that are easy to administer and could easily be incorporated at any activity level and sport; (2) the target population chosen for the study, once there are few studies with young female ballet dancers with the age selected in the present study using the YBT and mainly four horizontal hop tests to evaluate the muscle power and dynamic

balance, thus the study becoming very relevant by the sport specificity and age of the sample. Furthermore, another important point was the analysis of four hop tests providing new very interesting information about the use of these tests in ballet dancers. Limitations of this study must also be noted.

## Study limitations

Regarding the study limitation, although the sample size of the current investigation agrees with similar studies<sup>1,36</sup>, the sample size based on convenience represents a limitation; so, future studies investigating muscle power and dynamic balance in ballet should use a large sample size to increase the external validity of research with ballet dancers.

## Conclusion

In summary, these findings provide important take-home messages. Young female ballet dancers do not have asymmetry inter-limbs in both functional tests used and this may be due that the specific training of dance that stimulates the functional symmetric in jump tasks. However, they have a deficit in dynamic balance demonstrated by the YBT composite score, which might increase the risk of lower limb musculoskeletal injury. Considering that dynamic balance is affected by maturation and growth, this result can be explained by the dancers' age. However, further studies are needed to better understand the ballet dancers' functional performance of lower limbs. These results will also encourage and help multidisciplinary dance teams monitor injuries and can be used as a tool to implement strategies or rehab protocols that aid in the prevention of injuries in ballet dancers.

## Ethical approval

The work included in this manuscript was approved by the Ethical Committee at the University of Caxias do Sul.

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## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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# Rehabilitation through high-intensity exercise in early stages of stroke: Systematic review and meta-analysis

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## Summary

**Introduction:** High intensity training (HIT) has been shown to be safe and feasible, and to report many health related benefits to stroke patients. The objective of this review was to examine the effects of high intensity exercise on functional recovery and health related quality of life in the acute and subacute phases of stroke.

**Material and method:** Six databases were searched up to october 2023, looking for studies that compared the effect of HIT to other exercise interventions in the first six months after having a stroke.

**Results:** Seven papers were identified 163 patients were studied with a mean age of 65 years. Statistically significant differences were found for the variables of quality of life and health (average standardized mean difference [SMD] 1,07, with a 95% Confidence Interval [95%CI] of 0,94-1,33;  $p < 0,001$ ), and balance (SMD 0,86, 95%CI 0,41-1,30;  $p = 0,0002$ ); while for the variable mental health (SMD 0,05, 95%CI -0,33-0,44;  $p = 0,79$ ) and cardiorespiratory fitness (SMD 0,56, 95%CI -0,01-1,14;  $p = 0,055$ ) the results of the meta-analysis were not significant.

**Conclusions:** These results suggest that the implementation of HIT protocol has positive results on quality of life and health of stroke patients, and is safe during the acute and subacute stages of stroke.

## Key words:

Physical Condition. Therapeutic exercise. Quality of life. Health.

## Rehabilitación mediante ejercicio de alta intensidad en las fases tempranas del ictus: revisión sistemática y metaanálisis

### Resumen

**Introducción:** El ejercicio de alta intensidad (HIT) ha demostrado ser un modelo seguro y factible que ofrece beneficios en la salud de los pacientes con ictus. El objetivo de este metaanálisis fue examinar los efectos del ejercicio de alta intensidad sobre la recuperación funcional y la calidad de vida relacionada con la salud en las fases aguda y subaguda del ictus.

**Material y método:** Se realizó una búsqueda en seis bases de datos de hasta octubre de 2023 de ensayos clínicos que investigaron los efectos de HIT comparado con otras intervenciones de ejercicio en los primeros seis meses tras haber sufrido un accidente cerebrovascular.

**Resultados:** Se identificaron siete artículos en los que se estudió a 163 pacientes con una media de edad de 65 años. Se hallaron diferencias estadísticamente significativas para las variables de calidad de vida y salud (diferencia de medias estandarizadas [DME] promedio 1,07, con un intervalo de confianza del 95% [IC95%] de 0,94-1,33;  $p < 0,001$ ), y para el equilibrio (DME 0,86, IC95% 0,41-1,30;  $p = 0,0002$ ); mientras que para la variable salud mental (DME 0,05, IC95% -0,33-0,44;  $p = 0,79$ ) y capacidad cardiorrespiratoria (DME 0,56, IC95% -0,01-1,14;  $p = 0,055$ ) los resultados del metaanálisis fueron no significativos.

**Conclusiones:** Estos resultados sugieren que la implementación de un protocolo HIT es beneficioso para la mejora de la calidad de vida y la salud, así como mostrarse como una estrategia segura en pacientes en fases aguda y subaguda del ictus.

## Palabras clave:

Condición física. Ejercicio terapéutico. Calidad de vida. Salud.

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## Introduction

Progressive and significant ageing has been observed in western populations over recent decades. This has led to an increased incidence of age-related disorders, with strokes being the third most relevant pathology within that group in 2019<sup>1</sup>. Over 12 million new cases of stroke were recorded worldwide in that same year, as well as seven million deaths<sup>2</sup>. Both in Spain and throughout Europe, stroke is the second most widespread cause of dementia, behind Alzheimer's Disease, and the most widespread cause of disability<sup>3</sup>.

The main consequences in patients who have suffered a stroke are reduced motor control and changes in sensitivity<sup>4</sup>. Furthermore, their cardiorespiratory capacity is reduced by 50%<sup>5</sup>, which leads to greater physical inactivity<sup>6</sup> and therefore increased risk of a recurrent stroke<sup>7</sup>.

High-intensity exercise includes any type of exercise that achieves at least 70% of the heart rate reserve (HR reserve) or maximal oxygen uptake (VO<sub>2</sub>max), 75% of the maximum heart rate (HRmax) or a score of 14 on the Borg perceived exertion scale (RPE)<sup>8</sup>. It can be applied continuously or in intervals, through short high exertion bursts alternated with periods of low activity<sup>9</sup>.

At present, rehabilitation programmes for stroke patients place limited emphasis on the recovery of aerobic capacity<sup>10</sup>. However, owing to the benefits and safety reported by HIT protocols in healthy individuals and patients with other chronic diseases<sup>11,12</sup>, the inclusion of this type of exercise has been proposed with a view to reducing morbidity in stroke patients<sup>10</sup>. Moreover, there is also evidence to show that its use would be safe and beneficial for the cardiopulmonary health of these patients<sup>13-15</sup>, although the best exercise protocol to use is still being discussed<sup>10,16</sup>.

It has been shown that functional recovery potential is greater in the first months following the appearance of stroke<sup>4</sup>, but the majority of existing evidence studies the impact of high-intensity exercise in the rehabilitation from this disease while including all its stages or the chronic stage only. Hence, the goal of this review was to study the effect of HIT during the acute and sub-acute stages in stroke patients.

## Material and method

This systematic review with meta-analysis was carried out according to the PRISMA guide - "Preferred Reporting Items for Systematic Reviews and Meta-Analyses"<sup>17</sup>.

### Search Strategy

All those clinical trials that studied the effects of HIT in patients in the acute and sub-acute stages were included. The studies were considered for inclusion regardless of size, provided that they included a control group for the comparison of results.

The search for articles was conducted using the following databases: *Medline via PubMed*, *Cochrane Library (Willey)*, *Web of Science (Clarivate)*, *Embase via embase.com (Elsevier)*, *SportDiscus (EBSCOhost)* and

*BVSsalud (Literatura Latino Americana e do Caribe em Ciências da Saúde-LILACs)*, up to October 2023. Controlled vocabulary was used (MeSH terms), based on keywords and their synonyms, to refine the search. The references in articles included in systematic reviews were checked in order to identify other potentially eligible studies. A combination of the following terms was used: "stroke", "ischemic stroke", "haemorrhagic stroke", "cerebrovascular accident", "cerebrovascular disorder", "intensity training", "intensity exercise", "aerobic intensity", "physical therapy", "high intensity training", "high intensity exercise", "aerobic interval training", "continuous moderate exercise".

This study was registered in PROSPERO *International Prospective Register of Systematic Reviews* (CRD42023432785). Study titles and summaries that could be relevant to this review were obtained. Two authors checked the criteria for inclusion of the studies that were found. Whenever discrepancies arose regarding this matter, a consensus was reached based on a joint agreement. The complete text of the articles was subsequently assessed by using the criteria for inclusion and exclusion.

### Selection of the Studies and Eligibility Criteria

The following criteria for inclusion were established: 1) clinical trials; 2) with described intervention that included high intensity based on ESC criteria; and 3) stroke in acute and sub-acute stages.

The following criteria for exclusion were chosen: 1) stroke in chronic stage; 2) measurement of intensity using another variable besides VO<sub>2</sub>, HR or RPE; and 3) interventions that did not include aerobic exercise, defined as any activity that uses large muscle groups, can be maintained continuously and is of a rhythmic nature<sup>18</sup>.

### Extraction of Data and Bias and Quality Risk Analysis

The following information was gathered from the original studies selected: authors, year of publications, characteristics of the patients (age and average time since the appearance of the CVA), characteristics of the intervention (duration and intensity of the sessions) and the measurements of result with their statistical significance (Table 1).

The quality of the studies was assessed using the PEDro<sup>19</sup> scale, as well as the level of evidence using the tool from the University of Oxford Centre for Evidence-Based Medicine (OCEBM)<sup>20</sup>.

### Statistical Analysis

Jamovi v2.3.21 was used to carry out this meta-analysis. In all the studies that presented continuous data variables, the standardised mean difference (SMD) between the pre- and post-intervention values was chosen with a confidence interval of 95% as measured result (Table 2). For the variable present in more than two studies, the random effects model with statistical approach was used. As for all the other variables, the fixed effects model was used for analysis when comparing between only two studies<sup>21</sup>.

Table 1. Comparison of studies.

Authors/ Year/Study Type	Sample	Experimental Intervention	Control	Objective	Conclusions	Measurement
Hornby <i>et al.</i> 2022  Secondary analysis	n=44 (HIT n=27 / conventional physiotherapy control n=17) Subjects with locomotive deficiencies of 1-6 months post CVA 18-75 years	Walking (steps, floor, treadmill) reaching 80% of HR res 40 sessions, over 10 weeks. 40 min of walking per session	Functional tasks at lower intensities (<40% of HR res)	To conduct an economic analysis by comparing the costs and efficacy of the HIT programme with conventional physical therapies in subjects with sub-acute CVA	The costs were higher with the HIT protocol, although the benefits obtained by the subjects (AVAC and SSS) favoured this group, which would justify its application	ICERs AVAC (Physical SF-36) SSS
Leddy <i>et al.</i> 2016  Secondary analysis	n= 33 (HIT n=21 / conventional intervention n=12)	Practice of continuous walking in multiple environments maintaining 70-80% of HRR/RPE of 15-17 (Borg Scale) Treadmill, floor and steps 40 sessions, 8-10 weeks 1 hour sessions (40 min of walking)	Standard physiotherapy	To assess changes in the performance of aerobic exercise in patients with sub-acute CVA after high-intensity training when compared with conventional therapy	Significant improvements in VO <sub>2</sub> submax after the experimental training, with lower reductions, insignificant, in the VO <sub>2</sub> peak and VO <sub>2</sub> max, in favour of the intervention group Substantial gains in metabolic and locomotive functions in favour of the HIT group	Pulse oximeter 6MWT Portable indirect calorimeter
Sandberg <i>et al.</i> 2016  Randomised controlled trial	n= 56 (HIIT n=29 / control n=27) Median of 20 days post CVA Average age 70 years (53-87) Sessions in hospital (not admitted)	60 min of aerobic exercise 2/week, over 12 weeks Cycle ergometer Intervals: to reach ≥75% VO <sub>2</sub> max / 80% HR max 14-15 Borg Scale	No kind of rehabilitation. General advice on trying to regain pre-CVA capabilities Low intensity: walking/ stretching	To examine the effects of intense aerobic activity 2/ week over 12 weeks on physical function and quality of life in subjects with sub-acute CVA	Improvement in aerobic capacity and the distance travelled in favour of the intervention group Improvement in the self-perceived measurements (EQ-5D and SIS) in favour of the intervention group	GCTT-TT 6MWT MWS10m TUG SLS EQ-5D SIS HR
Mahtani <i>et al.</i> 2017  Secondary analysis	n= 36 (HIT n=23 / control n=13) 1-6 months post CVA 18-75 years Outpatient	40 sessions, 60 min/ session over 10 weeks, 4-5 sessions/week 70-80% HR res or 15-17 Borg scale Continuous exercise Treadmill	Conventional physiotherapy interventions 40 sessions over 10 weeks	To assess the effect of 10 weeks of high-intensity walking training compared with conventional interventions on gait kinematics in individuals with sub-acute CVA	Significant improvement in speed, symmetry and kinematics on the sagittal plane in favour of the intervention group Associated increase in compensatory conduct	Speed, cadence, stride length, spatial and temporal symmetry ROM in the joints Motion capture system with 8 cameras and 32 reflective markers
Wijkman <i>et al.</i> 2017.  Secondary analysis	n= 53 (HIIT n=29 / control n=27 / 3 subjects excluded during the process) Average age 70 years (53-87) Median of 22 days post CVA Sessions in the hospital (not admitted)	60 min sessions, 2/week, over 12 weeks HIIT: 14-15 Borg scale / 75% VO <sub>2</sub> max / 80% HR max Cycle ergometer	General advice on physical activity, no specific programme	To determine whether the exaggerated increase in blood pressure from exercise in subjects with CVA is modulated by aerobic activity	The subjects in the intervention group reach higher working levels, and their aerobic and functional capacity is benefited when compared with the control group Systolic BP remains unchanged after 12 weeks of programme	HR BP WR

