Universidad de Deusto
Deustuko Unibertsitatea
University of Deusto

Facultad de Educación y Deporte

Programa de Doctorado en Educación

Impacto de un programa de ejercicio físico en el ángulo de fase y su correlación con la salud física y mental en pacientes de cáncer durante y después de la pandemia de COVID-19

Impact of a physical exercise program on the phase angle and its correlation with physical and mental health in cancer patients during and after the COVID-19 pandemic.

Borja Gutiérrez Santamaría

Bilbao, 2023

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“Antes de curar a alguien, pregúntale si él está dispuesto a renunciar a las cosas que le enfermaron."

-Hipócrates-

“Before you heal someone, ask him if he’s willing to give up the things that make him sick.”

-Hippocrates-

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Eskerrik asko

Muchas gracias

TÍTULO:

RESUMEN:

Durante el período de emergencia sanitaria, se evidenció un marcado decremento en la actividad física y un aumento en el sedentarismo entre los pacientes oncológicos objeto de estudio, lo que incidió negativamente en la fuerza muscular y la capacidad respiratoria. En contrapartida, los aspectos psicológicos y la composición corporal no manifestaron alteraciones significativas. La preservación de niveles adecuados de actividad física se erige como un pilar fundamental para salvaguardar la salud física de esta comunidad vulnerable.

En el contexto de las evaluaciones clínicas realizadas en los pacientes con cáncer, se examinó el ángulo de fase (PhA) como un nuevo parámetro con el propósito de establecer correlaciones con aspectos tanto físicos como psicológicos de estos individuos. El objetivo fue evaluar la utilidad del PhA, obtenido mediante técnicas de bioimpedancia, en la monitorización de pacientes oncológicos a lo largo de su tratamiento. Este análisis reveló una relación entre el PhA y el rendimiento físico, donde un aumento en el PhA se asoció con mejoras en la capacidad de marcha, la fuerza muscular y el consumo de oxígeno. Cabe destacar que la edad ejerció una influencia significativa en esta relación.
El PhA se postula como una herramienta prometedora en la práctica clínica para la valoración del estado físico de los pacientes oncológicos durante su tratamiento.

Paralelamente, se emprendió una indagación sobre la posible relación entre el PhA y los factores de orden psicológico en los pacientes con cáncer. Los resultados arrojaron una correlación estadísticamente significativa entre el PhA y los cuestionarios que evaluaron la salud mental y el bienestar psicológico, indicando que un PhA más elevado se relacionó con una mejor percepción de la salud mental. No obstante, se advirtió que la relación no se mantuvo uniforme en todas las escalas de síntomas evaluadas. A pesar de este hallazgo prometedor, se destaca la necesidad de continuar investigando para asegurar la implementación confiable del PhA en la práctica clínica, especialmente en lo que respecta a aspectos psicológicos específicos.

PALABRAS CLAVE:

Cáncer, Actividad física, Ejercicio físico, Ángulo de fase, Fuerza, VO_{2max}

TITLE:

SUMMARY:

During the health emergency period, a significant decrease in physical activity and an increase in sedentary behavior were observed among the studied oncology patients, negatively impacting muscular strength and respiratory capacity. In contrast, psychological aspects and body composition did not show significant alterations. Preserving adequate levels of physical activity emerges as a fundamental pillar to safeguard the physical health of this vulnerable community.

In the context of clinical assessments conducted on cancer patients, the phase angle (PhA) was examined as a new parameter with the purpose of establishing correlations with both physical and psychological aspects of these individuals. The goal was to assess the utility of PhA, obtained through bioimpedance techniques, in monitoring oncology patients throughout their treatment. This analysis revealed a relationship between PhA and physical performance, where an increase in PhA was associated with improvements in walking capacity, muscular strength, and oxygen consumption. It is worth noting that age exerted a significant influence on this relationship.

PhA is posited as a promising tool in clinical practice for evaluating the physical condition of oncology patients during their treatment.

Simultaneously, an inquiry was undertaken to explore the potential relationship between PhA and psychological factors in cancer patients. The results yielded a statistically significant correlation between PhA and questionnaires assessing mental health and psychological well-being, indicating that a higher PhA was related to a better perception of mental health. However, it was noted that the relationship was not uniform across all evaluated symptom scales. Despite this promising finding, the need for further research to ensure the reliable implementation of PhA in clinical practice, especially concerning specific psychological aspects, is emphasized.

KEYWORDS:

Cancer, Physical Activity, Exercise, Phase Angle, Strength, VO_{2max}

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CAPÍTULO 1:

INTRODUCCIÓN Y MARCO TEÓRICO

Capítulo 1. Introducción y Marco Teórico

Chapter 1: Introduction and theoretical framework

Justificación de la Temática

Justification of the Topic

Cancer is a leading cause of death and a major obstacle to increasing life expectancy in all countries of the world (Bray et al., 2021). It was estimated that 19.3 million new cancer cases and almost 10 million cancer deaths would occur worldwide in 2020. Female breast cancer has overtaken lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0%), prostate (7.3%) and stomach (5.6%). Lung cancer remained the leading cause of cancer deaths, with an estimated 1.8 million deaths (18%), followed by colorectal (9.4%), liver (8.3%), stomach (7.7%) and female breast (6.9%) cancers. The overall incidence was 2-3 times higher in transition countries for both genders (Sung et al., 2021).

On the other hand, the global cancer burden is expected to be 28.4 million cases in 2040, an increase of 47% over 2020 (latest reported data) (Sociedad Española de Oncología Médica (SEOM), 2023), with a greater increase in countries in transition due to demographic changes, although this may be exacerbated by increased risk factors associated with globalisation and a growing economy. Building a sustainable infrastructure for the dissemination of cancer prevention measures and the provision of cancer care in countries in transition is critical for global cancer control (Sung et al., 2021).

In Spain, it is estimated that the incidence of cancer will reach around 341,000 cases by 2040, although this figure is difficult to estimate due to the unknown impact of the COVID-19 pandemic on cancer. According to data from the National Health System (SNS), a decrease in the number of patients discharged with an oncological diagnosis in 2020 of 37,260 patients was reported, being 12.2% lower than in 2019. The difference between communities varied between 1.8-34.8%. During the first months of the pandemic, between March and May 2020, the number of first visits to oncology services decreased by 12%, this decrease is justified due to the limitation in healthcare activity as well as the patient's refusal to go for consultation at the time of the highest incidence of COVID-19. During the following months, until February 2021, a return to normal activity was possible (Sociedad Española de Oncología Médica (SEOM), 2023). In 2023, 279,260 cases of cancer are expected to be diagnosed in Spain, distributed as follows: in the population under 45 years of age, men would suffer 6,070 cases and women 10,315; for the population between 45 and 64 years of age, 51,418 cases are estimated for men and 47,054 for women; and for those over 65 years of age, cases would amount to 101,057 cases in men and 63,346 for women. It is important to bear in mind that these numbers may be affected by the pandemic and possible delays in diagnosis, underlining the need to continue working on prevention and early diagnosis of cancer. According to predictions, the most frequently diagnosed cancers in Spain in 2023 for both sexes would be colon and rectum (42,721 new cases), breast (35,001), lung (31,282), prostate (29,002) and urinary bladder (21,694). In terms of the most common types of cancer, men have a higher incidence of prostate cancer (29,002), colon and rectum (26,357), lung (22,266) and urinary bladder (17,731), while breast cancer (35,001) and colon and rectum (16,364) are the most frequent in women.

According to the latest data on cancer in the Basque Autonomous Community (BAC) published in 2023, between 2013 and 2017, a total of 70,746 cases of cancer were diagnosed in the Basque Country, with an average of 14,150 new cases per year, 8,230 in men and 5,920 in women (Lopez de Munain & Audicana, 2023). During this period, the crude incidence rate was 778.1 per 100,000 in men and 530 per 100,000 in women, which is equivalent to a ratio of 1.7 higher in men than in women. The most common cancers in men during the same period, according to the most recent data (Lopez de Munain & Audicana, 2023), were prostate (8,376 cases), colon-rectum (6,278), lung (5,872) and bladder (3,418). In the case of women, the most frequent were breast cancer (8,031 cases), colon-rectum (3,991), lung (2,024) and uterus (1,709).

Similarly, taking into account the latest published data (Lopez de Munain & Audicana, 2023), deaths in the BAC between 2017 and 2021 totalled 30,766 deaths due to cancer, with an average of 6,153 deaths per year, 3,702 in men and 2,451 in women (Lopez de Munain & Audicana, 2023). With these figures, cancer is the leading cause of death in the BAC, accounting for 28.1% of total deaths, 33.7% in men and 22.4% in women.

In addition to causing suffering, the disease is costly and represents a significant burden in terms of care, management and monitoring for the health system.

Coste asociado al cáncer

Cost associated with cancer

A report by the Spanish Association Against Cancer commissioned a strategic consultancy to carry out a detailed estimate of the costs associated with cancer in Spain (Oliver Wyman, 2020). The report analyses the costs associated with cancer patients in Spain during a specific year, based on the incidence data of new cases detected in that period. The projected costs are spread over the patient's lifetime, excluding relapses. Direct medical costs include expenditures for treatment, follow-up, pharmacy, palliative care, reconstruction and fertility preservation. In addition, non-medical direct costs are included, such as transport, accommodation, subsistence and equipment, as well as expenses related to the care of the patient both by professionals and informal care provided by the family. Finally, indirect costs are added which encompass the loss of productivity of both the patient and his or her family, including loss of income of active patients, decreased household income and loss of productivity due to premature death (Oliver Wyman, 2020).

Following the independent study, it was concluded that the overall cost of cancer in Spain is 19.3 billion euros (1.3% of Spain's GDP) of which 48% (9.33 billion euros) is spent on direct medical costs, 12% (2.22 billion euros) on non-direct medical costs and 40% (7.75 billion euros) on indirect costs. Of the total expenditure, 55% of the costs are borne by the healthcare system and 45% by patients' families (Oliver Wyman, 2020).

In 2018, average costs per patient per year varied according to cancer type and stage. For example, colorectal cancer in local stage had an average cost of €16,529/patient/year, while in metastatic stage the cost rose to €34,738/patient/year. This pattern was also observed in breast cancer, with an average cost of €8,271/patient/year in the local state and €35,732/patient/year in the metastatic state. On the other hand, prostate cancer had an average cost of €5,321/patient/year locally and €14,129/patient/year metastatically. However, haematological cancers proved to be the most expensive, with an average cost of €55,578/patient/year, regardless of the patient's stage (Oliver Wyman, 2020).

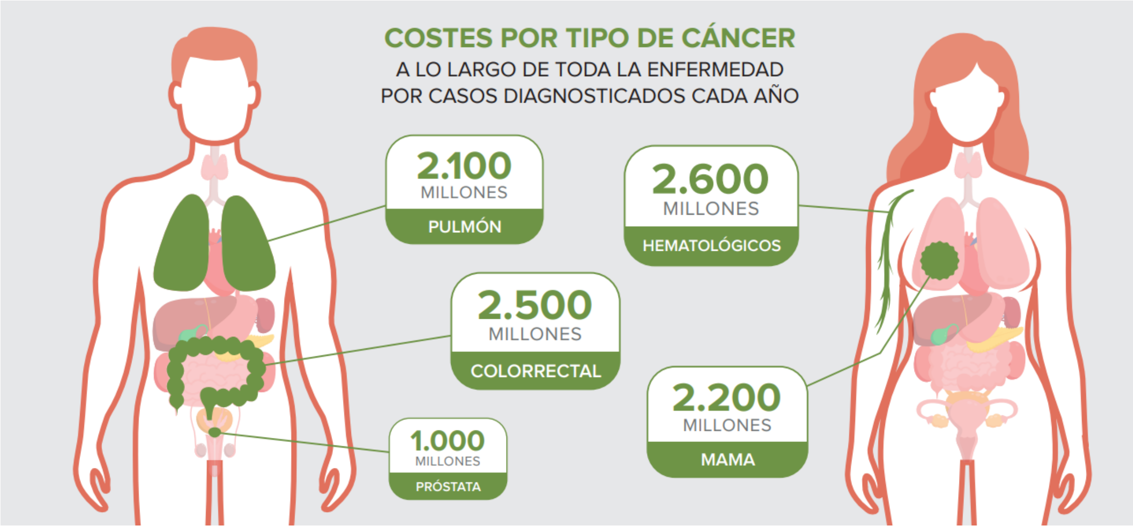

Figura 1 : *Costes al año por tipo de cáncer a lo largo de toda la enfermedad (obtenido de Oliver Wyman, 2020)*

In the Basque Country, there are very few studies on the costs of cancer. Only one article has been found that addresses the subject. This article focuses on the data on cancer costs in the Basque Country in 2010 and 2011 and shows that there were a total of 9,333 deaths from malignant neoplasm in that period. 65.4% of the deaths were men and 61.5% were aged 70 or over. The average age of the deceased was 72.9 years and 71.1% of them died in hospital. The average cost of those who died in hospital was almost twice as high compared to those who died at home (€14,794 and €7,491, respectively; $p<0.001$) (Nuño-Solinís et al., 2017).

Due to the high economic cost and social impact of cancer, non-pharmacological therapies have been developed to mitigate the negative effects of the disease and its possible side effects. In this sense, physical exercise has been widely supported by the scientific community as an effective tool. Both the disease itself and the treatments used to combat it can increase psychosocial distress, depression, cognitive impairment, pain and fatigue in patients. They also lead to a significant reduction in cardiorespiratory capacity and muscle strength (accelerated processes of sarcopenia and cachexia) and losses in bone mass (Schmitz et al., 2010). As a result, cancer survivors experience a decreased quality of life and an increased risk of developing comorbidities (Caan et al., 2018).

Over time, the importance of maintaining optimal physical condition in the context of a potential cancer diagnosis has been emphasized. This perspective is based on its capacity to enhance, in most instances, the prognosis and subsequent viability post-diagnosis while simultaneously mitigating the burdensome impacts that cancer can entail in physical, psychological, and economic terms. Within the realm of contemplated physical fitness, the most scrutinized aspects for improving prognosis and survival revolve around maximal oxygen consumption as VO_{2max}, musculoskeletal robustness, and body composition.

In the specific domain of VO_{2max}, a high level of cardiovascular fitness has consistently been correlated with more favourable outcomes in individuals afflicted by the oncological entity. The effective execution of physical exercise translates into greater tolerance for therapeutic procedures such as chemotherapy and radiation therapy, ultimately enabling the implementation of more intensive and effective treatments (Jones et al., 2010)

Further research has borne witness to the fact that enhancing muscular strength and functionality yields superior results in the context of oncological pathology, empowering the confrontation of the disease with a plethora of additional assurances (Williams et al., 2020)

Additionally, maintaining a body weight in accordance with health parameters and mitigating adipose deposits have been shown to positively influence therapeutic response, concurrently reducing the risk of metabolic complications, as elucidated by a review focused on diet and body composition. In this regard, arriving at the cancer diagnostic stage with an appropriate body weight and configuration could emerge as a defensive factor concerning diagnosis and subsequent survival (Williams et al., 2020).

Even if you are not in good physical condition, you can always improve your physical condition once diagnosed with a good adapted physical exercise plan and obtain benefits, although these will be lower.

Efectos del ejercicio físico en pacientes afectados de cáncer
Effects of physical exercise on cancer patients

Exercise has a multitude of health benefits, so in this section, we will focus on the most important ones related to cancer and its implications.

There is sufficient evidence to indicate how exercise can reduce tumour growth and cancer-specific mortality in a dose- and intensity-dependent manner. During exercise, several systemic factors, such as catecholamines and myokines, are released and other physiological processes, such as increased blood flow, occur. These acute long-term effects lead to a reduction in systemic inflammation and oxidative stress. In addition, changes in hormones and their receptors (insulin, growth factors, sex-steroid hormones, among others) together with intratumoural adaptations, such as improved blood perfusion, enhanced immune system, and adjustments in gene expression and metabolism, contribute to slower tumour progression and may reduce the ability of cancer cells to form tumours in distant tissues (Dethlefsen et al., 2016; L. Pedersen et al., 2015). However, walking alone does not bring these benefits per se; a certain minimum threshold of intensity needs to be exceeded to bring about the aforementioned benefits (Urhausen et al., 1994). It has been estimated that approximately one third of cancer deaths are related to obesity, lack of physical activity and poor nutrition and could have been prevented (American Cancer Society, 2012). Growing evidence has shown that cancer survivors who achieve a physical activity dose of 8 METs-h/week or an equivalent of 150 min/week of moderate to vigorous physical activity (MVPA) recommended by the ACSM (Schmitz et al., 2010) and the Australian Sports Medicine Association (Hayes et al., 2019) reduce the risk of recurrence by 50% and cancer-specific mortality by 25%.

Physical exercise is the most powerful intervention available to break the vicious circle of asthenia, anorexia, weakness, muscle atrophy, bone loss, decreased cardiorespiratory capacity, cognitive decline, anxiety and depression caused by the disease itself and the oncological, radiotherapeutic and surgical treatments they receive (Schmitz et al., 2010; Wolin et al., 2012).

Due to the reasons explained above, exercise is a powerful tool in managing the side effects of cancer patients, as well as improving the health of patients. As a result, there are physical exercise programs within the Spanish healthcare system that aim to provide this tool to a growing number of cancer-affected patients.

Before starting an exercise program, it is essential to conduct a battery of tests to assess the patient's condition and needs, in order to tailor the exercise regimen to their specific requirements. This individualized approach aims to potentially improve the patient's physical aspects as well as their overall disease condition. In the following section, the most commonly used physical and psychological tests in oncology patients will be mentioned and detailed to assess their physical and psychological health status.

Aproximación de batería de pruebas físicas y psicológicas en pacientes con cáncer
Approach to a battery of physical and psychological tests in cancer patients.

There are a multitude of tests used in physical exercise programs, both in research and clinical practice. This section aims to briefly explain a series of tests that the author of this doctoral thesis considers most important in the comprehensive assessment of the patient. Another characteristic of these tests is the balance between the quantity and quality of information they provide. They are designed to offer the most information with minimal cost, which can sometimes be high.

Evaluation of Cardiorespiratory Capacity: This test assesses the ability of the cardiovascular and respiratory systems to supply oxygen to the muscles during exercise. It is measured through stress tests, where the patient walks or pedals on a treadmill or stationary bicycle while their heart rate, blood pressure, and other physiological parameters such as oxygen consumption, gas exchange, and ventilatory quotient are recorded among the most important ones. Cardiorespiratory capacity is a crucial indicator of overall physical fitness and can impact cancer treatment tolerance and the ability to perform daily activities. Evaluating it allows for the adaptation of the exercise program and setting realistic goals for the patient(Machado et al., 2022; Schmitz et al., 2010; Wolin et al., 2012).

A typical stress test starts at a low intensity and gradually increases until the patient reaches their maximum effort or shows signs of fatigue or exercise intolerance. An example of a common protocol is the Bruce protocol, which includes progressive increments in treadmill speed and incline.

Measurement of Muscle Strength: This test evaluates the strength and capacity of the patient's muscles to generate tension and movement against resistance. Different muscle groups, such as grip strength, leg strength, or trunk strength, can be measured using dynamometers or resistance machines.

Muscle strength loss is common in cancer patients due to treatment and immobilization, which can impact functional capacity and quality of life. Measuring muscle strength helps identify potential weaknesses and design a specific exercise program to strengthen the affected muscles(Galvão et al., 2009; Minnella et al., 2018).

To measure grip strength, a hand dynamometer is used, and the patient squeezes with maximum force for a few seconds. To assess leg or trunk strength, specific exercises such as knee extension or trunk flexion can be performed using resistance machines.

Body Composition: Body composition assesses the distribution of lean mass (muscle and non-fat tissue), fat mass, and bone mineral density in the patient's body. It can be measured using techniques such as electrical bioimpedance (BIA) or dual-energy X-ray absorptiometry (DEXA).

Cancer patients may experience changes in body composition due to the loss of muscle mass (cachexia) or alterations in fat distribution. These changes can affect physical function, quality of life, and treatment response(Prado et al., 2008, 2009). Measuring body composition helps identify issues and design specific interventions to maintain or improve lean mass and bone density.

Electrical bioimpedance measures the body's electrical resistance and uses algorithms to estimate body composition. DEXA employs low-dose X-rays to scan the body and provides precise measurements of lean mass, fat mass, and bone density.

Both techniques are reliable, but BIA has a significantly lower cost compared to DEXA. However, when discussing result reliability, although BIA has high significance, DEXA results are considered the gold standard.

It is important to note that the aforementioned physical and psychological tests should be conducted under the supervision of qualified healthcare professionals, such as physiotherapists, psychologists, medical oncologists, or exercise physiologists. Moreover, it is necessary to tailor these tests to the individual needs and limitations of each patient to ensure their safety and effectiveness in evaluating their physical and psychological health status.

The questionnaires used in cancer patients are standardized tools designed to assess specific aspects of the patients' physical, emotional, and social well-being during cancer treatment and recovery. These questionnaires provide a systematic and reliable way to gather information about the patient's quality of life, emotional state, and overall health. They are validated and reliable tools for measuring specific aspects of quality of life, emotional well-being, and general health in cancer patients. Additionally, they provide objective and quantifiable information about the impact of the disease and its treatment on the patient's life, which helps healthcare professionals tailor treatment and provide more personalized care. Furthermore, they allow for comparisons between different patient groups, evaluate progress over time, and assess the effectiveness of frequently used interventions and treatments in research projects. Below, the main characteristics of some of the most commonly used questionnaires in cancer patients are explained:

1. FACIT (Functional Assessment of Chronic Illness Therapy): This questionnaire is designed to evaluate health-related quality of life in patients with chronic illnesses, including cancer. It measures aspects such as functional capacity, fatigue, pain, social support, and emotional well-being. Its main objective is to provide a comprehensive view of the impact of the disease and its treatment on the patient's quality of life(Al-shair et al., 2012).

2. QLQ-C30 (Quality of Life Questionnaire-Core 30): This questionnaire was developed by the European Organization for Research and Treatment of Cancer (EORTC) and is one of the most commonly used instruments to measure quality of life in cancer patients. The QLQ-C30 assesses various aspects such as physical and emotional functioning, cancer and treatment-related symptoms, and the overall impact of the disease on the patient's daily life(Fayers P, Aaronson N, Bjordal K, 2001; Fayers P. M. et al, 2001).

3. SF-36 (Short Form-36): This widely used questionnaire evaluates quality of life in various populations, including cancer patients. The SF-36 measures aspects such as physical and emotional functioning, pain, vitality, and mental health. It is a versatile tool that provides an overall view of the patient's perceived health and well-being(Brazier et al., 1992; Bunevicius, 2017; Ware Jr & Sherbourne, 1992).

4. GHQ-12 (General Health Questionnaire-12): This questionnaire is designed to detect mental health problems in the patient, such as anxiety, depression, and stress. It focuses on screening symptoms and emotions that may negatively affect the patient's mental health(Goldberg et al., 1997; Sánchez-López & Dresch, 2008).