(continues)

**Table 1. Comparison of studies (continued).**

Authors/ Year/Study Type	Sample	Experimental Intervention	Control	Objective	Conclusions	Measurement
Hornby <i>et al.</i> 2016  Randomised controlled trial	n=32 (HIT n=15 / control n=17) 1-6 months post CVA (average of 101 days) Outpatient	40 sessions, 60 min/ session over 10 weeks, 4-5 sessions/week 70-80% de HR res / Borg scale ≥14 Continuous exercise Initially treadmill. Later treadmill / floor / steps	Conventional physiotherapy, 40 sessions over 10 weeks Walking on treadmill or floor 30-40% HR res	To examine the effectiveness of walking-based high-intensity training on the ability to walk and other functional areas in subjects 1-6 months post CVA, compared with conventional therapy	Greater improvement in ability to walk and participation for HIT Significant differences in SSS and 6MWT for HIT Differences in spatial-temporal symmetry Balance in bipedalism and STS present similar results between groups	6MWT SSS STS
Krawczyk <i>et al.</i> 2019  Randomised controlled trial	n= 71 (HIIT n=40 / control n= 31) 1-21 days post CVA	Conventional care, HIIT protocol 3x3 min + 2 min of active recovery 5 sessions/week, over 12 weeks 77-93% HRmax / 14-16 Borg scale / TT Own choice method To encourage comple- tion, a static bicycle was provided if necessary	Motivational talk on changes to life habits, suggestion of different types of aerobic exercise, measurement (secondary prevention), monitoring of activity	To know whether HIIT training is effective and safe for patients with lacunar CVA	HIIT is safe and effective for patients with lacunar CVA The patients can engage in this activity early in their own home when they choose the type of exercise In 3 months, there were no effects on cardiorespiratory capacity The increase in physical activity did not lead to improvement in GCT-TT power production HIIT did not significantly improve overall wellbeing (depression, chronic stress, fatigue, cognition and quality of life) or cardiovascular function (blood pressure and endothelial function)	CRF with GCT-TT MFI-20 MDI WHO-5 MoCA PAS2 Venous blood biomarkers Blood pressure monitor (EndoPAT 2000) Body composition monitor (OMRON IMC) Accelerometer (AX3) Algometer

n: number of subjects; CVA: cerebrovascular accident; HIT: high-intensity training; HIIT: high-intensity interval training; HR: heart rate; HR max: maximal heart rate; HR res: heart rate reserve; BP: blood pressure; VO2 max: maximal oxygen uptake; VO2 submax: submaximal oxygen uptake; AVAC: years of life adjusted by quality of life; SSS: self-selected speed; ICERs: incremental cost-effectiveness ratios; Physical SF-36: health questionnaire SF-36; EQ-5D: health questionnaire EuroQol-5D; SIS: stroke impact scale; RPE: rate of perceived exertion; h: hours; min: minutes; ROM: range of movement; STS: sit-to-stand test; CRF: cardiorespiratory function; 6MWT: 6-minute walk test; GCT: cycle ergometer stress test; TT: talking test; MWS10m: maximum walking speed 10 m; WR: work rate; TUG: getting up and walking test; SLS: single leg stance test; WHO-5: general wellbeing test WHO-5; MFI-20: multidimensional fatigue inventory; MDI: major depression inventory; MoCA: Montreal cognitive assessment; PAS2: physical activity scale version 2.1.

Secondary studies on the same trial are included in this meta-analysis in such a way that they cannot be analysed despite the existence of comparable variables between them, thereby limiting the scope of this work. This is a hindrance to analysis because, having taken them into consideration would have magnified the effect given that they are variables measured in the same patients.

## Results

### Systematic Review

As can be seen in the PRISMA flowchart (Figure 1), 2,052 studies were identified and seven articles were finally included in the review.

### Characteristics of the Studies Included

Of the seven articles, three of them are randomised controlled trials (RCT)<sup>22-24</sup> and the remaining four are secondary analyses of those trials<sup>25-28</sup>. Hornby *et al.* 2022<sup>28</sup>, Leddy *et al.*<sup>26</sup> and Mahtani *et al.*<sup>27</sup> are secondary analyses of Hornby *et al.* 2016<sup>23</sup>; Wijkman *et al.*<sup>25</sup> is a secondary analysis of Sandberg *et al.*<sup>24</sup>; and Krawczyk *et al.*<sup>22</sup> is independent.

The studies were published between 2016 and 2022. They were carried out in different countries, including Denmark, Sweden and the United States.

### Characteristics of the Participants

The participants who formed part of the studies analysed were aged between 18 and 75. The participants were required to have a minimum



Table 2. Standardised measurements for the meta-analysis variables.

Variables	Article	Result to measure	N° of subjects	Intervention group			Control group		
				Ni	DMi	DE DMi	Nc	DMc	DE DMc
Cardiorespiratory capacity	Sandberg <i>et al.</i> 2016	6MWT (m)	56	29	105.1	76.2	27	35.9	93.2
	Hornby <i>et al.</i> 2016	6MWT (m)	32	15	116.0	101.4	17	29.0	77.5
	Krawczyk <i>et al.</i> 2019	GCT-TT (Watts)	63	31	7.7	31.7	32	6.7	32.7
Quality of life and health	Sandberg <i>et al.</i> 2016	EQ5D VAS	56	29	14.9	16.6	27	0.7	12.9
	Hornby <i>et al.</i> 2016	Physical SF36	32	15	9.0	4.9	17	2.0	5.3
Mental health	Krawczyk <i>et al.</i> 2019	WHO-5	63	31	4.0	15.3	32	5.0	12.4
	Hornby <i>et al.</i> 2022	Subdomain mental health	44	27	3.0	13.1	17	0.0	10.6
Balance	Sandberg <i>et al.</i> 2016	SLS	56	29	10.4	7.4	27	0.9	7.6
	Hornby <i>et al.</i> 2016	Berg scale	32	15	8.0	10.6	17	5.0	10.8

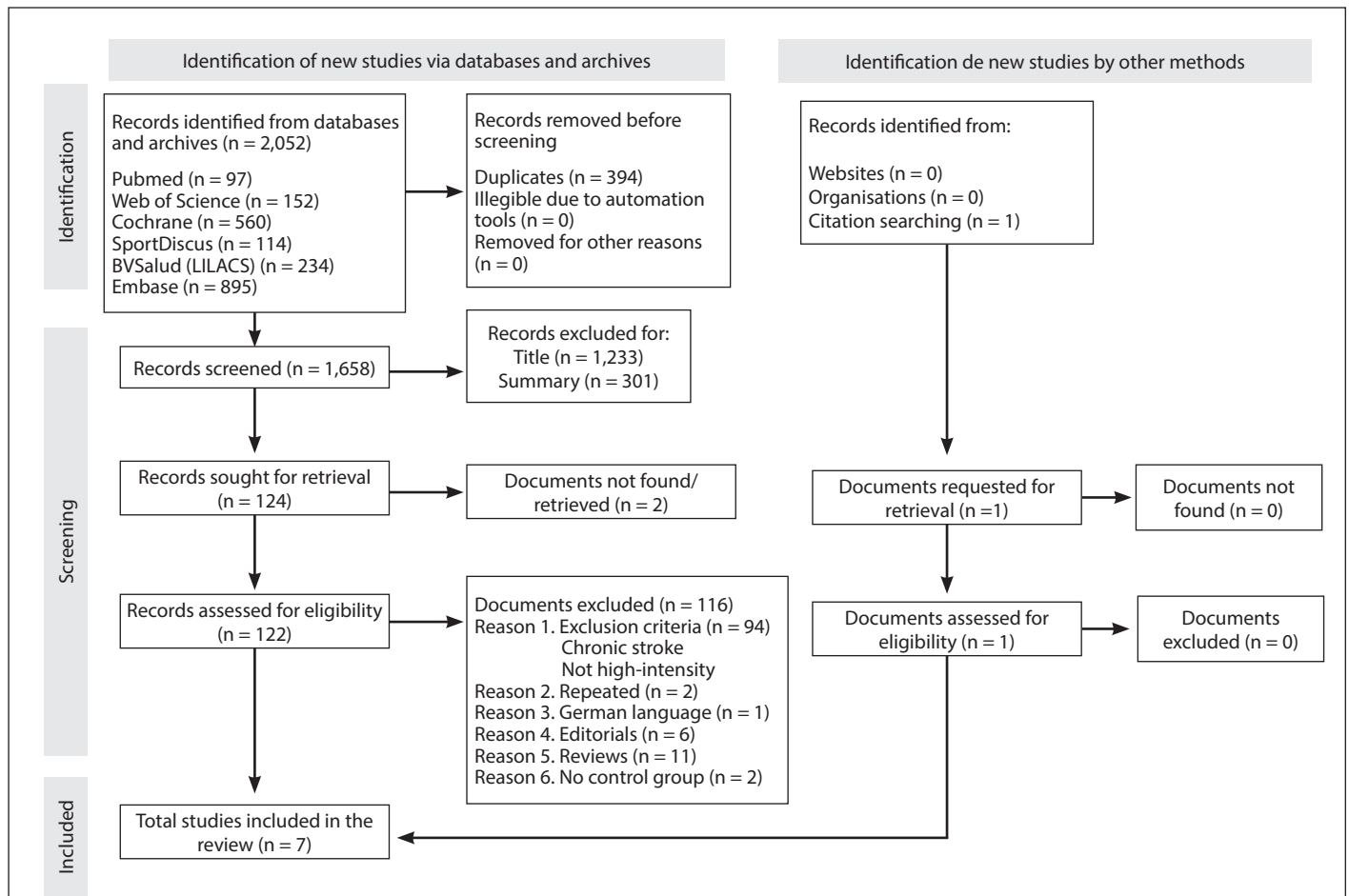
Variables	Article	Result to measure	Ni	Intervention group					
				PREi value	DE PREi	POSTi value	DE POSTi	DMi	DE DMi
Cardiorespiratory capacity	Sandberg <i>et al.</i> 2016	6MWT (m)	29	394.7	114.7	499.8	93.1	105.1	76.2
	Hornby <i>et al.</i> 2016	6MWT (m)	15	116.0	88.0	232.0	149.0	116.0	101.4
	Krawczyk <i>et al.</i> 2019	GCT-TT (Watts)	31	118.5	43.1	126.2	46.3	7.7	31.7
Quality of life and health	Sandberg <i>et al.</i> 2016	EQ5D VAS	29	72.3	22.3	87.2	9.1	14.9	16.6
	Hornby <i>et al.</i> 2016	Subdominio mental health	15	35.0	7.3	44.0	6.1	9.0	4.9
Mental health	Krawczyk <i>et al.</i> 2019	WHO-5	31	65.0	23.0	69.0	16.0	4.0	15.3
	Hornby <i>et al.</i> 2022	Physical SF36	27	51.0	19.0	54.0	18.0	3.0	13.1
Balance	Sandberg <i>et al.</i> 2016	SLS	29	9.6	10.3	20.0	10.6	10.4	7.4
	Hornby <i>et al.</i> 2016	Berg scale	15	32.0	16.0	40.0	11.0	8.0	10.6