It is important to note that these questionnaires should be administered under the supervision and guidance of healthcare professionals, and the patient's responses should be treated with confidentiality and sensitivity. The use of these questionnaires can significantly contribute to comprehensive and patient-centered care during their cancer journey.

One of the parameters that has experienced significant growth in recent years is the Phase Angle (PhA), so we will dedicate an entire section to understanding this parameter, as it is a fundamental pillar within this doctoral thesis.

Angulo de fase (PhA)

Phase angle (PhA)

Physical exercise and other strategies, such as proper nutrition, increasing muscle mass and decreasing body fat, have been shown to improve a substantial number of health markers including phase angle. The cell membrane consists of a phospholipid bilayer composed of a hydrophilic (water-affinity) head and a hydrophobic (water-repellent) tail. The conducting ball of the membrane straddles an insulating (hydrophobic) medium that forms the cell membrane. When two conductive materials surround an insulator, we speak of a capacitor. A capacitor is a device that stores electrons. This is what the membrane mainly does. It acts as a condenser, like a battery.

Phase angle has long been linked to nutritional status. This marker is rapidly becoming recognised as a global health marker in the assessment of total body health. When the cell membrane loses its ability to function effectively (i.e. in cases of malnutrition or disease) it effectively loses its ability to store electrons and can no longer function as an effective membrane. This is captured by the phase angle. The phase angle is the measure of the functionality of the cell membrane, i.e. how well our battery is functioning. If there is leakage in the cell membrane, the cell membrane's ability to retain voltage will decrease, so the phase angle will decrease.

There are two elements to the phase angle: the reactance (X) and the resistance (R). It should be noted that this measurement is a direct assessment of the cell membrane, and not a calculation based on indirect equations. The phase angle φ is the displacement between the AC current and the voltage at the measured impedance (50 kHz). The expression for the phase angle φ is:

$\varphi = \text{arctg } X/R$

The reactance (X) reflects the cell mass of the body, and the resistance (R) reflects the water or fluid in the body. Therefore, fluid and muscle mass will influence the phase angle. A greater phase angle could mean an increase in muscle mass (body cell mass) or a decrease in fluid, either from recovery from infection, injury or a decrease in fluid from dehydration. A loss of fat could also increase the phase angle. A lower phase angle could mean a loss of muscle mass, or an increase in fluid, when caused by rehydration, or conversely when it is a sign of inflammation or infection.

A low phase angle will alert for further assessment of what might be the cause. Previous research has looked at different cancers to provide cut-off points where special attention should be paid, such as 4.5° or 5.3° in lung cancer, 5.57° in colorectal cancer, 5.08° in pancreatic cancer or 5.6° in breast cancer (Norman et al., 2012).

One of the most important aspects of PhA is that it is modifiable, and one of the most powerful interventions to improve this parameter is physical activity. It has been shown that the practice of physical activity and specific physical exercises in cancer patients can have a positive effect on PhA levels and, as a result, on health outcomes(Alexandre Duarte Martins et al., 2022; Short et al., 2022).

Programa Bizi Orain durante la pandemia por COVID-19
Bizi Orain Program during the COVID-19 pandemic

To improve disease management and the side effects of treatment in cancer patients, a physical exercise programme has been launched and is offered to cancer patients who meet certain criteria for inclusion in the programme (Arietaleanizbeaskoa et al., 2021). The information for the present doctoral thesis has been obtained from the Bizi Orain (BO) research project, which is a hybrid, randomised clinical and implementation trial in which 312 cancer patients were randomly assigned to two parallel groups. The BO group carried out the supervised exercise plan immediately for 3 months and the other group received advice and a standardised prescription of physical activity, diet and smoking cessation plans to be carried out autonomously, thus forming a comparison or control group (Grandes et al., 2008; Sanchez et al., 2015). At the end of the trimester, the comparison group also received the BO supervised exercise plan. Functional capacity and quality of life were measured as secondary outcome variables at 0, 3, 6 and 12 months (Arietaleanizbeaskoa et al., 2021)

BO is a programme that promotes a biopsychosocial approach in the health system to promote health, not just treat disease. It is based on cooperation between health organisations, universities and community actors. Patients learn to exercise autonomously thanks to the education provided during the programme. However, the project was affected by an extremely rare and shocking event, which affected a large part of society. This event had a major impact on the world society and caused inconvenience to the BO project's sample of cancer patients. The coronavirus came to light in December 2019 and was highly relevant in Spain in early 2020. The coronavirus known as SARS-CoV-2 spread worldwide and caused the COVID-19 pandemic. The symptomatic severity of COVID-19 infection appeared to vary with age and the presence of comorbidities. Elderly patients with underlying chronic diseases, such as cancer, appeared to be more vulnerable (Chen et al., 2020; Liang et al., 2020; Wu & McGoogan, 2020; Yue et al., 2020).

During its first phase of expansion outside China, Italy and Spain were the countries most affected and reported the most cases and deaths. As a result, they were the first nations to declare a state of emergency in Europe. In Spain it was declared on 17 March and the government ordered a blockade to restrict travel and cancel non-essential services in order to stop the spread of the disease.

Social distancing and confinement were instrumental in stopping the spread of the coronavirus. However, confinement across the country is unprecedented and it is unknown how it may have affected the health and well-being of the general population and in particular cancer patients, a group of interest in this paper. In these circumstances, the sudden and stressful situation, in addition to prolonged stays at home, may imply a radical change in lifestyle behaviour, such as physical activity (Castañeda-Babarro et al., 2020), eating habits, mental health, quality of sleep, among others (Altena et al., 2020; Jiménez-Pavón et al., 2020; WHO Mental Health, 2020).

The project had to be interrupted due to confinement between March and June, and was not resumed until October 2020. During this time, a covid-free protocol was developed to ensure the safety of patients from any possible infection.

Whilst the project was temporarily halted, efforts were redirected towards the completion of a protocol article, culminating in a co-authorship on the publication titled "Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial"(Arietaleanizbeaskoa et al., 2021), which is appended in the annexes.

CAPÍTULO 2

OBJETIVOS E HIPÓTESIS

Capítulo 2. Objetivos e Hipótesis

El proyecto de tesis que se presenta tiene como objetivo analizar el impacto del COVID-19 en los pacientes de cáncer. En este análisis se estudiará tanto el impacto físico como psicológico que la enfermedad ha generado en los pacientes. Además, se analizará el parámetro de bioimpedancia conocido como ángulo de fase (PhA) y su posible relación con los parámetros físicos y psicológicos estudiados previamente. Para alcanzar estos objetivos se han planteado las siguientes hipótesis:

Objetivo principal

Analizar el comportamiento de los aspectos físicos y psicológicos en los pacientes de cáncer analizados, la influencia del COVID-19 y la relación de los parámetros físicos y psicológicos con el PhA.

Hipótesis

Para el Artículo 1 "Physiological and mental health changes in cancer patients during the COVID-19 state of emergency":

Hipótesis 1. Los pacientes de cáncer de Bizkaia sufren un deterioro tanto a nivel fisiológico como psicológico durante el estado de alarma por COVID-19.

Para el Artículo 2 "Association between PhA and Physical Performance Variables in Cancer Patients":

Hipótesis 2. Las variables de rendimiento físico se ven relacionados con los valores de PhA debido a la influencia de la integridad celular en el rendimiento físico.

Para el Artículo 3 "Association between Phase Angle and Subjective Perceptions of Health Variables in Cancer Patients":

Hipótesis 3. Las variables de estado psicológico y estado de salud autopercibido se ven relacionados con los valores de PhA debido a la influencia de la calidad de integridad celulares en el estado psicológico.

Objetivos específicos

Para el Artículo 1 "Physiological and mental health changes in cancer patients during the COVID-19 state of emergency":

1. Evaluar en pacientes de cáncer de Bizkaia el estado fisiológico y psicológico antes y después del estado de emergencia por COVID-19.
2. Evaluar en pacientes de cáncer de Bizkaia, el efecto fisiológico y psicológico generado durante el estado de emergencia por COVID-19 en España.

Para el Artículo 2 "Association between PhA and Physical Performance Variables in Cancer Patients":

3. Evaluar la relación entre el PhA y la aptitud física.
4. Determinar cómo afectan la edad y el sexo a la relación entre el PhA y el rendimiento físico en pacientes con cáncer en Bizkaia.

Para el Artículo 3 "Association between Phase Angle and Subjective Perceptions of health Variables in Cancer Patients"

5. Evaluar la relación entre el PhA y el estado psicológico y la autopercepción de la salud.
6. Analizar la viabilidad de una metodología de predicción del estado psicológico utilizando el PhA como valor medido.

En la tabla 1 observamos la síntesis de la relación entre los manuscritos y los objetivos e hipótesis planteadas en este capítulo.

TABLA 1: *Resumen de la relación entre manuscritos y los objetivos e hipótesis planteadas*

Artículo	Estado del trabajo	Objetivo	Hipótesis
Physiological and mental health changes in cancer patients during the COVID-19 state of emergency	Publicado	1-2	1
Association between PhA and Physical Performance Variables in Cancer Patients	Publicado	3-4	2
Association between Phase Angle and Subjective Perceptions of health Variables in Cancer Patients	Publicado	5-6	3

CAPÍTULO 3

METODOLOGÍA

Capítulo 3. Metodología

Contextualización

La presente Tesis Doctoral está compuesta por tres artículos que tienen la siguiente estructura: Introducción, Materiales y Métodos, Resultados, Discusión, Conclusiones y Referencias. El apartado de Referencias de cada artículo contiene la bibliografía incluida en cada uno de ellos. El apartado Referencias (Capítulo 6 de este documento), incluye las referencias mencionadas en la Justificación del Tema, Marco Teórico, Metodología y Discusión. Los tres artículos que se muestran en esta Tesis Doctoral han sido publicados en diversas revistas científicas:

- Artículo 1: Sport Science for Health (https://www.springer.com/journal/11332).
- Artículo 2: International Journal of Environmental Research and Public Health (https://www.mdpi.com/journal/ijerph).
- Artículo 3: Healthcare (https://www.mdpi.com/journal/healthcare)

La publicación de los tres artículos ha permitido presentar la tesis en la modalidad de "tesis por compendio de artículos", por lo cual en el siguiente capítulo 4. Resultados, los artículos se presentan publicados en revistas científicas. A continuación, se citan los 3 artículos y se explica cuál ha sido la aportación del autor de la tesis a cada uno de los trabajos (tabla 3). Las referencias completas a los artículos son:

- Artículo número 1: Gutiérrez-Santamaría, B., Castañeda-Babarro, A., Arietaleanizbeaskoa, M. S., Mendizabal-Gallastegui, N., Grandes, G., & Coca, A. (2022). Physiological and mental health changes in cancer patients during the COVID-19 state of emergency. *Sport sciences for health*, 1–8. Advance online publication. https://doi.org/10.1007/s11332-022-01008-w

- Artículo número 2: Gutiérrez-Santamaría, B., Martinez Aguirre-Betolaza, A., García-Álvarez, A., Arietaleanizbeaskoa, M. S., Mendizabal-Gallastegui, N., Grandes, G., Castañeda-Babarro, A., & Coca, A. (2023). Association between PhA and Physical Performance Variables in Cancer Patients. *International journal of environmental research and public health*, 20(2), 1145. https://doi.org/10.3390/ijerph20021145

- Artículo número 3: Gutiérrez-Santamaría B, Martinez Aguirre-Betolaza A, García-Álvarez A, Arietaleanizbeaskoa MS, Mendizabal-Gallastegui N, Grandes G, Coca A, Castañeda-Babarro A. Association between Phase Angle and Subjective Perceptions of Health Variables in Cancer Patients. *Healthcare*. 2023; 11(13):1852. https://doi.org/10.3390/healthcare11131852

El autor de la tesis ha realizado las siguientes contribuciones en los tres artículos: conceptualización, recolección de datos, análisis formal, investigación, metodología, recursos, redacción inicial del artículo, redacción-revisión y edición (tabla 8).