Variables	Article	Result to measure	Nc	Control group					
				PREc value	DE PREc	POSTc value	DE POSTc	DMc	DE DMc
Cardiorespiratory capacity	Sandberg <i>et al.</i> 2016	6MWT (m)	27	384.3	131.9	420.2	131.6	35.9	93.2
	Hornby <i>et al.</i> 2016	6MWT (m)	17	131.0	108.0	160.0	111.0	29.0	77.5
	Krawczyk <i>et al.</i> 2019	GCT-TT (Watts)	32	119.5	44.0	126.2	47.9	6.7	32.7
Quality of life and health	Sandberg <i>et al.</i> 2016	EQ5D VAS	27	80.4	18.9	81.1	17.5	0.7	12.9
	Hornby <i>et al.</i> 2016	Physical SF36	17	36.0	7.5	38.0	7.4	2.0	5.3
Mental health	Krawczyk <i>et al.</i> 2019	WHO-5	32	64.0	18.0	69.0	17.0	5.0	12.4
	Hornby <i>et al.</i> 2022	Subdomain mental health	17	63.0	12.0	63.0	16.0	0.0	10.6
Balance	Sandberg <i>et al.</i> 2016	SLS	27	11.8	10.8	12.7	10.7	0.9	7.6
	Hornby <i>et al.</i> 2016	Berg scale	17	33.0	16.0	38.0	14.0	5.0	10.8

Ni: sample size in intervention group; DMi: standardised average difference in intervention group; DE DMi: standard deviation of the standardised average difference of the intervention group; Nc: sample size in control group; DMc: standardised average difference in control group; DE DMc: standard deviation of the standardised average difference of the control group; PREi value: pre-intervention average of the experimental group; DE PREi: standard deviation of the pre-intervention of the experimental group; PREc value: pre-intervention average of the control group; DE PREc: standard deviation of the pre-intervention of the control group; 6MWT: 6-minute walking test; GCT-TT: stress test on cycle ergometer with talking test; EQ5D VAS: questionnaire EuroQol-5D; Physical SF36: health questionnaire SF36; Subdomain mental health: health questionnaire SF-36, subdomain mental health; WHO-5: general wellbeing index WHO-5; SLS: single leg stance test; m: metres; Watts: watts.

Figure 1. PRISMA flowchart.



Page MJ, McKenzie JE, Bossuyt PM, Bouiron I, Hoffman TC, Mulrow CD, et al. The PRISMA 2020 statement: an update guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71. For more information <http://www.prisma-statement.org/>

level of stability and mobility that would enable the exercise (ability to walk five metres with minimal or moderate assistance), as well as the ability to understand written and spoken instructions, including the capacity to give informed consent<sup>22-28</sup>.

### Characteristics of the Interventions and Conditions of the Control Groups

Table 3 shows the information gathered on the intervention in the studies for this work, including RCTs and secondary analyses. An intervention model based on exercise at intervals was used in three studies<sup>22,24,25</sup>, while the other four used continuous exercise. Different instruments were used for the rehabilitation: a treadmill was used in four of the studies<sup>23,26-28</sup>, an ergometer in three<sup>22,24,25</sup> and steps or walking on flat ground was also used in another three<sup>23,26,27</sup>.

Different parameters were used to measure the intensity of the exercise, it being possible to use several of them in each study:

VO<sub>2</sub>max and HRmax was used in two studies<sup>24,25</sup>, HR reserve in five<sup>23,26-29</sup> and the RPE score in another five<sup>22,23,25-27</sup>.

The intervention was spread over between eight and twelve weeks. In terms of the session frequency, this was two days a week in two publications<sup>24,25</sup> and between four and five days a week in the others. Only one of the studies had a duration of less than 40 minutes<sup>22</sup>. Finally, six studies were carried out in an outpatient environment and only one in a hospital environment<sup>25</sup>.

A "(+12)" is added in brackets in certain sections. This corresponds to patients of the Holleran *et al.*<sup>29</sup> protocol, a preliminary study that was carried out to know whether it was possible to carry out the Hornby *et al.*<sup>23</sup> study and which therefore follows the same intervention but the patients of which were not added to the tables because there is no control group.

### Quality Assessment

The methodological quality of each study is represented in Table 4. It can be seen that five of the publications included present a good quality<sup>22-25,28</sup> given that they obtained a rating of between 6 and 8 points out of 10. Of the remaining two, one obtained a score of 5<sup>27</sup> and

**Table 3. Comparison of interventions.**

Intervention	Subtype	RCTs and secondary analyses	Participants
Type	HIT	4	86(+12)
	HIIT	3	98
Method	Treadmill	4	86(+12)
	Cycle ergometer	3	98
	Floor/steps	3	63(+12)
Intensity measurement	VO <sub>2</sub> max	2	58
	RHmax	2	85
	HR res	5	99(+12)
	RPE (Borg)	5	128(+12)
Time	≤40 min	1	40
	≥40 min	6	144(+12)
Frequency	≤4 days/week	2	58
	4-5 days/week	5	126(+12)
Programme duration	8-12 weeks	7	184(+12)
Environment	Hospital	1	29
	Outpatient	6	155(+12)

HIT: high-intensity training; HIIT: high-intensity interval training; VO<sub>2</sub>max: maximal oxygen uptake; HRmax: maximal heart rate; HR res: heart rate reserve; RPE (Borg): rate of perceived exertion (Borg scale); "(+12)" corresponds to the subjects in the Holleran *et al.* protocol.

the other obtained a score of 4<sup>26</sup>, this being considered an acceptable level of evidence.

The selection criteria were specified in all the studies and they began with groups of patients who presented similar baseline characteristics.

Except in one<sup>26</sup>, all the subjects were given a random and concealed allocation. The assessors were blinded in some<sup>22-24,26</sup>. Except in two<sup>26,27</sup>, results were presented from all the participants to whom the intervention was allocated or who were allocated to the control group. When this was not possible, the data were analysed on an "intention-to-treat" basis. Finally, in none of the studies were the measurements of the results obtained in more than 85% of the patients. This was because they did not reach that percentage or because no explicit mention was made of it.

On the other hand, all the trials met the requirements of a randomised clinical trial and were classified as level 1b.

### Meta-analysis

- *Cardiorespiratory capacity.* A total of three studies reported pre- and post-intervention data for cardiorespiratory capacity. The SMDs varied between 0.03 and 0.95, with all the estimates being positive. The average estimated SMD based on the random effects model was 0.56, with a confidence interval of 95% (CI95%) of between -0.01 and 1.14. The average result presented no significant differences ( $z = 1.92$ ,  $p = 0.055$ ). The Q test for heterogeneity was not significant. However an average heterogeneity in the results was observed ( $Q(2) = 5.83$ ,  $p = 0.05$ ,  $\tau^2 = 0.16$ ,  $I^2 = 64.8\%$ ). The

prediction interval of 95% given for the results varies between -0.42 and 1.54 (Figure 2).

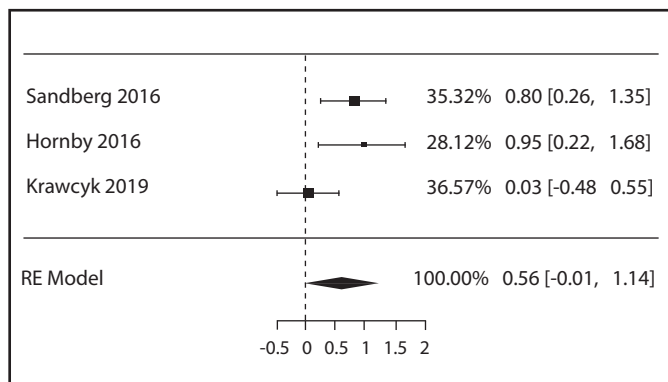
- *Quality of life and health.* A total of two studies reported pre- and post-intervention data for quality of life and health. The SMDs varied between 0.94 and 1.33, with all the estimates being positive. The average estimated SMD based on the fixed effects model was 1.07, with a CI95% of between 0.62 and 1.52. The average result presented no significant differences ( $z = 4.69$ ,  $p < 0.0001$ ). According to the Q test, there was no significant amount of heterogeneity in the true results ( $Q(1) = 0.67$ ,  $p = 0.41$ ,  $I^2 = 0.00\%$ ) (Figure 3).
- *Mental health.* A total of two studies reported pre- and post-intervention data for mental health. The SMDs varied between -0.07 and 0.24, with half of the estimates being negative (50%). The average estimated SMD based on the fixed effects model was 0.05, with a CI95% of between -0.33 and 0.44. The average result presented no significant differences ( $z = 0.27$ ,  $p = 0.79$ ). According to the Q test, there was no significant amount of heterogeneity in the true results ( $Q(1) = 0.61$ ,  $p = 0.44$ ,  $I^2 = 0.00\%$ ) (Figure 4).
- *Balance.* A total of two studies reported pre- and post-intervention data for balance. The SMDs varied between 0.27 and 1.25, with all the estimates being positive. The average estimated SMD based on the fixed effects model was 0.86, with a CI95% of between 0.41 and 1.3. The average result presented no significant differences ( $z = 3.79$ ,  $p = 0.0002$ ). According to the Q test, the true results are apparently heterogeneous ( $Q(1) = 4.49$ ,  $p = 0.03$ ,  $I^2 = 77.75\%$ ) (Figure 5).

**Table 4. PEDro scale (Physiotherapy Evidence Database).**

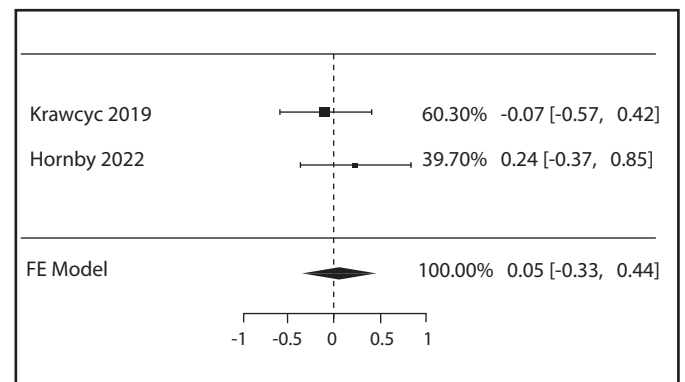
Studies	1	2	3	4	5	6	7	8	9	10	11	Total PEDro scale
Hornby <i>et al.</i> 2022	X	X	X	X					X	X	X	6/10
Leddy <i>et al.</i> 2016	X			X			X			X	X	4/10
Krawczyk <i>et al.</i> 2019	X	X	X	X			X		X	X	X	7/10
Sandberg <i>et al.</i> 2016	X	X	X	X			X		X	X	X	7/10
Mahtani <i>et al.</i> 2017	X	X	X	X						X	X	5/10
Wijkman <i>et al.</i> 2018	X	X	X	X					X	X	X	6/10
Hornby <i>et al.</i> 2016	X	X	X	X			X		X	X	X	7/10

1 selection criteria; 2 random allocation; 3 concealed allocation; 4 baseline comparison of the groups; 5 blinded subjects; 6 blinded therapists; 7 blinded assessors; 8 key outcome measurements in >85% subjects; 9 "intention to treat" monitoring and analysis; 10 comparison between groups; 11 point estimates and variability. An "X" indicates a "yes" score and its absence a "no".