Muestras y Procedimiento

En la tabla 5 se indica un resumen detallado de las muestras de cada artículo.

Muestra del artículo 1

Treinta y tres participantes fueron remitidos por sus oncólogos o hematólogos en los hospitales de Cruces, Basurto y Galdakao en Bizkaia, como parte del proyecto principal, de los cuales, n=28 (84.8%) participantes eran mujeres y n=5 (15.2%) eran hombres. Los participantes tenían edades comprendidas entre los 38 y los 80 años con una media de 55.9 ±10.9 años. La altura comprendía los 143-180cm con una media de 162.11±8.30 cm. Un peso entre 51.9-115.1kg con 70.50 ±15.54kg de media y un IMC comprendido entre 19.89-43.64 Kg/m^2 con una media en el grupo de 26.80 ±5.43. Los diagnósticos de los cánceres en esta muestra se distribuyen de la siguiente forma: cáncer de mama, n=18 (54.5%); linfomas, n=6 (18.2%); canceres digestivos, n=4(12.1%) y finalmente otros, n=5 (15.2%).

TABLA 2: *Descripción de la muestra del artículo 1*

	N (%)	Mean±SD	Min-Max
Age (years)	33	55.9±10.9	38-80
Height (cm)	33	162.11±8.30	143-180
Weight (kg)	33	70.50±15.54	51.9-115.1
BMI (kg/m^2)	33	26.80±5.43	19.89-43.64
Surgery	25 (75.76)		
Metastatic	8 (24.2)		
DIAGNOSTIC			
Breast	18 (54,5)		
Lymphoma	6 (18,2)		
Digestive	4 (12,1)		
Others	5 (15,2)		
TREATMENT			
Chemotherapy	16 (48,5)		
Radiotherapy	2 (6,1)		
Hormone therapy	1 (3)		
Chemotherapy+Radiotherapy	8 (24,2)		
Chemotherapy + Radiotherapy + Hormone therapy	2 (6,1)		
Radiotherapy+ Hormone therapy	4 (12,1)		
SEX			
Female	28 (84.8)		
Male	5 (15.2)		

Notes: SD=standard deviation; Min=minimum; Max= Maximum; N=number of participants; BMI: Body mass index.

Muestra del artículo 2

311 pacientes formaron parte de la muestra para el artículo 2, de los cuales, n=225 (72.3%) participantes eran mujeres y n=86 (27.7%) eran hombres. La edad media fue de 55.54±10.98 años, altura 164.7±8.7 cm, peso 70.93±14.52 kg y BMI 26.1±4.9 kg/m^2.
En este artículo cabe destacar el valor medio de PhA 4.88±0.68 grados.
De los 311 pacientes incluidos en el estudio, 309 tenían al menos una medición de PhA, 239 tenían al menos dos, 201 tenían al menos tres y 94 tenían cuatro mediciones, respectivamente. Por lo tanto, los datos totales fueron 843 mediciones de PhA.

TABLA 3: *Descripción de la muestra del artículo 2*

Variable	n (%)	Mean ± SD
AGE (years)	311(100)	55.54 ± 10.98
SEX		
FEMALE	225(712.3)	
MALE	86(27.7)	
HEIGHT (cm)		164.7 ± 8.7
WEIGHT (kg)		70.93 ± 14.52
BMI (kg/m^2)		26.1 ± 4.9
PhA(°)		4.88 ± 0.68
400 mWT(seg.)		278.73 ± 53.37
VO_{2peak}(ml/kg/min)		15.31 ± 4
VT1		54.09 ± 16.81
VT2		80.97 ± 23.17
UBS		61.70 ± 23.17
LBS		33.26 ± 13.37
SURGERY	164(52.9)	
METASTATIC	50(19.6)	
CANCER STAGE		
I	48(15.4)	
II	80(25.7)	
III	62(19.9)	
IV	121(38.9)	

BMI: body mass index; PhA: phase angle;400 mWT: 400 m walking test; VO_{2peak}: peak consumption of VO_2; VT1: first ventilatory threshold; VT2: second ventilatory threshold; UBS: upper-body strength; LBS: Lower-Body strength.

Muestra del artículo tres

311 pacientes formaron parte de la muestra para el artículo 3, de los cuales, n=225 (72.3%) participantes eran mujeres y n=86 (27.7%) eran hombres. La edad media fue de 55.54±10.9 años, altura 164.7±8.7 cm, peso 70.9±14.5 kg y BMI 26.1±4.9 kg/m^2.

En este artículo cabe destacar el valor medio de PhA 4.9±0.7 grados.

De los 311 pacientes incluidos en el estudio, 309 tenían al menos una medición de PhA, 239 tenían al menos dos mediciones, 205 tenían al menos tres mediciones y 121 tenían cuatro mediciones. Por lo tanto, los datos totales son 874 mediciones de PhA.

TABLA 4: *descripción de la muestra del artículo 3*

Variable	n (%)	Mean±SD
AGE (years)	311(100)	55.5±10.9
SEX		
FEMALE	225(72.3)	-
MALE	86(27.65)	
HEIGHT (cm)		164.7±8.7
WEIGHT (kg)		70.9±14.5
BMI (kg/m^2)		26.1±4.9
PhA(º)		4.9±0.7
VO_{2peak} (ml/kg/min)		15.3±4
CHEMOTHERAPY	274(88.1)	
RADIOTHERAPY	92(29.6)	
BONE METASTASES	50(16.1)	
SURGERY	164(52.9)	
CANCER STAGE		
I	48(15.4)	
II	80(25.7)	
III	62(19.9)	
IV	121(38.9)	
CANCER TYPE		
Breast	132(42.4)	
Colorectal	24(7.7)	
Hematologic	69(22.2)	
Ovary	14(4.5)	
Pancreas	17(5.5)	
Lung	19(6.1)	
Other	36 (11.6)	
SMOKING		
Never	169(54.3)	
Ex-smoker	94(30.2)	
Smoker	48(15.4)	
COMORBILITIES		
Diabetes	27(8.7)	
COPD	16(5.1)	
Heart failure	8(2.6)	
Hypertension	68(21.9)	
Hyperlipidemia	70(22.5)	

BMI: body mass index; PhA: phase angle; VO_{2peak}: peak consume of VO_2; COPD: Chronic Obstructive Pulmonary Disease

TABLA 5: *Resumen de las muestras de cada artículo*

	Tipo de muestreo	Tamaño inicial de la muestra	Distribución por sexos
Muestra artículo 1	Muestreo aleatorio simple	N= 33	Mujeres=84.8% Hombres= 15.2%
Muestra artículo 2	Muestreo aleatorio simple	N=311	Mujeres= 72.3% Hombres= 27.7%
Muestra artículo 3	Muestreo aleatorio simple	N=311	Mujeres= 72.3% Hombres= 27.7%

Instrumentos de medición

Artículo uno

El presente estudio llevó a cabo una evaluación de múltiples variables en pacientes de cáncer, a fin de determinar el impacto del COVID-19 en su salud física y psicológica. El cuestionario utilizado para evaluar los niveles de AF fue el IPAQ versión corta (IPAQ-S) validado en español que pregunta sobre tres tipos específicos de actividad realizada durante los 7 días anteriores en los cuatro dominios (tiempo libre, trabajo, actividades domésticas y transporte). Se completó un IPAQ-S durante y después del estado de emergencia actividad cuando la evaluación se realizó después de las restricciones COVID-19.

La estatura de los sujetos se midió con un tallímetro de pared (Seca, Alemania) y la composición corporal con un analizador de bioimpedancia In-body 770 (In-body, Seúl, Corea). La frecuencia cardiaca en reposo y la presión arterial Omron X3 Comfort (HEM-7155-EO) (OMRON, Kyoto, Japón) se midieron sentados en una habitación tranquila.

Para determinar el VO_{2peak} (el valor VO_2 máximo en los últimos 30 segundos de la última etapa de la prueba submáxima realizada por los sujetos), se llevó a cabo una prueba en un cicloergómetro de frenado eléctrico (Ergostik, Geratherm Respiratory, Bad Kissingen, Alemania). Tras un calentamiento sin carga de 5 minutos, la carga se incrementó 10 W por minuto partiendo de una carga inicial de 20 W. Se indicó a los participantes que mantuvieran una cadencia superior a 65 rpm. El intercambio de gases se analizó durante toda la prueba con un analizador de gases (Ergostik, Sanro, España). El primer y segundo umbrales ventilatorios (VT1 y VT2) se obtuvieron utilizando el primer aumento exponencial del equivalente ventilatorio (VE) de oxígeno (O_2) (VE/VO_2). El VT2 o punto de compensación respiratoria (PCR) se determinó utilizando el cociente del equivalente ventilatorio (VE/VCO2). La prueba se llevó a cabo hasta que los sujetos alcanzaron su VT2 o frecuencia cardiaca al 85% de su máximo teórico.

Mediante la prueba de cinco repeticiones máximas (5RM) y utilizando máquinas de ejercicios de fuerza, se evaluó la fuerza muscular general con ejercicios de press de pecho (L070, BH, España), press de piernas (L050, BH, España). El protocolo utilizado fue el aplicado anteriormente consistente en un calentamiento de 10 repeticiones con un peso fácil (~50% de 5RM) y las 3-5 progresivas de 5RM hasta el agotamiento (~65,75,85,95% de 5RM).

Se utilizó una serie de cuestionarios para evaluar la calidad de vida específica del cáncer. La calidad de vida específica del cáncer se evalúa mediante el cuestionario 16 de la Organización Europea para la Investigación y el Tratamiento del Cáncer (EORTC QLQ-C-30), con una escala de 1 a 100; las puntuaciones más altas representan una mayor función/calidad de vida. Este cuestionario incluye cinco dominios funcionales (función física, cognitiva, emocional y social; las puntuaciones más altas representan una mayor función/calidad de vida) y tres escalas de síntomas (fatiga, dolor y náuseas; las puntuaciones más bajas indican una mayor calidad de vida/menor gravedad de los síntomas). Para evaluar la calidad de vida general relacionada con la salud se utilizó la Encuesta de Salud Breve de 36 ítems del Estudio de Resultados Médicos (SF-36) (escala de 1 a 100; las puntuaciones más altas indican una mayor calidad de vida) en los ámbitos del funcionamiento físico, el funcionamiento del rol físico, el dolor corporal, la salud general, la vitalidad, el funcionamiento social, el funcionamiento del rol emocional y la salud mental.

Artículo dos

La evaluación de las pruebas físicas de los pacientes comienza con la medición de la composición corporal, seguida de la evaluación de los 400 mWT y, por último, una prueba de fuerza de la parte superior e inferior del cuerpo.

La altura de los sujetos se midió con un tallímetro de pared (Seca, Alemania) y la composición corporal con un analizador de bioimpedancia Inbody 770 (In-body, Seúl, Corea) conforme al protocolo de medición (Walter-Kroker et al. 2011).

Los protocolos de marcha de 400 m consistían en una marcha rápida de 400 m administrada por personal formado y certificado. La caminata se realizó en un pasillo largo con conos en ambos extremos, separados por 20 m (Lange-Maia et al. 2015; Arietaleanizbeaskoa et al. 2021).