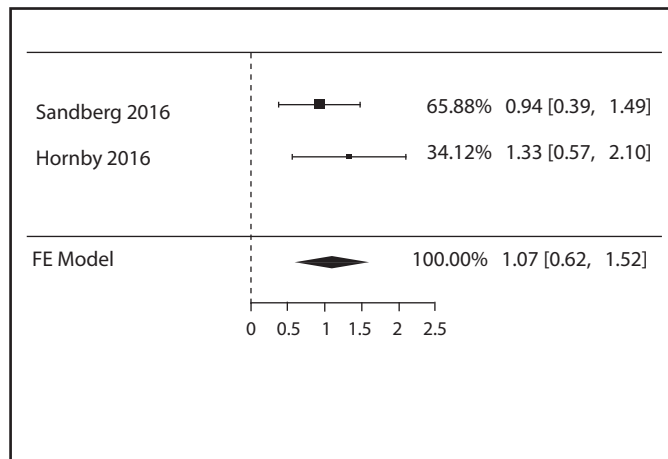
**Figure 2. Forest plot for cardiorespiratory capacity.**



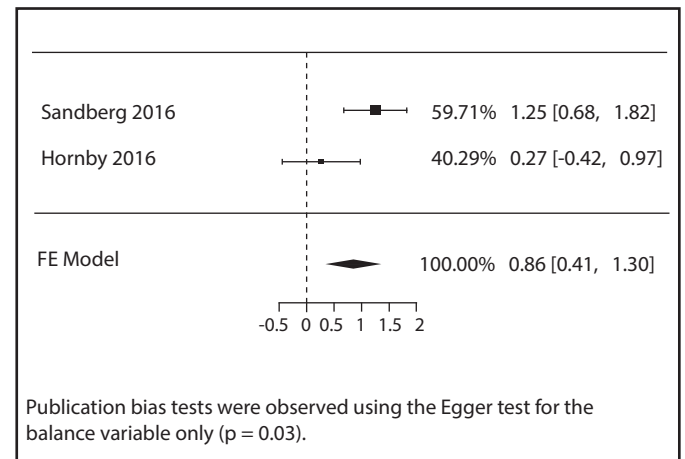
**Figure 4. Forest plot for mental health.**



**Figure 3. Forest plot for quality of life and health.**



**Figure 5. Forest plot for balance.**



## Adverse Events

The adverse episodes found were analysed in depth, with no significant differences observed between groups. The groups were similar in terms of the number of events. The events included fractures, wounds, falls without damage, joint and muscle pain, as well as cardiorespiratory events (high blood pressure, angina and bronchoaspiration), which required hospital admission<sup>23,26</sup>. Two articles do not record this information<sup>27,28</sup>, one article presented no adverse events related to the intervention<sup>22</sup> and another two presented no serious adverse events throughout the full duration of the trial<sup>24,25</sup>.

## Discussion

Based on the data presented in this meta-analysis, we suggest that a protocol of high-intensity exercise has beneficial effects on quality of life and health, as well as balance, but not significant in terms of mental health and cardiorespiratory capacity in the early stages of patients with stroke when compared with conventional interventions. It was possible to include four of the seven articles in the quantitative analysis section, with good evidence quality.

### Cardiorespiratory Capacity and Haemodynamic Variables

We found positive results, albeit insignificant for cardiorespiratory capacity in the intervention group. In a previous meta-analysis, in which chronic patients were included, significant beneficial effects were reported from HIT on cardiorespiratory capacity<sup>13</sup>. This could be because the patients at this stage of recovery usually begin with reduced cardiovascular capacity, meaning they present a greater margin of improvement. However, in the early stages of stroke, the potential for capacity recovery to pre-stroke values is greater given that the patients have not been suffering the consequences of their disease for as long and, therefore, have not deteriorated due to inactivity over such a long time. Furthermore, greater aerobic capacity has been linked to a reduction in cardiovascular and recurrent stroke risk factors, partly due to the decrease it causes in blood pressure and serum cholesterol levels<sup>30</sup>. Our analysis did not study haemodynamic levels, although the original articles by Krawczyk *et al.*<sup>22</sup> and Wijkman *et al.*<sup>25</sup> did observe a significant improvement in the heart rate reduction, in favour of the intervention.

### Quality of Life and Health

Previous studies have confirmed that aerobic exercise not only improves cardiorespiratory capacity and disability but also mobility and balance at any stage of recovery with a strong level of evidence<sup>7,16</sup>, which has a direct impact on quality of life. In this regard, we were able to confirm that HIT significantly improves quality of life and health in the intervention group when compared with the control group. No-

netheless, this does not correspond to the results described previously by other authors<sup>31</sup>. This discrepancy could be explained by the lower intensity to which the intervention group in said study was subjected (60-80% HR reserve).

### Mental Health and Cognition

In terms of mental health, this study did not observe that the HIT model offers any greater benefits than classic rehabilitation protocols. In this regard, the impact had by aerobic exercise on existing depression and mental wellbeing is not conclusive<sup>16</sup>. This could be due to the limited number of patients recruited, meaning that the results produced may not be definitive.

### Balance

Our quantitative analysis coincides with the conclusions reached in the review by Saunders *et al.*<sup>16</sup>, in which it is established that aerobic exercise produces a greater improvement in balance when compared with conventional rehabilitation interventions at any stage of recovery with a strong level of evidence.

### Kinematics

The changes in kinematics were studied from different perspectives. Hence, Holleran *et al.*<sup>29</sup> reported a significant improvement in the speed, cadence and length of stride. This implies that high-intensity exercise may be a factor that improves the prognosis when recovering the capacity of an efficient gait, although the evidence to date is limited due to the number of studies found.

### Adverse Events

No serious adverse events were observed in any of the studies included. However, it should be stressed that they were only analysed in depth in two of the seven articles without showing a clear link to the intervention<sup>23,26</sup>. Others mention the lack of serious adverse events during the trial<sup>24,25</sup>; Krawczyk *et al.*<sup>22</sup> found no other kind of adverse event; and this is not mentioned in the last two<sup>27,28</sup>.

Other reviews strengthen the safety of HIT in patients with stroke at all stages of recovery, such as Luo *et al.*<sup>13</sup>, Anjos *et al.*<sup>15</sup>, and Fahey *et al.*<sup>32</sup>, in which no significant differences were found between the high-intensity exercise groups and the control groups, there being no increase in the rate of adverse events when compared with conventional rehabilitation.

The available evidence suggests that the model is safe and well tolerated. However, despite the safety of these protocols, Wijkman *et al.*<sup>25</sup> observed a significant elevation in systolic blood pressure in response to the exercise. For this reason, we consider it essential that this model of exercise be prescribed and supervised by trained professionals and carefully adapted to the individual needs of each subject, together with rigorous control of the physiological variables of each patient during the intervention.

## Strengths and Limitations

It should be taken into consideration that different terminology is used to define the intensity of exertion. In our case, it was decided to follow the indications of the European Society of Cardiology (ESC). For that reason, a number of studies were rejected under this criteria, mainly because the levels of intensity they proposed were lower than the established. On the other hand, the search was performed in major databases, so we therefore believe that we successfully grouped together the most relevant studies on the topic.

Due to the recent nature of this line of research (the earliest study was conducted in 2016), there is little literature available. This is a limitation and we should be cautious in the contributions presented here. Nonetheless, the analysis of methodological quality confirms that five trials obtained a good level of quality and an acceptable level of evidence in the remaining two.

## Conclusions

Our meta-analysis suggests that use of an HIT protocol is beneficial in improving quality of life and health, as well as showing itself to be a safe strategy in patients in acute and sub-acute stages of stroke.

## Conflict of Interest

The authors declare no conflict of interest whatsoever.

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# Early detection of increased blood pressure and its relation to the study of fingerprints among young football players in the city of Bogotá

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## Summary

Blood pressure as a hemodynamic variable is a useful and key diagnostic element for the detection of arterial hypertension (HTA), since through this variable it is possible to recognize optimal cardiovascular functioning in addition to quickly identifying the risk of suffering from this disease, which unfortunately is identified late, since in most cases the patients do not show symptoms. Determining predisposing factors to develop the disease is of great importance for public health and in this sense dermatoglyphics becomes an alternative that allows, through the recognition of genetic markers, the early identification of this pathology. Therefore, the objective of this work is to identify the relationship between fingerprint dermatoglyphics and increased blood pressure in athletes. Male university athletes between 18 and 26 years old were included for the study. Those who were divided into two groups, controls and cases, according to their blood pressure figure, the case definition corresponds to high blood pressure figures (120-129 and <80 mmHg). While the definition of control linked those participants who presented normal blood pressure values (<120 and <80 mmHg). A questionnaire was carried out in which the data of blood pressure, weight, height, family and personal history were recorded, additionally, the fingerprinting of the Cummins and Midlo (1942) protocol was carried out. As a result, it was found that in the group of football players with high blood pressure (TAA), a greater count of whorls in the left hand was identified  $1.54 \pm 1.50$  in relation to the normotensive group  $1.49 \pm 1.47$ . The appearance of whorls was found in the TAA group when they had a family history of cardiovascular disease with an OR 3.9 ( $P < 0.000$ ). Therefore, it is concluded that there are fingerprint dermatoglyphic patterns associated with the predisposition to increased blood pressure.

## Key words:

Dermatoglyphics. Arterial Pressure. Football.

## Detección temprana de aumento de presión arterial y su relación con la dermatoglifia dactilar en futbolistas jóvenes de la ciudad de Bogotá

### Resumen

La presión arterial como variable hemodinámica, se constituye en un elemento diagnóstico útil y clave para la detección de la hipertensión arterial (HTA), ya que mediante esta variable se logra reconocer el funcionamiento cardiovascular óptimo. Determinar factores predisponentes a desarrollar la enfermedad es de gran importancia para la salud pública y en ese sentido la dermatoglifia se convierte en una alternativa que permite mediante el reconocimiento de marcadores genéticos la identificación precoz de esta patología. Por ello el objetivo de este trabajo es identificar la relación entre la dermatoglifia dactilar y el aumento de tensión arterial en futbolistas de Bogotá. Para el estudio se incluyeron deportistas hombres entre 18 a 26 años, quienes se dividieron en dos grupos, controles y casos, según su cifra de tensión arterial, la definición de caso corresponde a cifras tensionales altas (120-129 y <80 mmHg). Mientras que la definición de control vinculó aquellos participantes que presentaron cifras tensionales normales (<120 y <80 mmHg). Se realizó un cuestionario en el cual se registraron los datos de presión arterial, peso, talla, antecedentes familiares y personales, adicionalmente, se realizó la toma de huellas del protocolo de Cummins y Midlo (1942). Como resultados se encontró que el grupo de futbolistas con tensión arterial alta (TAA) se identificó un mayor recuento de verticilos en mano izquierda  $1,54 \pm 1,50$  con relación al grupo normotensos  $1,49 \pm 1,47$ . Se encontró en el grupo de TAA la aparición de verticilos cuando se tienen antecedentes familiares cardiovasculares con un OR 3,9 ( $p < 0,000$ ). Por lo tanto, se concluye que existen patrones dermatoglíficos dactilares asociados a la predisposición del aumento de la tensión arterial.

## Palabras clave:

Dermatoglifia. Presión arterial. Fútbol.