Para determinar el VO_{2peak} (el valor máximo de VO_2 en los últimos segundos de la última etapa de la prueba submáxima realizada), se realizó una prueba en un cicloergómetro con freno eléctrico (Ergostik, Geratherm Respiratory, Bad Kissingen, Alemania). Tras un calentamiento de 5 minutos sin carga, se aumentó la carga en 10 W por minuto a partir de una carga inicial de 20 W. Se indicó a los participantes que mantuvieran una cadencia superior a 65 rpm. El intercambio de gases se analizó durante toda la prueba con un analizador de gases (Ergostik, Sanro, España). El primer y segundo umbrales ventilatorios (VT1 y VT2) se obtuvieron mediante el primer aumento exponencial del oxígeno (O2) ventilatorio equivalente (VE/VO_2). El VT2 o punto de compensación respiratoria (PCR) se desterró mediante el método de la relación equivalente ventilatoria (VE/VCO2). La prueba se realiza hasta la confirmación de al menos uno de los criterios siguientes 1) Se observa el segundo umbral ventilatorio o el llamado "punto de compensación respiratoria" (PCR) a partir de las cifras de Wasserman (equivalentes respiratorios y cambios de presión parcial de O2 y CO2); 2) La relación de intercambio respiratorio (RER) ≥1,05 y la calificación del esfuerzo percibido (RPE)>8 en la escala de Borg de 0-10 puntos; 3) Los participantes muestran agotamiento volitivo sin cumplir los criterios anteriores (Gil-Rey et al. 2014; Mishra et al. 2012).

A través de la prueba de cinco repeticiones máximas (5RM) y utilizando máquinas de ejercicios de fuerza, se evaluó la fuerza muscular general con ejercicios de prensa de pecho (L070, BH, Vitoria, España), prensa de piernas (L050, BH, Vitoria, España) (Kraemer , Fleck, Steven J.,, 2005).

Artículo tres

La estatura de los pacientes se midió con un estadiómetro de pared (Seca, Alemania), las mediciones de la composición corporal se obtuvieron utilizando un analizador de bioimpedancia Inbody 770 (Inbody, Seúl, Corea). Estos procedimientos de medición siguieron estrictamente el protocolo establecido para garantizar la precisión y la coherencia. Las mediciones se realizaron de pie porque las investigaciones han demostrado que la posición interfiere con algunos de los valores de los que se toma el PhA, por lo que siempre se debe conocer la forma en que se midió la bioimpedancia. La PhA está compuesta por dos elementos: la reactancia (X) y la resistencia (R). Debe tenerse en cuenta que esta medición es una evaluación directa de la mem-brana celular, y no un cálculo basado en ecuaciones indirectas. La fórmula para el ángulo de fase es:

$\varphi = \text{arctg } X/R$

Se utilizó una serie de cuestionarios con buenas propiedades psicométricas para evaluar la salud general, la calidad de vida específica del cáncer y la fatiga relacionada con el cáncer. Estos cuestionarios son los utilizados en la práctica de los clínicos de los hospitales que participaron en el estudio. La Encuesta de Salud de Forma Corta de 36 ítems del Estudio de Resultados Médicos (SF-36) se utiliza para evaluar la calidad de vida general relacionada con la salud y la calidad de vida específica del cáncer se evalúa mediante el Cuestionario Básico de Calidad de Vida (QLQ-C-30). El SF-36 consta de ocho escalas de puntuación obtenidas mediante la suma ponderada de las preguntas de cada sección. Cada escala se transforma directamente en una escala de 0-100, asumiendo que cada pregunta tiene el mismo peso. Cuanto menor es la puntuación, mayor es el impedimento. Cuanto mayor es la puntuación, menor es la discapacidad. El Cuestionario de Salud General (GHQ-12) evalúa la morbilidad psicológica y los posibles trastornos psiquiátricos. Los ítems del GHQ-12 se puntúan en una escala de 4 puntos utilizando un marco temporal de "las dos últimas semanas". Hay tres formas de puntuar el GHQ-12: el método de puntuación bimodal GHQ (0-0-1-1), recomendado por los autores del test para su uso en entornos clínicos, y el método de puntuación Likert (0-1-2-3), que se utiliza habitualmente en investigación, y el método de puntuación C-GHQ, en el que se puntúan los ítems con frases positivas (0-0-1-1) y los ítems con frases negativas (0-1-1-1). Cuanto más grave es el problema, mayor es la puntuación (con un máximo de 9 para cada una de las subescalas). Por último, la fatiga relacionada con el cáncer se evalúa mediante la escala Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatiga). La escala de fatiga FACIT es una herramienta breve, de 13 ítems y fácil de administrar que mide el nivel de fatiga de una persona durante sus actividades diarias habituales en la última semana. El nivel de fatiga se mide en una escala Likert de cuatro puntos (4 = nada fatigado a 0 = muy fatigado); las puntuaciones más bajas indican mayor fatiga.

Análisis Estadísticos

Artículo uno

Se utilizó la prueba T para examinar las diferencias en los parámetros fisiológicos (masa musculoesquelética, masa grasa, grasa visceral, Wmax, WVT2 y fuerza corporal superior e inferior) y parámetros psicológicos de calidad de vida (EORTCQLQ- 30 y SF-36) en dos periodos de tiempo (tiempo: pre-post restricciones pandémicas). Para los análisis psicométricos, se evaluaron la agrupación y el escalado originales para las dimensiones múltiples de los de los cuestionarios y, antes del análisis, se utilizó la prueba de fiabilidad Alfa de Cronbach antes del análisis. Todos los análisis se realizaron en SPSS v.26 con un nivel alfa fijado en 0,05.

Artículo dos

La relación entre el ángulo de fase y las pruebas físicas se analizó mediante modelos de regresión lineal mixta (SAS: PROC MIXED), que tienen en cuenta las correlaciones entre mediciones repetidas de cada paciente. La edad y el sexo se utilizaron como variables de ajuste, y el mejor modelo se eligió siguiendo una estrategia paso a paso hacia atrás mediante pruebas de razón de verosimilitudes (con un criterio de significación de la razón de verosimilitudes) (con un criterio de significación de $p < 0,05$). También se realizaron pruebas de correlación entre el PhA y las variables físicas. Se realizaron análisis de subgrupos para estudiar si la relación entre el PhA y las variables de resultado era diferente en función del sexo o la edad, probando términos de interacción entre estas covariables y la fase angular ($p < 0,01$).

Todos los análisis se realizaron con SAS 9.4 (SAS Institue Inc., Cary, NC, EE.UU.) y R.4.2.2 (The R Foundation, Viena, Austria).

Artículo tres

Se emplearon modelos de regresión lineal mixta para examinar la asociación entre el PhA y las pruebas psicológicas (SAS: PROC MIXED), que tienen en cuenta las correlaciones inherentes observadas en las mediciones repetidas en cada paciente. Se incorporaron al análisis variables de ajuste como la edad, el sexo, el tipo de cáncer, el estadio, los tratamientos, el hábito de fumar y las comorbilidades. Cabe destacar que ninguna de estas variables presentaba valores perdidos. Se empleó una estrategia regresiva por pasos para identificar el modelo más apropiado, guiada por pruebas de cociente de verosimilitudes. El proceso de selección consistió en desplazar iterativamente las variables que no contribuían significativamente a la capacidad explicativa del modelo, con un criterio de significación fijado en $p < 0{,}05$. El modelo final se determinó siguiendo este procedimiento. La proporción de varianza explicada por las variables fijas en los modelos se comunicó mediante la R cuadrada marginal obtenida por el método de Nakagawa. También se realizaron pruebas de correlación entre el PhA y las variables psicológicas. Todos los análisis se realizaron con SAS 9.4 y R.

Garantías Éticas de la Investigación

El presente proyecto de investigación cumplió los requisitos la de declaración de Helsinki de la Asociación Médica Mundial de principios éticos para las investigaciones médicas en seres humanos.

Antes del inicio de cualquier valoración, se solicitó la aprobación del estudio por el Comité de Ética del país vasco, que fue concedida con el código “PI2019016". El proyecto considera el reglamento de protección de datos personales (UE 2016/679) aprobado por la Comisión y el Consejo de la UE en abril de 2016 relacionado con el I) procedimiento de consentimiento informado; II) el acceso a los datos personales; III) el uso de datos para el interés público; y IV) las responsabilidades de los investigadores responsables del proyecto. Para garantizar la exactitud de la recogida de datos y la comprensión por parte de los alumnos de la naturaleza del estudio, el investigador principal del estudio estuvo presente durante la administración de los cuestionarios. Antes de la administración del cuestionario, se informó a todos los participantes de su voluntad de participar y de la confidencialidad de los datos recogidos.

CAPÍTULO 4

RESULTADOS

Capítulo 4. Resultados

En este apartado presentamos los tres artículos que constituyen el núcleo de esta tesis doctoral, todos ellos ya publicados (ver tabla 6). La tabla 3 muestra un resumen de las conclusiones destacadas de cada una de las publicaciones, las cuales dan respuesta a los objetivos e hipótesis planteados en el presente proyecto.

TABLA 6: *Resumen de artículos y resultados presentados que componen la tesis*

Modelo de Estudio	Artículos	Objetivos	Conclusiones
1. observacional descriptivo	Gutiérrez-Santamaría, B., Castañeda-Babarro, A., Arietaleanizbeaskoa, M. S., Mendizabal-Gallastegui, N., Grandes, G., & Coca, A. (2022). Physiological and mental health changes in cancer patients during the COVID-19 state of emergency. *Sport sciences for health*, 1–8. Advance online publication. https://doi.org/10.1007/s11332-022-01008-w	1-2	Una menor actividad física conlleva una adaptación fisiológica negativa, que afecta especialmente a los niveles cardiovasculares y de cardiovascular y de fuerza. Si bien es importante mantener la cantidad e intensidad de ejercicio de la población general, la capacidad física de este grupo especialmente vulnerable es vital para su salud y bienestar. La capacidad física de este grupo especialmente vulnerable es vital para su salud y bienestar.
2. observacional descriptivo	Gutiérrez-Santamaría, B., Martinez Aguirre-Betolaza, A., García-Álvarez, A., Arietaleanizbeaskoa, M. S., Mendizabal-Gallastegui, N., Grandes, G., Castañeda-Babarro, A., & Coca, A. (2023). Association between PhA and Physical Performance Variables in Cancer Patients. *International journal of environmental research and public health*, 20(2), 1145. https://doi.org/10.3390/ijerph20021145	3-4	Se ha demostrado que los datos de PhA obtenidos directamente de la prueba BIA están muy relacionados con rendimiento físico y, por tanto, proporcionan información sobre los cambios del paciente durante el tratamiento. En particular, se ha demostrado que la relación con el mWT 400 es una prueba muy válida para predecir problemas de sarcopenia y estimar el $VO_{2Máx}$ de los pacientes, especialmente en adultos mayores, e incluso para relacionarse con la muerte por cualquier causa.
3. Observacional descriptivo	Gutiérrez-Santamaría, B.; Martinez Aguirre-Betolaza, A.; García-Álvarez, A.; Arietaleanizbeaskoa, M.S.; Mendizabal-Gallastegui, N.; Grandes, G.; Coca, A.; Castañeda-Babarro, A. Association between Phase Angle and Subjective perceptions of Health Variables in Cancer Patients.*Healthcare* 2023, 11, 1852. https://doi.org/10.3390/healthcare11131852	5-6	El PhA es una herramienta útil para evaluar la percepción subjetiva de la salud de los pacientes con cáncer, especialmente en lo que respecta a los factores psicológicos. Aunque existe una correlación estadísticamente significativa, es necesario seguir investigando antes de aplicarlo con confianza en la práctica clínica. El valor predictivo actual de este predictor para determinados aspectos psicológicos es limitado.