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## Introduction

Dermatoglyphics has been considered a useful tool based on the use and identification of fingerprint patterns. These uses initially focussed on analysis and detection of aspects related to the subjects' physical condition and provided an understanding of processes associated with embryonic development and genetic implications that might affect health conditions in the future. It is important to note that the configuration of these patterns is unique and it lasts throughout each human being's lifetime, explaining why each dermatoglyphic pattern provides information related to the subject's embryonic development, health and development conditions, demonstrating a high capacity to identify chronic illnesses such as diabetes, cancer and hypertension<sup>1-3</sup>.

Regarding hypertension, this pathological entity is clearly a multifactorial disease which is largely silent. Having said that, referencing the systematic review by Wijerathne *et al.*<sup>4</sup>, hypertension is a pathology that has contributed to overloading public health resources due to the concomitant development of cardiovascular and cerebrovascular events, among others. In Colombia, the prevalence of arterial hypertension varies by the region of the country being analysed. Nevertheless, it is concerning that, according to García *et al.*<sup>5</sup>, 59.6% of the population has not had an assertive and early diagnosis.

In this respect, early recognition of the underlying factors is imperative for public health actions that seek to prevent the on-going risk<sup>6</sup>. Genetic inheritance through fingerprints appears in the mother's intrauterine environment during the third and sixth month of pregnancy<sup>6,7</sup>. These genetic markers contain information on the predisposition of individuals both at a physical (somatotype) and physiological level. The study of fingerprints is currently considered a valid, reliable test because they are unique and unchanging in each human being<sup>8-10</sup>.

Although this is true, studies such as Kulkarni *et al.*<sup>11</sup>, which involved 200 subjects randomly divided into case groups and control groups, managed to identify differences in the presentation of dermatoglyphic patterns where there are clear changes in the size of the whorls and the ulnar loops; these changes were also clear in the study by Tafazoli *et al.*<sup>12</sup>, which not only identified changes in the whorl size but also demonstrated an increase in their frequency among the hypertensive group.

Likewise, various studies that compared the dermatoglyphic patterns between the hypertensive and normotensive population found that subjects who suffered from AHT commonly present radial loops while normotensive persons mainly present ulnar loops. In turn, the ATD angle in hypertensive individuals tends to be greater than among normotensive subjects and whorls are the most frequent dermatoglyphic pattern among persons who suffer from arterial hypertension<sup>12-14</sup>.

Simultaneously, a great difference is seen in the number of lines and the ulnar loops between subjects with hypertension and the

healthy group. In addition, there is a statistically significant difference in the ulnar loop pattern in the fifth finger of the left hand, and the fourth and fifth on the right hand; this pattern frequently appeared in the hypertensive group<sup>9</sup>.

Other findings have managed to demonstrate the possible relationship between certain fingerprint patterns and the presence of arterial hypertension (AHT), by means of quantitative analysis of the frequency and the type of designs on an individual, to discriminate persons who might have inherited AHT. Various studies focus on the analysis of dermal ridges on the palms and soles. However, this study will be based on the distal phalanges of the hands which are closely related to potential biophysical capacities, and a predisposition to develop certain illnesses<sup>13-15</sup>.

Some physiological approaches that help to explain the relationship between these dermatoglyphic changes and the presence of arterial hypertension would be associated with biological processes derived from embryonic instability during pregnancy, plus impacts on nutrition and maternal stress. On the other hand, it is relevant that some studies have involved the genetic component in determining fingerprints and vascular endothelium although it is true that the genes responsible for developing the different layers of skin and blood vessels can be key to shaping dermatoglyphic patterns. Part of the research has identified the SMARCAD1 gene as one of the genes responsible for forming dermatoglyphics, although its role is not clear in the whole vascular endothelial context and so research is continuing in this respect. It certainly cannot be ignored that the shape of these fingerprint patterns and the genetic basis of a subject would be directly influenced by other factors during foetal development such as infections, consumption of psychoactive substances, among other elements alter the mother's uterine environment<sup>16,17</sup>.

According to the above, the aim of this research is to work from dermatoglyphics to identify the presence of digital traits which concur with previous research, making it possible to recognise the presence of arterial hypertension in young football players.

## Material and method

### Study design

Analytical study of cases and controls.

### Participants

The study included 86 football players aged between 18 and 26 years old who trained more than three times a week; the players must have belonged to the group for at least six months, and played in competitions for their category (second division professional football). The case definition was football players who had high blood pressure readings (120-129 and <80 mmHg), according to definitions from the *American Heart Association* regarding high blood pressure<sup>18</sup>. The control definition was any subjects with normal blood pressure readings



(<120 and <80 mmHg) according to definitions by the *American Heart Association* regarding normotensive subjects<sup>18</sup>. As exclusion criteria, the study did not consider participants presenting diagnoses of hypothyroidism, AHT, burns on their hands, congenital deformations on their hands, partial or total hand amputation.

**Data collection instruments**

A questionnaire was produced for continuous variables which recorded data for arterial pressure, weight, height and family and personal history (morbid, orthopaedic trauma, surgical, pharmacological, neonatal) in an open format for this purpose. It is important to clarify that family history was recorded to acknowledge any history of hypertension in their family. The oscillometric blood pressure was taken using a Ri-champion N digital blood pressure monitor (Ries-ter, Jungingen, Germany), with the participant seated and relaxed for around 5 minutes, their feet resting on the floor and their back against the backrest, their arm supported on a fixed surface. It was taken twice and the average of the two readings was used to record blood pressure for the individuals (desktop-table); the user was not allowed to tighten their muscles as this affects the real values. The measurements were taken on one day between 7:00 and 8:00 am. The height was measured using the Holtain® height rod (0-209 cm; accurate to 0.1 cm) and the Tanita® scales were used to measure the weight. Finally, fingerprints were taken using the Cummins and Midlo protocol<sup>19</sup>. They were taken from all 10 fingers of each subject on a biometric Futronic FS-50 fingerprint scanner reader, which considered the following variables: a) patterns from the fingers on each hand (arches, loops, whorls); b) total ridge count on the fingers (SQTL); c) design of the fingerprint types. Subsequently, they were reclassified taking into account the average of the Arch, Loop and Whorl figures, and the sum of the ridges. Using the data collected in dermatoglyphics, they were re-categorized into nominal Yes and No variables, and so all values above the average were re-classified into the Yes category and any below the average were put into the No category. This provided the corresponding odds ratios (OR).

The information was recorded in an Excel document, alongside the data from each user, which were coded due to information confidentiality. Subsequently, the data were divided into cases and controls, finding 35 cases and 51 controls.

**Results analysis**

Version 25 of the IBM SPSS statistics programme was used. The averages and the standard deviation were described for the quantitative dermatoglyphic data from cases and controls. Subsequently, a Chi Squared test was applied to determine if there were statistically significant differences for the dermatoglyphic variable. The exposure prevalence (population, cases and controls) and odds ratio (OR) were determined.

**Ethics Committee**

The research took place according to the Declaration of Helsinki<sup>20</sup>, Resolution No. 008430 of 1993 from the Colombian Ministry of Health.

Additionally, the research project was approved by the Committee of Ethics, Bioethics and Scientific Integrity for research from the Santo Tomás University on 27 June 2019 in document no. 10.

**Results**

A total of 86 people took part in the research, with an average age of 19 ± 2.82 years old. The average height for the sample was 1.74 ± 0.07 metres and the average weight was 66.5 ± 9.97 kg. All the participants did sport at least 3 times a week. After dividing the group according to their blood pressure readings, the high blood pressure (HBP) group comprised 35 persons and the normotensive group comprised 51 persons (Table 1).

It was found that radial loops and arches are the variables least presented by both study groups (Table 1). The average number of arches in both hands is slightly higher in the HBP group, although there is no significant difference. Regarding the ulnar loops on the right hand, they have a lower average in the group of football players with high blood pressure compared to the normotensive group.

On the other hand, no significant difference was found in the radial loops on both hands and ulnar loops on the left hand. A slightly greater whorl average was found on the right hand in the HBP group and a lower average in the SQTL of the right hand in football players with HBP. Finally, no significant difference was found in the LH and D10 SQTL variables.

Among the data collected in the population, family history was determined as a parameter to recognise genetic predisposition to high blood pressure finding that there was no significant statistical

**Table 1. Descriptive statistics for the dermatoglyphic characterisation of the sample by group.**

Variables	Players with HBP		Normotensive players	
	Average	S.D.	Average	S.D.
RH arches	0.17	±0.45	0.10	±0.36
LH arches	0.29	±0.83	0.18	±0.48
RH radial loops	0.20	±0.41	0.20	±0.45
LH radial loops	0.14	±0.36	0.27	±0.49
RH ulnar loops	2.60	±1.46	2.94	±1.36
LH ulnar loops	2.97	±1.40	3.10	±1.27
RH whorls	2.07	±1.63	1.75	±1.43
LH whorls	1.54	±1.50	1.49	±1.47
RH SQTL	94.34	±40.02	94.98	±42.27
LH SQTL	90.86	±41.89	90.82	±43.89
Sum of SQTL	185.20	± 79.96	185.80	± 84.88
D10	13.11	±3.55	12.98	±3.13

HBP: high blood pressure; RH: right hand; LH: left hand; SQTL: sum of quantity of total lines; D10: delta index in the designs.

relationship between the normotensive and high blood pressure groups. However, by relating the background history with what was found in the fingerprints, Table 2 shows a relationship between history of hypertension and the presence of whorls on the left hand. Additionally, a relationship was found between the sum of total ridges and the sum of ridges on the left hand with family history of hypertension.

## Discussion

The aim of this study was to find patterns that made it possible to use the study of fingerprints to identify the increase in blood pressure among young football players in the city of Bogotá. The findings initially highlight a larger whorl count on the left hand and the right hand for the group which presents high blood pressure. These results concur with the study by Kulkarni *et al.*<sup>11</sup> which stated that hypertensive patients tend to present a higher frequency of whorl patterns which appear alongside a higher average ridge count than the controls<sup>15</sup>.

Likewise, in a study performed with 200 people who suffered from arterial hypertension and a group of 200 people with normal blood pressure, Ganesh *et al.*<sup>21,22</sup> stated that the sample of hypertensive persons showed a significant frequency in the number of whorls in all ten fingers, plus a decrease in ulnar loops and the ATD angle.

**Table 2. Odds ratio according to dermatoglyphic patterns, groups and family history of hypertension.**

<b>Whorls on left hand (WLH)</b>				
		<b>No</b>	<b>Yes</b>	<b>P value</b>
No		3.0	-3.0	
Yes	OR	-3.0	3.0	0.002
<b>Whorls on left hand with history of hypertension (WLHAHT)</b>				
		<b>No</b>	<b>Yes</b>	<b>P value</b>
No		3.9	-3.9	
Yes	OR	-3.9	3.9	0.000
<b>Designs on little finger with history of hypertension (DLHAHT)</b>				
		<b>No</b>	<b>Yes</b>	<b>P value</b>
No		2.6	-2.6	
Yes	OR	-2.6	2.6	0.008
<b>Sum of total ridges with history of hypertension (STLHAHT)</b>				
		<b>No</b>	<b>Yes</b>	<b>P value</b>
No		2.1	-2.1	
Yes	OR	-2.1	2.1	0.032
<b>Sum of ridges on left hand with history of hypertension (SLHAHT)</b>				
		<b>No</b>	<b>Yes</b>	<b>P value</b>
No		2.1	-2.1	
Yes	OR	-2.1	2.1	0.032

Own work.

It was also possible to identify a larger arch count on the left hand in the group with high blood pressure, similar to the result in a study carried out by Igbigbi *et al.*<sup>23</sup>, which assessed 99 persons aged between 25 and 66 years old. The study sample was divided into three groups (27 patients with type 2 diabetes, 21 patients with hypertension and 51 patients with diabetes and hypertension). This study looked for variability in the fingerprint and footprint patterns. The differences in the fingerprint patterns showed that the male diabetic patients did not have arches on their thumb, although hypertensive women did display arches.