En la tabla 7 se muestran las características de las revistas en las que se han publicado los artículos mencionados.

TABLA 7: *Índice de calidad de las revistas*

Revista	ISSN	Categoría	PR	FI	Q	Editorial
Sport Sciences for Health	1824-7490	Sport sciences	SI	1,5	3	Springer
International Journal of Environmental Research and Public Health	1660-4601	Special Issue *"Application of Bioelectrical Impedance Analysis (BIA) in Human Health and Life"*	SI	4,614	1	MDPI
HealthCare	2227-9032	Health Policy	SI	2,8	2	MDPI

Nota: ISSN: International Standard Serial Number; FI: Factor de Impacto; PR: Revisión por pares; Q: cuartil (JCR)

A continuación, en la tabla 8 se indica la aportación exacta realizada por cada uno de los autores en los diferentes artículos que se presentan. Posteriormente, se adjuntan los artículos que conforman este manuscrito.

TABLA 8: *Participación de los autores en cada uno de los manuscritos*

Contribución	Artículo 1	Artículo 2	Artículo 3
Conceptualización	B.G.-S., A.C.-B, A.C.	B.G.-S., A.M.A.-B., M.S.A., G.G., A.C.	B.G.-S., A.M.A.-B., M.S.A., G.G., N.M.-G.; A.C.
Recolección de datos	B.G.-S.	B.G.-S.	B.G.-S.
Análisis formal	B.G.-S., A.C.	A.G.-Á., A.C.	A.G.-Á., A.C.
Investigación	B.G.-S., A.C.-B. and A.C.	B.G.-S., A.M.A.-B., A.C.-B.; A.C.	B.G.-S., A.M.A.-B., A.C.-B.; A.C.
Metodología	B.G.-S., A.M.A.-B., G.G., A.C.-B., A.C.	B.G.-S., A.M.A.-B., G.G., A.C.-B., A.C.	B.G.-S., A.M.A.-B., A.C.-B., G.G.; A.C.
Supervisión	B.G.-S., A.C.-B., A.C	B.G.-S., A.M.A.-B., A.C.-B., A.C	B.G.-S., A.M.A.-B., A.C.-B., A.C

Redacción inicial del artículo	B.G.-S.	B.G.-S., A.M.A.-B., A.C.-B.	B.G.-S., A.M.A.-B., A.C.-B.
Redacción-revisión y edición	B.G.-S., M.S.A., N.M.-G., G.G., A.C.-B., A.C.	B.G.-S., A.M.A.-B., M.S.A., N.M.-G., G.G., A.C.-B., A.C.	B.G.-S., A.M.A.-B., M.S.A., N.M.-G., G.G., A.C.-B., A.C.
Nota B.G.-S.=Borja Gutiérrez Santamaría; A.M.A.-B.= Aitor Martínez de Aguirre; M.S.A.= María Soledad Arietaleanizbeaskoasarabia; A.G.-Á. =Arturo García Álvarez; N.M.-G.= Nere Mendizábal Gallastegui; G.G.= Gonzalo Grandes; A.C.-B.=Arkaitz Castañeda Babarro; A.C.=Aitor Coca. Todos los autores han leído y aceptado la versión publicada del manuscrito.			

Artículo uno

Physical Physiological and mental health changes in cancer patients during the COVID-19 state of emergency

RESUMEN

Antecedentes

Debido a la pandemia de COVID-19 a la que nos enfrentamos actualmente, muchos gobiernos de todo el mundo han declarado el estado de emergencia e incluso el confinamiento. Esta situación estresante, además de las estancias prolongadas en casa, puede implicar un cambio radical en el comportamiento del estilo de vida y la actividad física (AF). El objetivo de este estudio es evaluar los efectos fisiológicos y psicológicos en pacientes oncológicos que cambiaron sus hábitos de AF durante el estado de emergencia COVID-19 en España.

Métodos

Se evaluó a 33 participantes antes y después del estado de emergencia. Se utilizó una serie de cuestionarios para evaluar la calidad de vida específica del cáncer.

Resultados

Los resultados más relevantes revelaron un tiempo significativamente menor de caminar ($p < 0,001$) y de estar sentado ($p = 0,014$). La fuerza de la parte superior e inferior del cuerpo también disminuyeron significativamente ($p = 0,009$ y 0,012, respectivamente) y el consumo de oxígeno (VO_{2pico}) ($p = 0,023$). Ninguno de los parámetros analizados mostró diferencias significativas para los aspectos psicológicos (QLQ-C-30y SF-36) y la composición corporal.

Conclusiones

Una menor actividad física conlleva una adaptación fisiológica negativa, que afecta especialmente a los niveles cardiovasculares y de cardiovascular y de fuerza. Si bien es importante mantener la cantidad e intensidad de ejercicio de la población general, la capacidad física de este grupo especialmente vulnerable es vital para su salud y bienestar.

Sport Sciences for Health
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ORIGINAL ARTICLE

Physiological and mental health changes in cancer patients during the COVID-19 state of emergency

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Abstract

Backgrounds Due to the COVID-19 pandemic that we are currently facing, many governments across the world have declared a state of emergency and even confinements. This stressful situation, in addition to prolonged stays at home, may imply a radical change in lifestyle behavior and physical activity (PA). The aim of this study is to evaluate the physiological and psychological effects in cancer patients who changed their PA habits during the COVID-19 state of emergency in Spain.

Methods Thirty-three participants were evaluated pre- and post-state of emergency. A series of questionnaires was used to assess cancer-specific quality of life.

Results The most relevant results revealed significantly lower walking time ($p<0.001$) and sitting time ($p=0.014$). Upper and lower body strength also decreased significantly ($p=0.009$ and 0.012, respectively) and oxygen consumption (VO2 peak) ($p=0.023$). None of the parameters analysed showed significant differences for psychological aspects (QLQ-C-30 and SF-36) and body composition.

Conclusion Lower physical activity leads to negative physiological adaptation, particularly affecting cardiovascular and strength levels. While it is important to maintain the general population's amount and intensity of exercise, this particularly vulnerable group's physical capacity is vital to their health and well-being.

Keywords QLQ-C-30 · SF-36 · IPAQ-S · Cancer · Physical activity

Introduction

Cancer is one of the principal causes of morbi-mortality in the world with around 19 million new cases recorded in 2020 and population estimates indicate that the number of new cases is expected to rise in the next 2 decades to 29.5 million by 2040 [1]. Almost half of the world population will be diagnosed with cancer at some point in their lives and many of these new cases will receive intensive treatment that will reduce their quality of life and produce functional alterations in other organs, increasing the risk of suffering from other types of diseases [2]. Nevertheless, due to advances

Dr. Coca had been part of Deusto University (affiliation 1) during the most part of the study.

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in medicine in general, and cancer treatments in particular, there are an increasing number of cancer survivors (CS) (person who suffers from cancer, measured from the moment of the diagnosis until the end of his or her life) [3].

It has been observed that physical inactivity ranks fourth among the risk factors for global mortality (6% of deaths registered worldwide). Additionally, physical inactivity is estimated to be the primary cause of approximately 21 to 25% of colon and breast cancers, 27% of diabetes cases, and approximately 30% of the burden of ischemic heart disease (WHO, 2010).

Exercise contributes to improved health and functional outcomes in the cancer population [4] and, based on review of published evidence regarding the safety and efficacy of exercise in cancer survivors, Schmitz and colleagues state that physical activity (PA) is completely safe and recommend it [2].

A large body of evidence has recommended that cancer patients meet the public health guidelines for PA and the necessary exercise prescription particularly requires consideration of many aspects to positively and safely impact individuals with a cancer diagnosis [5]. Despite being PA recommendations for cancer survivors, they are the same as those set for the healthy population. However, in terms of PA, the same intensity cannot be recommended [6]. In some advanced stages of the disease, cachexia, among other secondary effects of cancer and its treatment, is one of the metabolic multifactorial syndromes that affect a large number of patients. It is caused by a combination of reduced food intake and abnormal metabolism which results in a negative balance of energy and protein synthesis [7].

From the psychological approach, an important revision from the American College of Sport Medicine [2] supports that PA is a consolidated therapy for prevention and management not only in depression and anxiety scenarios but also in several other psychological outcomes like self-esteem and mood during treatment. Moreover, physical exercise program intervention results in statistically significant improvements in quality-of-life (QoL) test scores [8].

Due to the COVID-19 pandemic that we are currently experiencing [9], many governments across the world have declared a state of emergency and even confinements, which is the case of the Government of Spain [10]. This stressful situation, in addition to prolonged stays at home, may imply a radical change in lifestyle behavior and physical activity [11]. However, its impact on the health and well-being of the general population, and the population with cancer in particular, is not known.

The aim of this study is to evaluate the physiological and psychological effect in cancer patients who changed their PA habits during the COVID-19 state of emergency in Spain.

We hypothesise that physiological and psychological parameters worsened during the COVID-19 state of alarm.

Materials and methods

Participants

Thirty-three participants, whose characteristics are shown in Table 1, were referred by their oncologists or hematologists at the Cruces, Basurto, and Galdakao hospitals in Bizkaia/Biscay, Basque Country, Spain, as part of the main project called Bizi Orain, which consist in 3 months of physical exercise (progressive resistance and aerobic training) supervised and controlled by professional physicians. Furthermore, the program had different physical and psychological valuations at the moment of the starting the program, at the 3, 6, and 12 months [12].

All patients were participants in a physical exercise intervention program Bizi Orain [12] for cancer patients. Although they had completed the first physical evaluation, they did not begin the training program due to the COVID-19 state of emergency declared in Spain. This evaluation consisted of pre-state of emergency measures of the different parameters in our study. After the state of emergency was lifted and once safety was guaranteed, the assessments were performed again to begin with the program. Thus, these are the assessments used as post-state of emergency for the present study.

Inclusion and exclusion criteria followed our protocol [12]. All the subjects were natives of Spain. The study protocol was conducted ethically according to international as well as journal standards [13] and was approved by the Institutional Research Ethics Committee (PI2019016). The trial was registered on January 18, 2019 (Clinical Trials.gov NCT03819595).

Measurement: outcome variables

Patients were physically and psychologically evaluated at the University of Deusto, (Biscay, Spain) at the same times of day (9:00 to 14:00) and in similar environmental conditions (temperature, ± 21 °C; relative humidity, 50–55%; barometric pressure, ± 720 mmHg).

On 14 March 2020, a state of alarm with the resulting confinement was declared in Spain and remained in effect until 21 June 2020, when restrictions were gradually lifted, but maintaining mobility restrictions, closure of sports facilities, gymnasiums, and nightlife venues. Curfews were imposed from 22:00 to 6:00 [10]. These restrictions may have influenced the amount of physical activity (Fig. 1).