In SQTl, the result was slightly higher in the high blood pressure group, as in the study by Tafazoli *et al.*<sup>12</sup>, which analysed the dermatoglyphics of the individuals who suffer from arterial hypertension and reported that in comparison with a normotensive group, the number of ridges is greater in the hypertensive population. It should be highlighted that the frequency of whorls and arches in all ten fingers is greater in comparison with a group of normotensive persons. In addition, the research performed by Arista *et al.*<sup>24</sup> concluded that the total ridge count is higher in the hypertensive population compared to normotensive subjects.

In the study by Nodari *et al.*<sup>9</sup>, including 268 adults, 134 individuals were diagnosed with hypertension finding a significant difference in all ten fingers. Additionally, it identified that fingerprint patterns such as ulnar loops on the fifth finger of the left hand and the fourth and fifth finger of the right hand are more frequent in individuals who suffer arterial hypertension.

In the same way, it was demonstrated that the fifth finger of the left hand, the fifth finger on the right hand and the fourth finger on the same hand contain an ulnar loop pattern that is more frequent in subjects in the hypertensive group, as opposed to results from this study, where despite having found a lower average of ulnar loops on the right hand and on the left hand, no statistically significant difference was found that would provide an indicator.

The article by Rudragouda *et al.*<sup>25</sup> which collected data from the fingerprints of a control group and a group with hypertension, identified that both the right hand and left hand of the hypertensive group presented more arches than the control group. In addition, the study group demonstrated a greater number of radial loops in both hands than in the control groups. However, more ulnar loops appeared in the control group, both in the left hand and the right hand. These results concur with figures obtained in this research, given that the group of football players with high blood pressure showed a higher arch and ulnar loop count in both hands than the group of normotensive football players.

Finally, the odds ratio was used to identify that there was a relationship with the presence of whorls on the left hand among the individuals with family history of high blood pressure. Likewise, there is a relationship between the total sum of the ridges and the sum of ridges on the left hand with family history of hypertension. These

results are not currently found in research because family history has not been used as an indicator. The odds ratios can be used as a variable of interest for future studies.

Limiting factors, which should be emphasised when developing this research, include a lack of information and research focused on the study of fingerprints, particularly in Colombia. As suggestions for future research, data should be taken from a larger number of participants than in this research project to improve the reliability and validity of results.

## Conclusions

It is thereby concluded that dermatoglyphics are a promising way of screening by recognising the risk factor related to the presence of high blood pressure in association with the subjects' family history, given the multifactorial nature of this disease. Dermatoglyphics could thereby be used as an early detection tool due to the characteristic profile presented by persons and athletes around the increase in arterial pressure and the possible development of arterial hypertension.

## Conflicts of interest

The authors declare that there is no conflict of interest.

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# Analysis of ventilatory equivalent responses for gases. Physiological significance

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## Summary

Although the respiratory equivalents for the two gases are parameters provided by the software of automated devices, are of great importance in the assessment of the response to exercise in healthy and sick people. This review work analyses the evolution of these parameters in both healthy people and patients with pathologies of the cardiovascular and respiratory systems. Their considerable physiological significance lies in the formulas that express these indices of respiratory function. However, if appropriate modifications are made to the ratios  $\dot{V}_E / \dot{V}O_2$  y  $\dot{V}_E / \dot{V}CO_2$  allows a better physiological significance, since they are determined by  $F_{E}O_2$  and  $F_{E}CO_2$ , so that a modification of these variables informs about the ratio  $\dot{V}_D / \dot{V}_E$  thus, indirectly, of the ratio  $\dot{V}_A / \dot{Q}$ . In healthy people, the response of the equivalents in the three classic phases described indicates a readjustment of the  $\dot{V}_A / \dot{Q}$  ratio (phases I and II) and a "potential" mismatch (phase III). On the other hand, in patients with cardiac or pulmonary pathology, the  $F_{E}O_2$  and  $F_{E}CO_2$  fractions clearly show an alteration of the  $\dot{V}_A / \dot{Q}$  ratio from the start of exercise, depending, of course, on the degree of impairment. Specifically, the change in the slope of the  $\frac{\dot{V}_E}{\dot{V}CO_2} / intensidad$  ratio has been a criterion accepted by cardiologists as a predictor of morbidity and mortality in cardiac patients with impaired ventricular function.

## Key words:

Respiratory gas equivalents.  
Ventilation/perfusion ratio.  
Healthy subjects. Heart disease.  
Pneumopathies.

## Análisis de la respuesta de los equivalentes respiratorios para los gases. Significación fisiológica

### Resumen

A pesar de ser únicamente unos parámetros de la información que aportan los softwares de los aparatos automatizados, los equivalentes respiratorios para los dos gases son de gran importancia en la valoración de la respuesta al ejercicio en personas sanas y enfermas. Este trabajo de revisión analiza la evolución de estos parámetros tanto en personas sanas como enfermas con patologías del sistema cardiovascular y respiratorio. Su considerable significación fisiológica radica en las propias fórmulas que expresan estos índices de función respiratoria. Pero, si se realizan las oportunas modificaciones de los cocientes  $\dot{V}_E / \dot{V}O_2$  y  $\dot{V}_E / \dot{V}CO_2$  La forma de expresar los equivalentes respiratorios para los gases según las ecuaciones 3 y 5 aporta una mejor significado fisiológico, pues vienen determinados por las  $F_{E}O_2$  y  $F_{E}CO_2$ , de manera que una modificación de estas variables informan de una modificación de la relación  $\dot{V}_D / \dot{V}_E$  y por consiguiente, de forma indirecta, de la relación  $\dot{V}_A / \dot{Q}$ . En las personas sanas la respuesta de los equivalentes en las tres fases clásicas descritas indica un reajuste de la relación  $\dot{V}_A / \dot{Q}$  (fases I y II) y un desajuste "potencial" (fase III). Por el contrario, en los enfermos con alguna patología cardíaca o pulmonar, las fracciones de las  $F_{E}O_2$  y  $F_{E}CO_2$  muestran claramente una alteración de la relación  $\dot{V}_A / \dot{Q}$  desde el comienzo del ejercicio, naturalmente según el grado de deterioro. Concretamente, ha sido la modificación de la pendiente de la relación  $\frac{\dot{V}_E}{\dot{V}CO_2} / intensidad$  un criterio admitido por la cardiología como predictor de la morbilidad y mortalidad en cardiopatas con alteración de la función ventricular.

## Palabras clave:

Equivalentes respiratorios para los gases.  
Relación ventilación/perfusión.  
Sujetos sanos. Cardiopatías.  
Neumopatías.

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## Introduction

Among the many parameters provided by software for modern-automated appliances<sup>1</sup>, ventilatory equivalents for gases ( $\dot{V}_E / \dot{V}O_2$  y  $\dot{V}_E / \dot{V}CO_2$ ) are widely used in stress test assessments, both for healthy and sick persons.

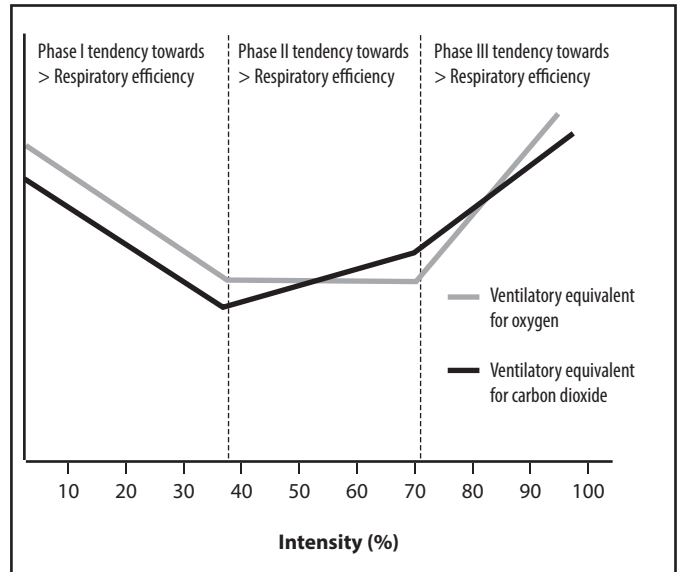
In the physiology field, for many years physiologists looked at the critical intensity which causes the accumulation of lactic acid<sup>2,3</sup>. Various non-invasive methods, based on continuous measurement of respiratory gases have been used to determine the "critical intensity". One of these methods involves looking at how  $\dot{V}_E / \dot{V}O_2$   $\dot{V}_E / \dot{V}CO_2$  behave during increasingly intense exercise<sup>4</sup>.

Given that ventilatory equivalents for gases are an indirect measurement of respiratory system efficiency (see physiological significance), Klebert *et al.*,<sup>5</sup> Guazzi *et al.*,<sup>6,7</sup> and Shafiq A<sup>8</sup> proposed that the  $\dot{V}_E / \dot{V}CO_2$  slope is an important morbidity and mortality predictor among heart failure patients. Specifically, the noticeable increase in the  $\dot{V}_E / \dot{V}CO_2$  / exercise intensity ratio slope is a prognostic value for heart failure patients independently of the fraction value<sup>6-8</sup>. On the other hand, Dumitrescu D *et al.*<sup>9</sup> have demonstrated in patients with pulmonary vasculopathy, that the response changes for PETCO<sub>2</sub> and  $\dot{V}_E / \dot{V}CO_2$  and other ventilatory exchange parameters make it possible to determine differences from other alterations in ventilatory exchange during exercise.

In principle, the physiological significance of  $\dot{V}_E / \dot{V}O_2$  y  $\dot{V}_E / \dot{V}CO_2$  is very simple. As these are dimensionless quotients, they represent a measurement of efficiency, as they indicate the quantity of air that the respiratory system mobilises in one minute ( $\dot{V}_E$ ) to consume one litre of oxygen ( $\dot{V}O_2$ ) or remove one litre of carbon dioxide ( $\dot{V}CO_2$ ), for the  $\dot{V}_E / \dot{V}O_2$  and  $\dot{V}_E / \dot{V}CO_2$ , respectively. Consequently, it seems logical to think that the larger the  $\dot{V}_E$  the less efficient the respiratory system in terms of the physiological integration parameters represented by  $\dot{V}O_2$  and  $\dot{V}CO_2$ : pulmonary, cardiovascular and muscular functions, all controlled by the nervous system.

However, the "arithmetical" consideration of the equivalents as ventilatory efficiency parameters is clearly not entirely accurate. As shown in Figure 1, the "numerical values" of the equivalents tend to gain (phase I), maintain (phase II) and lose ventilatory efficiency (phase III). Naturally, this raises an obvious question: at rest, when the equivalents' values are higher than at the end of phase I, is the respiratory system less efficient? The answer seems to be logical: the respiratory system is not less efficient at rest than during light exercise. Therefore, our aim in this review is to clarify, as far as possible, the physiological significance of the ventilatory equivalents for both gases and, from there, apply it to physiological conditions (health and performance) and pathological conditions (pathologies of the cardiovascular system and the respiratory system). As a starting point, the physiological significance is difficult to understand and so simple pulmonary function models will be used, aware of the limitations this implies.

**Figure 1. Representation of the EqO<sub>2</sub>/intensity and EqCO<sub>2</sub>/intensity functions. The three phases are shown, described in the usual way, from the point of view of respiratory efficiency.**



## Physiological significance of the ventilatory equivalents for the gases

As the arithmetic expression of the ventilatory equivalents does not provide enough information to find out what they represent physiologically, it is advisable to express them as follows.