The questionnaire used to evaluate the levels of PA was the IPAQ short version (IPAQ-S) validated in Spanish

Table 1 Characteristics of the sample

	N (%)	Mean±SD	Min-Max
Age (years)	33	55.9±10.9	38–80
Height (cm)	33	162.11±8.30	143–180
Weight (kg)	33	70.50±15.54	51.9–115.1
BMI (kg/m2)	33	26.80±5.43	19.89–43.64
Surgery	25 (75.76)		
Metastatic	8 (24.2)		
Diagnostic			
Breast	18 (54,5)		
Lymphoma	6 (18,2)		
Digestive	4 (12,1)		
Others	5 (15,2)		
Treatment			
Chemotherapy	16 (48,5)		
Radiotherapy	2 (6,1)		
Hormone therapy	1 (3)		
Chemotherapy+radiotherapy	8 (24,2)		
Chemotherapy + radiotherapy + hormone therapy	2 (6,1)		
Radiotherapy+ Hormone therapy	4 (12,1)		
Sex			
Female	28 (84.8)		
Male	5 (15.2)		

Notes: *SD* standard deviation; *Min* minimum; *Max* Maximum; *N* number of participants; *BMI* Body mass index

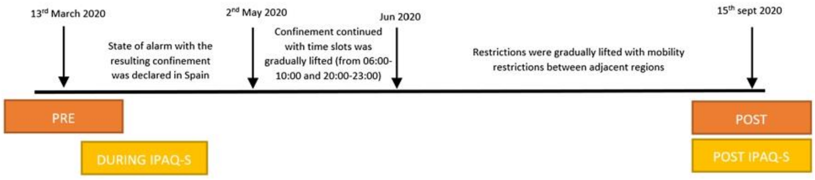

Fig. 1 Evolution of phases during the COVID-19 pandemic and restrictions

(Wolin et al. 2008) which asks about three specific types of activity undertaken during the previous 7 days in the four domains (leisure time, work, household activities, and transport). An IPAQ-S during and post-state of emergency activity was completed when the evaluation was performed after the COVID-19 restrictions.

The subjects' height was measured using a wall stadiometer (Seca, Germany) and body composition with an Inbody 770 bioimpedance analyzer (In-body, Seoul, Korea). Resting heart rate and blood pressure Omron X3 Comfort (HEM-7155-EO) (OMRON, Kyoto, Japan) were measured seated in a quiet room.

To determine the VO2peak (the peak VO2 value in the last 30 s of the last stage of the test sub-maximal test perform by the subjects), a test performed on an electric braking cycle-ergometer (Ergostik, Geratherm Respiratory, Bad Kissingen, Germany). Following an unloaded 5-min warm-up, the load was increased 10 W per minute starting from an initial load of 20 W. Participants were instructed to maintain cadence over 65 rpm. Gas exchange was analysed throughout the test with a gas analyser (Ergostik, Sanro, Spain). The first and second ventilatory thresholds (VT1 and VT2) were obtained using the first exponential increase in the oxygen (O2) ventilatory (VE) equivalent (VE/VO2). The VT2 or respiratory compensation point (RCP) was determined using the ventilatory equivalent method (VE/VCO2) ratio [6, 14]. The test was carried out until the subjects reached their VT2 or heart rate at 85% of their theoretical maximum.

Through the test of five maximum repetitions (5RM) and using strength exercise machines, general muscular strength was evaluated with chest press exercises (L070, BH, Spain) and leg press (L050, BH, Spain). The protocol used was the one previously applied [15], consisting of 10 repetitions warm-up with an easy weight (~50% of 5RM) and the 3–5 progressive 5RM until exhaustion (~65,75,85,95% of 5RM).

A series of questionnaires was used to assess cancer-specific quality of life. Cancer-specific quality of life is evaluated by the European Organization for Research and Treatment of Cancer (EORTC QLQ-C-30) questionnaire [16] scaled from 1 to 100, and higher scores represent greater function/quality of life. This questionnaire includes five functional domains (physical, cognitive, emotional, and social role; higher scores represent greater function/quality of life) and three symptom scales (fatigue, pain, and nausea; lower scores indicating a higher quality of life/less symptom severity). The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (scaled from 1 to 100, higher scores indicating greater quality of life) was used to assess general health-related quality-of-life status across physical functioning, physical role functioning, bodily pain, general health, vitality, social functioning, emotional role functioning, and mental health domains [17].

Statistical analysis

T test was used to examine differences in physiological parameters (musculoskeletal mass, fat mass, visceral fat, Wmax, WVT2, and Upper and Lower body strength) and psychological parameters of quality of life (EORTC-QLQ-30 and SF-36) in two time periods (time: pre-versus post-pandemic restrictions). For the psychometric analyses, grouping and scaling based on the original papers [18, 19] were assessed for the multi dimensions of the questionnaires and Cronbach´s Alpha reliability test was used prior to the analysis. All analyses were performed in SPSS v.26 with alpha level set at 0.05.

Results

As shown in Table 2, body composition values remained similar both before and after the state of alarm. Musculoskeletal mass measures did not evidence significant differences ($p = 0.934$). The percentage of fat mass presented a slight insignificant decrease ($p = 0.354$), and finally, visceral fat also showed an insignificant reduction ($p = 0.791$).

Table 3 shows the differences in PA, sitting time (ST), and walking time (WT). Regarding vigorous physical activity (VPA) and moderate physical activity (MPA), no significant differences were observed between the activity measurements during and after the state of emergency. It

Table 2 Body composition levels and physical and physiological parameters pre and post the break in PA due to the state of emergency

Variable	Pre (Mean ± SD)	Post (Mean ± SD)	*P* value	*d*-Cohen
Musculoskeletal mass (kg)	23.8 ± 5.4	23.8 ± 5.6	0.934	0
Fat mass (%)	37.1 ± 8.4	35.5 ± 10.7	0.354	0.16
Visceral fat (cm2)	134.2 ± 54.2	132.4 ± 55.3	0.791	0.03
VO2peak (mL•min•kg^{-1})	17.03 ± 5.08	15.42 ± 3.98	0.023*	0.35
WMAX (W)	90.34 ± 28.85	86.55 ± 27.03	0.078	0.14
WVT2 (W)	88.57 ± 26.06	85 ± 26.60	0.106	0.13
Lower body strength (kg)	61.96 ± 22.10	52.86 ± 23.18	0.012*	0.40
Upper body strength (kg)	30.39 ± 14.46	24.95 ± 14.27	0.009*	0.38

*$p < 0.05$; *WMAX* Watts maximum; *WVT2* Watts at ventilatory threshold 2

Table 3 Variations in levels of PA and time sitting during and after the state of emergency due to COVID-19.

Variable	During	Post	*P* value	*d*-Cohen
VPA (min/week)	1.88 ± 10.61	0	0.325	<0.01
MPA (min/week)	117.50 ± 160.02	91.56 ± 124.24	0.349	0.18
Walking time (min/week)	76 ± 113.08	327.50 ± 206.92	< 0.001*	1.51
Sitting time (hours/day)	7.53 ± 2.66	6.63 ± 5	0.014*	0.47

VPA vigorous physical activity; *MPV* moderate physical activity
(*$p < 0.05$)

should be noted that no patient except one reported vigorous-intensity activity during the state of emergency and no patients reported VPA post-state of emergency. Alternatively, with walking and sitting time, significant differences were reported in both variables with p values < 0.001 and 0.014, respectively. Meanwhile, considerable growth was observed in the number of hours invested in walking in comparison to such time during the state of emergency ($d = 1.51$). As for the sitting hours, a slight but significant decrease was observed after the state of emergency.

Large but insignificant decreases ($p = 0.0789$) were found for cardiovascular condition (Table 2) in the amount of Wmax the patients were capable of moving. In turn, the measure of the VT2 watts was also slightly lower after the state of emergency. However, in spite of observing a slight watt decrease of 4.1%, the reduction ($p = 0.106$) is not statistically significant. The last physiological parameter for cardiovascular function measured by peak oxygen consumption (VO2peak) shows a significant decrease ($p = 0.023$), evidenced by $n = 20$ who reduced their VO2peak and n = 8 who raised it. Finally, upper and lower body strength levels were significantly lower ($p = 0.012$ and $p = 0.009$, respectively).

Finally, the results shown in Table 4, obtained with the SF-36 and EORTC-QLQ-30 questionnaires, did not evidence significant differences in any of the variables measured therein.

Discussion

Fulfilling the objective of the research to observe the changes produced in terms of PA during the time of the state of alarm by COVID-19 and its implication in physiological and psychological aspects, the most relevant results revealed significantly lower WT and ST. Upper and lower body strength also decreased significantly. None of the parameters analysed showed significant differences for psychological aspects.

No modifications in body composition were found between the pre- and post-state of emergency levels. The patients' body composition may already have been modified by their disease, in which higher fat mass and lower muscle mass are often observed [20].

There is a growing body of evidence noting less physical activity during a state of alarm with restricted mobility such as that caused by COVID-19. For this reason, there are now systematic reviews on the general population's level of physical activity during the recent state of emergency [21]. The literature indicates less physical activity and more sitting time.

The sample studied did not show significant differences in VPA, which may be explained by the low levels of intense activity due to the pathology itself which induces chronic fatigue that could hinder exercise [22]. Due to the pathology, these patients are sometimes recommended to stop VPA given the risk of carrying out these activities without professional supervision, and that is why, many doctors advise against carrying out this type of intense practice [23]. However, breaking out of this vicious cycle and beginning to exercise are a good strategy to fight cancer-related chronic fatigue [24]. It is important to note that our sample does not reach the 75 min/week minimum levels of vigorous activity recommended by the WHO. While these are recommendations for the healthy population, compliance with the VPA and MPA guidelines tends to improve the prognosis of persons with pathologies, and particularly cancer survivors [25], 26. Intense or high-intensity activities are advisable as they result in adaptation similar to that generated by longer periods of moderate exercise but require less time (40% of the time). We could therefore state that vigorous exercise is more effective for achieving beneficial physicological adaptation, and is a safe option [25, 27, 28].

Higher levels have been noted with MPA and this indicates that this group does more MPA than VPA, although they do not reach the WHO's recommended minimum guidelines of > 150 min/week MPA [29]. The time devoted to walking was reduced during the state of emergency, possibly due to confinement (during the state of alarm) or restricted mobility between areas. However, once the mobility restrictions were lifted, a sharp rise in walking time was noted. The logical consequence of restrictions on mobility during the state of alarm would be for walking time to decrease, and likewise for walking time to increase as restrictions were lifted.

This may have been due to the subjects' perception that being outdoors involved a lower risk of COVID-19 infection. In addition, another important factor is the recommendation that the doctor gives to these patients to walk [30], age is

Table 4 Psychological differences between pre- and post-state of emergency due to COVID and their significance (p value)

Variable	Pre	Post	*P* value	*d*-Cohen
EORTC-QLQ-30				
Global health status	4.74 ± 1.15	4.83 ± 1.19	0.684	0.08
Emotion role	1.56 ± 0.63	1.55 ± 0.56	0.798	0.02
Social function	1.56 ± 0.83	1.67 ± 0.92	0.408	0.12
Cognitive function	1.53 ± 0.71	1.54 ± 0.75	0.851	0.01
SF-36				
Emotional role	1.77 ± 0.39	1.87 ± 0.38	0.096	0.26
Mental health	4.26 ± 0.82	4.14 ± 0.75	0.568	0.15

EORTC QLQ-C-30: European Organization for Research and Treatment of Cancer; SF-36: Short-Form Health Survey also a factor that makes patients walk more and perform less VPA or MPA [31].

As walking time was reduced, sitting time increased and then fell once again when walking time increased.

Although our sample is formed by a population that is being or has been treated for cancer, some similar patterns have been observed in a study with 3800 healthy subjects before and after the state of emergency. Performed by Spanish researchers, it showed lower VPA, MPA, and walking time but higher sitting time [11]. This behavior related to time devoted to physical activity was confirmed through reviews of articles on the effects of confinement on physical activity [21].

Lower physical activity leads to negative physiological adaptation, particularly affecting cardiovascular and strength levels. According to their age and prognosis, patients may even lose their autonomy [32].