The oxygen consumption analysed in respiration is given by the following equation:

$$\dot{V}O_2 = (\dot{V}_I \cdot F_{I}O_2) - (\dot{V}_E \cdot F_E O_2) \text{ (Equation 1)}$$

Where  $\dot{V}_I$  and  $\dot{V}_E$  are the ventilations when inhaling and exhaling and  $F_{I}O_2$  y  $F_E O_2$  are oxygen fractions in the air which is inhaled and exhaled, respectively. Unless the respiratory quotient is greater than the unit and it is necessary to apply Zunt's correction<sup>10</sup>, wrongly attributed to Haldane, it can be considered that  $\dot{V}_I$  and  $\dot{V}_E$  are equal, which simplifies equation 1:

$$\dot{V}O_2 = \dot{V}_E (F_I O_2 - F_E O_2) \text{ (Equation 2)}$$

Substituting for the oxygen equivalent in the formula gives the following equation:

$$Eq O_2 = \frac{\dot{V}_E}{\dot{V}_E \cdot (F_I O_2 - F_E O_2)} = \frac{1}{(F_I O_2 - F_E O_2)} \text{ (Equation 3)}$$

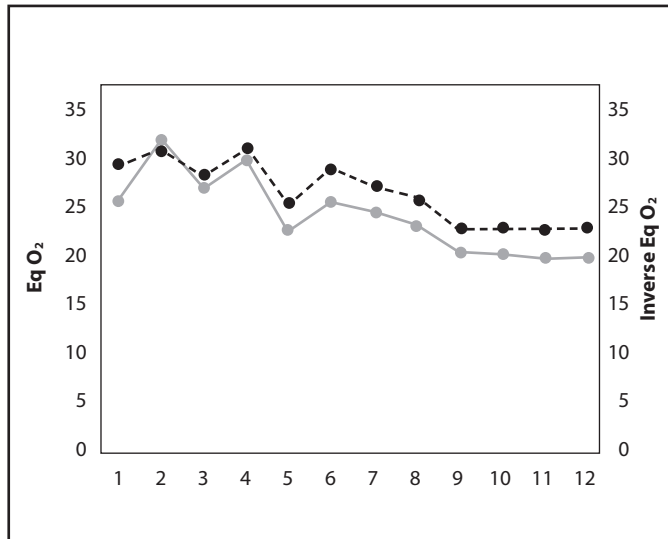
The same reasoning can be applied to carbon dioxide:

$$\dot{V}CO_2 = (\dot{V}_I \cdot F_I O_2) - (\dot{V}_E \cdot F_E CO_2) \text{ (Equation 4)}$$

Given that  $F_I O_2$  is practically zero, the ventilatory equivalent for carbon dioxide is:

$$Eq CO_2 = \frac{\dot{V}_E}{\dot{V}_E \cdot F_E CO_2} = \frac{1}{F_E CO_2} \text{ (Equation 5)}$$

**Figure 2. Representation of the ventilatory equivalent for oxygen in phase I, according to the usual expression ( $EqO_2 = \dot{V}_E / \dot{V}O_2$ ) and the expression corresponding to equation 3:  $Eq O_2 = 1 / (F_I O_2 - F_E O_2)$ .**



As shown, this equation does not add information regarding how  $\dot{V}_E / \dot{V}O_2$  behaves (Figure 2), as it is exactly the same. However, the information that it provides is important to understand it physiologically.

The behaviour of the exhaled fractions of oxygen ( $F_E O_2$ ) and carbon dioxide ( $F_E CO_2$ ) reflect the variations in the ratio between the physiologic dead space (anatomic + alveolar) and the flow volume  $\dot{V}_E / \dot{V}_E^{11}$ . When the respiratory system changes from a state of rest to light-moderate exercise, alveolar recruitment takes place, so that  $F_E O_2$  drops slightly and  $F_E CO_2$  rises. Consequently, the denominator of equations 3 and 5 increases, meaning that the ventilatory equivalents for the gases decrease. At this intensity, there is actually an increase in alveolar ventilation, and this produces a very slight change in the partial pressure of alveolar  $CO_2$  ( $P_a CO_2$ ) compared to pre-exercise values.

At high intensities, above 60%, there is a disproportionate increase in ventilation compared to the metabolic activity, reducing  $F_E CO_2$  and increasing  $F_E O_2$ . This behaviour is fundamental to attempt to regulate the acid-base state, because the "acidification" effects of the carbon dioxide can be completely eliminated by compensating the metabolic acidosis associated with the increase in the concentration of arterial lactate and protein concentration<sup>11</sup>. The  $F_E CO_2$  and  $F_E O_2$  variations at high intensities are indirect data of the  $\dot{V}_A / \dot{Q}$ , ventilation/perfusion ratio, that can be diverted towards unbalance values greater than the unit, indicating an inappropriate cardiovascular adjustment compared to the respiratory value<sup>12</sup>.

In summary, the way of expressing the ventilatory equivalents (equations 3 and 5) provides relevant information to understand the physiological significance for three reasons: 1) it does not represent a modification of the response of these parameters, 2) it makes it possible

to centre these parameters on strictly respiratory variables ( $F_E CO_2$  and  $F_E O_2$ ) and not on an integrating variable such as oxygen consumption and 3)  $F_E CO_2$  and  $F_E O_2$  are very useful parameters to estimate the  $\dot{V}_D / \dot{V}_E$  ratio, an indirect parameter of the  $\dot{V}_A / \dot{Q}$  ratio.

## Ventilatory equivalents in healthy subjects

Among other ergospirometry parameters, ventilatory equivalents are used to determine the aerobic-anaerobic transition, a more accurate term than anaerobic threshold, as this is a process not a particular time and, the confusion regarding these terms also makes it difficult to understand it physiologically. As stated by Chicharro and Legido<sup>13</sup>, the different denominations of the "break points" for ventilatory equivalents (Figure 1) have actually confused more than explained the physiological reasons that determine them, even more so when attempting to implement the phases determined by the variations of the equivalents in training<sup>14</sup>. Consequently, as one example, using Wasserman's terminology (Table 1), in intensive interval training it is not possible to qualify the intensity as an anaerobic threshold. This would be a considerable error regarding the conception of the aerobic-anaerobic transition phenomenon.

There has been wide debate around the relationship between the aerobic-anaerobic transition and the increase in concentration of lactic acid from Wasserman's description in 1986<sup>15</sup>. This paper does not intend to discuss this relationship, although it should be highlighted that many

**Table 1. Different designations for the first increment of the ventilation.**

Designation	Author
<b>First break point</b>	
Point of optimum efficiency	Hollman, 1959
Anaerobic threshold	Wasserman, 1964
Aerobic threshold	Kindermann, 1979; Skinner and McLellan, 1980
Individual aerobic transition	Passenhofer, 1981 Farrell, 1979
<b>Second break point</b>	
Aerobic-anaerobic threshold	Mader, 1976
Anaerobic threshold	Kindermann, 1981
Individual anaerobic threshold (IAT)	Stegman and Kindermann, 1981
Onset of lactate accumulation in blood	Sjodin and Jacobs, 1981
Ventilatory threshold 2	Orr, 1982
Anaerobic threshold	Skinner and McLellan, 1980

References not described in the manuscript. These are shown in reference<sup>13</sup>.

other physiological relationships have been established such as changes in the composition of saliva, electromyographic pattern, concentration of catecholamines and variation in the heart rate/intensity slope<sup>16</sup>. In this respect, Peinado *et al.*<sup>16</sup> indicate that all the changes which occur make up the “efferent” signal managed by the command or central generator. We thereby understand that the explanation of the ventilatory equivalents’ response for the gases is what is mentioned above, which we will explain succinctly and simply below.

In phase I, a readjustment of the ventilation/perfusion ratio takes place due to “alveolar recruitment” so that the ventilatory equivalents decrease. In phase II, according to elementary analysis of the equivalents, this would be the best linkage between the respiratory system and the cardiovascular system. In other words, the zone where the best health benefits are presumably obtained. Finally, the ventilation/perfusion ratio increases above the unit, suggesting that the cardiovascular system is unable to adjust<sup>12</sup>. In an interesting study carried out on pure-bred horses by McDonough *et al.*,<sup>17</sup> the ventilatory equivalent for oxygen does not increase as exercise becomes more intense. The authors attribute the response from  $\dot{V}_E/\dot{V}O_2$  to a linkage between the movement pattern (length of the stride) and the regulation of the respiration (linkage between current volume and respiratory frequency) and they indicate that, when alveolar recruitment must be increased, the  $V_D/V_T$  ratio is much higher in the pure-bred horses compared to human beings.

In another respect, it is worth considering whether the variations in ventilatory equivalents for the gases with training condition might be justified by the physiological significance indicated in the previous paragraph. In a review article, Benito *et al.*<sup>18</sup> indicate that the variation

between different training periods among professional cyclists was under 2% and in lower-level cyclists, it was between 3 and 15%. These small differences are due to the fact the  $F_{E}CO_2$  and  $F_{E}O_2$  do not vary considerably according to the training condition, so that the PET  $CO_2$  and the PET  $O_2$  cannot show obvious changes.

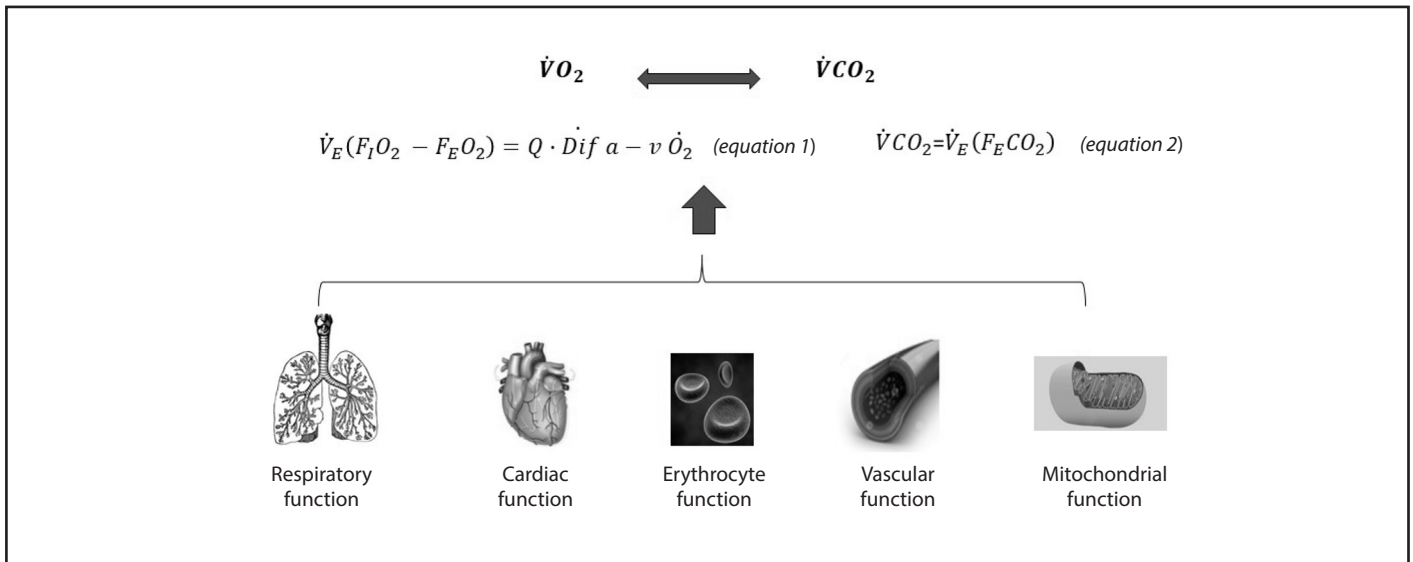
## Ventilatory equivalents for the gases in persons with various pathologies

Analysis of the ventilatory equivalents for respiratory gases during exercise in persons with various pathologies is even more complex than for healthy persons. Out of all their possible pathologies which might vary the body’s response to exercise, evaluated using ergospirometry, pathologies of the cardiovascular system, specifically the heart pump, and the respiratory system aroused the most interest. A careful study of the book by Wasserman and Whip<sup>19</sup> specifically shows that more than 80% of their practical cases focus on these pathologies.

Therefore, this section does not intend to exhaustively describe the physiological significance of these two parameters, but to analyse them from a didactic perspective. We think that with the appearance of the decree which regulates cross-cutting training for Health Science specialities, a previously-trained sports doctor or a doctor who might have trained on the job, must provide the knowledge acquired in their training to the different pathologies likely to be assessed using ergospirometry.

Figure 3 shows schematically how it is possible to impair the two central parameters of ergospirometry. A respiratory alteration lowers  $\dot{V}O_2$  and  $\dot{V}CO_2$  and can be explained by variations of equation 1 ( $\dot{V}_E(F_{I}O_2 - F_{E}O_2)$ ), and equation 4 ( $\dot{V}CO_2 = (\dot{V}_I \cdot F_{I}CO_2) - (\dot{V}_E \cdot F_{E}CO_2)$ ), respectively. On the

**Figure 3. Diagram of the organs, systems and tissues that determine oxygen consumption and carbon dioxide removal. Equation 1 is the result of equalling out the oxygen consumption by solving it in Fick’s principle and the oxygen consumption according to the respiratory exchange. The carbon dioxide removal is represented according to the respiratory exchange (equation 2).**



other hand, a cardiac alteration also leads to lower values of  $\dot{V}O_2$  and  $\dot{V}CO_2$  and can be explained by an alteration in cardiac output. Finally, a modification to the artery-vein oxygen difference ( $Dif_{a-v}O_2$ ) conditions lower values of  $\dot{V}O_2$  and  $\dot{V}CO_2$ , although it is more complex to assign this term only to a cardiac or respiratory pathology.

### The ventilatory equivalents for the gases in the response to exercise in respiratory system pathologies

Although it is common to divide the response to exercise in the respiratory system pathologies by the spirometry pattern (obstructive or restrictive), the contribution of the ventilatory equivalents will be analysed in general below<sup>20,21</sup>.

Figure 4 shows the differences in the ratios

$$\frac{\dot{V}_E}{\dot{V}O_2} / intensity \quad \frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

in a patient with obstructed airways (chronic obstructive pulmonary disease) and a healthy person. The patient's respiratory inefficiency is shown by the inability to reduce the denominator of equation 3. In other words, the patient presents difficulties to lower  $F_{E}O_2$  and raise  $F_{E}CO_2$  during phase I of the exercise (Figure 1) and the slope of

$$\frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

is high. This example matches the results from Dumitrescu D *et al.*,<sup>9</sup> who worked with patients with pulmonary vasculopathy to determine how the decrease in PET  $CO_2$  compared to the drop in the  $I \dot{V}_E / \dot{V}CO_2$  suggests a loss of blood vessels and can represent a sign of alteration of the left ventricular function, associated with this in these patients.

On the other hand, when establishing differences in the response to exercise in patients with a restrictive pattern (parenchymatous or extra-parenchymatous) compared to patients with an obstructive alteration of the airways, we consider that there is little physiopathological significance, as it is not feasible to compare the degree of damage from these pathologies that lead to modifications of the ventilatory equivalents which are difficult to differentiate. Furthermore, the possible differences do not determine clinical advantages.

### Ventilatory equivalents for the gases in the response to exercise in cardiovascular system pathologies

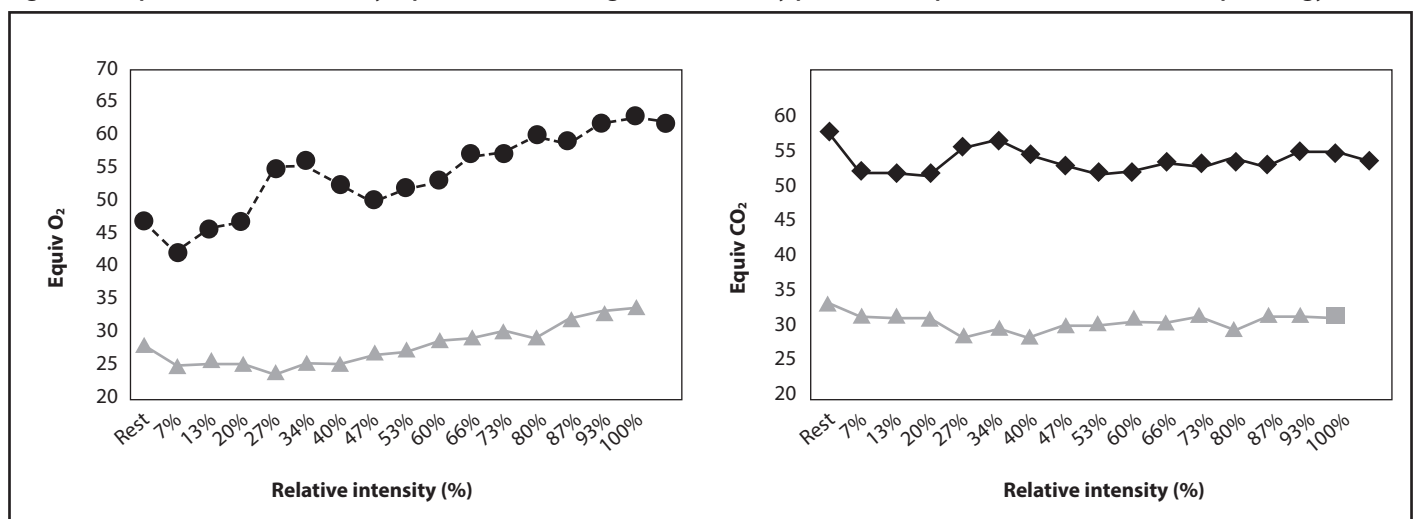
The "relative" problem of patients with heart failure is that the alterations in the ventricular function appear alongside alterations in the respiratory system. Consequently, the response from the ventilatory equivalents for the gases does not differ from the response corresponding to the patients with "strictly" respiratory pathologies, although according to various authors, it is one way of assessing the prognosis and evolution of the cardiac disease.

Miki *et al.*<sup>22</sup> assess the survival time in patients with heart failure by means of the slope of the ratio

$$\frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

Using multivariate analysis, these authors indicate that low ventilatory efficiency, measured indirectly by  $\dot{V}_E / \dot{V}CO_2$ , is an important predictive morbidity and mortality factor, independently of central hemodynamic activity. Concerning the factors being studied (slope of the  $PaO_2$ , the  $\dot{V}_E / \dot{V}CO_2$ , oxygen pulse, maximum oxygen consumption and age), the authors of this study confirm what other authors Kleber *et al.*<sup>23</sup> and Braga *et al.*<sup>24</sup> have mentioned: usefulness as survival prognosis predictors among these patients.

Figure 4. Response of the ventilatory equivalents for both gases in a healthy person and a patient with an obstructive pathology.





In the same way, in an interesting study on the possible influence of the inhibition of afferent information from the musculature on the respiratory pattern, Olson *et al.*<sup>25</sup> demonstrated that increased ventilation in patients with heart failure was produced by an increase in the respiratory frequency at the expense of the  $V_T/T_I$  ratio and an increase in the slope

$$\frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

plus a drop in the intensity and the peak oxygen consumption. According to these authors, they are partly due to the reduction of the information afferent to the respiration regulation centres, as when they pharmacologically cancel out the afferent inputs of the musculoskeletal system, the ventilatory response drops during exercise.

Finally, among other cardio-respiratory parameters, Takayanagi *et al.*<sup>26</sup> and Van Iterson<sup>27</sup> have raised the importance of the  $\dot{V}_E / \dot{V}CO_2$  during exercise to assess patients with heart failure. The former<sup>26</sup> showed that during the recovery of the variations experienced by the respiratory quotient, the  $\dot{V}_E / \dot{V}CO_2$  and the PET  $O_2$  were significantly greater among people with better ventricular function. The latter<sup>27</sup> show that the alteration of the slope

$$\frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

during exercise is better explained by the VD/VT ratio among patients with heart failure and a low ejection fraction compared to patients with heart failure and an ejection fraction within the normal range, emphasising the need to improve interpretation of the slope

$$\frac{\dot{V}_E}{\dot{V}CO_2} / intensity$$

in heart failure, fundamentally from the clinical point of view.

## Conflicts of interest

The author does not declare any conflict of interest.

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PEVERINI, AGUSTINA	218	326	2023				

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La dirección de Archivos de Medicina el Deporte desea agradecer a todos su desinteresada colaboración.

# Guidelines of publication Archives of Sports Medicine

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The ARCHIVES OF SPORTS MEDICINE Journal (Arch Med Deporte) with ISSN 0212-8799 is the official publication of the Spanish Federation of Sports Medicine. This journal publishes original works about all the features related to Medicine and Sports Sciences from 1984. This title has been working uninterruptedly with a frequency of three months until 1995 and two months after this date. Arch Med Deporte works fundamentally with the system of external review carried out by two experts (peer review). It includes regularly articles about clinical or basic research, reviews, articles or publishing commentaries, brief communications and letters to the publisher. The articles may be published in both SPANISH and ENGLISH. The submission of papers in English writing will be particularly valued.

Occasionally oral communications accepted for presentation in the Federation's Congresses will be published.

The Editorial papers will only be published after an Editor requirement.

The manuscripts accepted for publication will become FEMEDE property and their reproduction, total or partial, must be properly authorized. All the authors will have to send a written letter conceding these rights as soon as the article is accepted for publication.

## Submit of manuscripts

1. The papers must be submitted at the Editor in Chief's attention, written in double space in a DIN A4 sheet and numbered in the top right corner. It is recommended to use Word format, Times New Roman and font size 12. They must be sent by e-mail to FEMEDE's e-mail address: femede@femede.es.
2. On the first page exclusively it should include: title (Spanish and English), authors' first name, initial of the second name (if applicable), surname and optionally the second one; Main official and academic qualifications, workplace, full address and corresponding author e-mail. Supports received in order to accomplish the study – such as grants, equipments, medicaments, etc- have to be included. A letter in which the first author on behalf of all signatories of the study, the assignment of the rights for total or partial reproduction of the article, once accepted for publication shall be attached. Furthermore, the main author will propose up to four reviewers to the editor. According to the reviewers, at least one must be from a different nationality than the main author. Reviewers from the same institutions as the authors, will not be accepted.

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  - a. **ORIGINALS RESEARCH:** It will contain an introduction, which must be brief and will contain the aim of the work, written in such a way that the reader can understand the following text.  
**Material and method:** the material used in the work will be exposed, as well as its characteristics, selection criteria and used techniques, facilitating the necessary data in order to allow the reader to repeat the experience shown. The statistical methods will be detailed described.  
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9. After hearing the reviewers' suggestions (journal uses peer correction system), may reject the works which are not suitable, or indicate the author the modifications which are thought to be necessary for its acceptance.
10. The Editorial Board is not responsible for the concepts, opinions or affirmations supported by the authors.
11. Submissions of the papers: Archives of Sports Medicine. By e-mail to FEMEDE'S e-mail address: [femede@femede.es](mailto:femede@femede.es). The submission will come with a cover letter on which the work's examination for its publication in the Journal will be requested, article type will be specified, and it will be certified by all authors that the work is original and has not been partially or totally published before.

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# Campaña de aptitud física, deporte y salud



La **Sociedad Española de Medicina del Deporte**, en su incesante labor de expansión y consolidación de la Medicina del Deporte y, consciente de su vocación médica de preservar la salud de todas las personas, viene realizando diversas actuaciones en este ámbito desde los últimos años.

Se ha considerado el momento oportuno de lanzar la campaña de gran alcance, denominada **CAMPAÑA DE APTITUD FÍSICA, DEPORTE Y SALUD** relacionada con la promoción de la actividad física y deportiva para toda la población y que tendrá como lema **SALUD – DEPORTE – DISFRÚTALOS**, que aúna de la forma más clara y directa los tres pilares que se promueven desde la Medicina del Deporte que son el practicar deporte, con objetivos de salud y para la mejora de la aptitud física y de tal forma que se incorpore como un hábito permanente, y disfrutando, es la mejor manera de conseguirlo.

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