Oxygen consumption is a predictor of survival in the general population [33, 34] and in the cancer population [2, 35]. We found a significantly lower V02peak during the period studied. The V02peak depends on three main components: oxygen uptake, the blood's oxygen-carrying capacity to the muscles, and mitochondrial functionality [36]. When observing the effects of lack of exercise on the V02peak components, we find that 2 days of no exercise lowers plasma levels by 5 to 12% [37]. An 8% drop in cardiac output, responsible for carrying oxygen, was noted, together with other cardiac modifications after 21 days with no exercise training [38]. Muscular capillarisation also fell to pre-exercise training levels in just 4 weeks [39]. Finally, a 12 to 28% drop in mitochondrial production of ATP was noted 3 weeks after stopping exercise [39]. 8 weeks of combined exercise training followed by 8 weeks of no exercise in breast cancer patients evidenced 8% lower VO2peak for cardiovascular levels [40]. Seeing that the variations are important in a relatively short period of time in this patient is important to not been more than few days without exercise to maintain the adaptations. In turn, decreased PA led to significantly lower strength levels during the COVID-19 state of alarm.

The articles by Mujika and Padilla [41, 42] explain how strength levels can drop by 7–12% during an 8 to 12 week period of no exercise training. Although these patients were not totally inactive, their strength levels fell (14.68% for lower body and 17.9% for upper body) more than expected for the exercise population in the same situation. Mujika and Padilla's article is carried out in a young athlete population, and seeing that it does not differ much from our subjects, we could identify a pattern of loss of strength regardless of the age and sex of the subjects. It is true that the older you are, the loss of muscle mass and strength would be increased, but in this case, it behaves in a similar way. This loss may have been due to their treatment, although muscle mass loss was not found as was anticipated for these patients and their treatment [43, 44]. In line with this evidence, our study sample's strength levels decreased around 14 to 15%, which is similar to the losses expected in the healthy exercise population. The study cited above [40] found lower strength levels similar to the findings in our sample of cancer patients. Such reduced strength levels might have been due to neuronal disadaptation caused by lack of strength training as the peripheral adaptations (amount of muscle mass) did not change.

No significant psychological differences were observed in any of the variables measured with the SF-36 and EORTC QLQ-30 questionnaires. This may be explained by the negative results that these patients show on this type of questionnaire measuring quality of life, since their health problems cause them to have a poor perception of this aspect [45]. In studies on cancer patients, physical exercise was found to significantly improve the global health status measured by the EORTC-QLQ-30 questionnaire, although there were no significant differences when pre-intervention values were compared with those recorded during the state of emergency. No significant differences were found in any of the items when comparing pre-exercise training (without having begun the exercise programme) and the findings obtained after a state of emergency. Thus, the conclusion is that subjective values for quality of life would return to their initial levels after a state of emergency [40]. The emotional state item showed a tendency toward significance. The respondents' subjective assessment of their emotional state could have become worse due to the restrictions imposed during the state of alarm, which is the case of healthy people who evidenced greater anxiety, depression, and emotional impact.

In general, the behavior of the healthy population in the exceptional situation of COVID-19 had been studied, but little was known about cancer patients regardless of sex and age. Many parameters (nutrition, genetics, socio-economic situation, etc.) could have affected the results of our study, but we have been able to show how the results are in line with the results obtained in a healthy population.

Conclusion

Aware of the role that PA plays in individuals' health, functioning as a polypill with broad benefits in the case of chronic diseases [46], it is also important to highlight the importance of PA to the cancer population. While no differences in body composition or psychological state were found in our sample, possibly due to this group's poor parameters to begin with, there was a decline in strength and fitness level as well as less time of PA levels during this period. Attention should focus on maintaining or increasing PA levels in the event of another state of alarm in the future, because while it is important to maintain the general population's amount and intensity of exercise, this particularly vulnerable group's physical capacity is vital to their health and well-being [25] Even if there are no significant changes in psychological aspects, it is an important aspect to consider during treatment to provide them with the necessary help.

Strengths and limitations

This is one of the first studies that measures changes in lifestyle and psychological variables in cancer patients due to the new situation generated by the COVID-19 pandemic, considering psychological and physiological aspects.

The main limitations of this study are that the study was a part of larger project that was being conducted as the COVID-19 pandemic started. As such, the sample of this study was the patients that were evaluated to start the research project and did not initiate any activities. These patients were contacted again to start the project once it was allowed and we retested them. This explains that the sample is small and heterogenous (with a large age dispersion that has to be taken care of when reading the results), besides the study was not randomized. We also could not compare with a control group because of the nature of the study, and the COVID-19 was the same for all the patients.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study complies with the Declaration of Helsinki and its revisions, as well as with good clinical practice. The Ethics Committee of the Basque Country approved the study in the health centers ensuring it would be implemented in compliance with the established regulations. Regarding data confidentiality, only the study researchers have access to the data of individuals who agree to participate in the study, in compliance with the Organic Act 15/1999 of December 2013, on the protection of personal data and its 2011 revision.

Informed consent The project is part of a wider project on recovery-stress balance and injury in sport that has been approved by the IRB and participants provided informed consent.

References

1. Sociedad Española de Oncología Médica (2020). Las cifras del cáncer en España. https://seom.org/seomcms/images/stories/recursos/Cifras_del_cancer_2020.pdf
2. Schmitz KH, Courneya KS, Matthews C et al (2010) American college of sports medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 42(7):1409–1426. https://doi.org/10.1249/MSS.0b013e3181e0c112
3. Irwin M. 2012 ACSM's Guide to Exercise and Cancer Survivorship. Human Kinetics.
4. Midtgaard J, Hammer NM, Andersen C, Larsen A, Bruun D-M, Jarden M (2015) Cancer survivors' experience of exercise-based cancer rehabilitation - a meta-synthesis of qualitative research. Acta Oncol 54(5):609–617. https://doi.org/10.3109/0284186X.2014.995777
5. Wolin KY, Schwartz AL, Matthews CE, Courneya KS, Schmitz KH (2012) Implementing the exercise guidelines for cancer survivors. J Support Oncol 10(5):171–177. https://doi.org/10.1016/j.suponc.2012.02.001
6. Gil-Rey E, Quevedo-Jerez K, Maldonado-Martin S, Herrero-Roman F (2014) Exercise intensity guidelines for cancer survivors: a comparison with reference values. Int J Sports Med 35(14):e1–e9. https://doi.org/10.1055/s-0034-1389972
7. Cala MP, Agulló-Ortuño MT, Prieto-García E et al (2018) Multiplatform plasma fingerprinting in cancer cachexia: a pilot observational and translational study. J Cachexia Sarcopenia Muscle 9(2):348–357. https://doi.org/10.1002/jcsm.12270
8. Penttinen H, Utriainen M, Kellokumpu-Lehtinen P-L et al (2019) Effectiveness of a 12-month Exercise Intervention on physical activity and quality of life of breast cancer survivors; five-year results of the BREX-study. In Vivo 33(3):881–888. https://doi.org/10.21873/invivo.11554
9. WHO Director Media Briefing on Covid-19. 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19
10. Spain. Spanish Royal Decree 463/2020, Number 67:25390–25400. https://www.boe.es/diario_boe/txt.php?id=BOE-A-2020-3692
11. Castañeda-Babarro A, Arbillaga-Etxarri A, Gutiérrez-Santamaría B, Coca A (2020) Physical activity change during COVID-19 confinement. Int J Environ Res Public Heal 17(18):6878. https://doi.org/10.3390/ijerph17186878
12. Gutierrez Santamaria B GGAMGREMGNGÁADLFIDMSPSCA. Implementing exercise in standard cancer care: Bizi Orain hybrid, clinical and implementation randomized trial study protocol. JMIR Res Protoc. Published online 2021.
13. Harriss DJ, MacSween A, Atkinson G (2019) Ethical standards in sport and exercise science research: 2020 update. Int J Sports Med 40(13):813–817. https://doi.org/10.1055/a-1015-3123
14. Mishra SI, Scherer RW, Geigle PM et al (2012) Exercise interventions on health-related quality of life for cancer survivors. Cochrane database Syst Rev. https://doi.org/10.1002/14651858.CD007566.pub2

15. Fiuza-Luces C, Padilla JR, Valentin J et al (2017) Effects of exercise on the immune function of pediatric patients with solid tumors: insights from the PAPEC randomized trial. Am J Phys Med Rehabil 96(11):831–837. https://doi.org/10.1097/PHM.0000000000000757
16. Aaronson NK, Ahmedzai S, Bergman B et al (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in International Clinical Trials in oncology. J Natl Cancer Inst 85(5):365–376. https://doi.org/10.1093/jnci/85.5.365
17. Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care 30(6):473–483
18. Fayers P, Aaronson N, Bjordal KSM (2001) The EORTC QLQ-C30 Scoring Manual. Published online, Eur Organ Res Treat Cancer
19. Fayers PM et al (2001) EORTC QLQ-C30 scoring manual the EORTC QLQ-C30 introduction. Scoring Man 30:1–67
20. Brown JC, Cespedes Feliciano EM, Caan BJ (2018) The evolution of body composition in oncology-epidemiology, clinical trials, and the future of patient care: facts and numbers. J Cachexia Sarcopenia Muscle 9(7):1200–1208. https://doi.org/10.1002/jcsm.12379
21. Stockwell S, Trott M, Tully M et al (2021) Changes in physical activity and sedentary behaviours from before to during the COVID-19 pandemic lockdown: a systematic review. BMJ Open Sport Exerc Med 7(1):e000960. https://doi.org/10.1136/bmjsem-2020-000960
22. Cramp F, Daniel J (1996) Exercise for the management of cancer-related fatigue in adults. Cochrane database Syst Rev. https://doi.org/10.1002/14651858.CD006145.pub2
23. Bravo Bartra MI (2012) Actividad física intensa: Dulce o Amargo. Rev Clínica Med Fam 5:76
24. Lucía A, Earnest C, Pérez M (2003) Cancer-related fatigue: can exercise physiology assist oncologists? Lancet Oncol 4(10):616–625. https://doi.org/10.1016/s1470-2045(03)01221-x
25. McTiernan A, Friedenreich CM, Katzmarzyk PT et al (2019) Physical activity in cancer prevention and survival: a systematic review. Med Sci Sports Exerc 51(6):1252–1261. https://doi.org/10.1249/MSS.0000000000001937
26. de Rezende LFM, de Sá TH, Markozannes G et al (2018) Physical activity and cancer: an umbrella review of the literature including 22 major anatomical sites and 770 000 cancer cases. Br J Sports Med 52(13):826–833. https://doi.org/10.1136/bjsports-2017-098391
27. Wallen MP, Hennessy D, Brown S et al (2020) High-intensity interval training improves cardiorespiratory fitness in cancer patients and survivors: A meta-analysis. Eur J Cancer Care (Engl) 29(4):e13267. https://doi.org/10.1111/ecc.13267
28. Wewege M, van den Berg R, Ward RE, Keech A (2017) The effects of high-intensity interval training vs moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. Obes Rev An Off J Int Assoc Study Obes. 18(6):635–646. https://doi.org/10.1111/obr.12532
29. Bull FC, Al-Ansari SS, Biddle S et al (2020) World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 54(24):1451–1462. https://doi.org/10.1136/bjsports-2020-102955
30. Backman M, Wengström Y, Johansson B et al (2014) A randomized pilot study with daily walking during adjuvant chemotherapy for patients with breast and colorectal cancer. Acta Oncol (Madr) 53(4):510–520. https://doi.org/10.3109/0284186X.2013.873820
31. Frändin K, Grimby G, Mellström D, Svanborg A (1991) Walking habits and health-related factors in a 70-year-old population. Gerontology 37(5):281–288. https://doi.org/10.1159/000213272
32. Dias Reis A, Silva Garcia JB, Rodrigues Diniz R et al (2017) Effect of exercise training and detraining in autonomic modulation and cardiorespiratory fitness in breast cancer survivors. J Sports Med Phys Fitness 57(7–8):1062–1068. https://doi.org/10.23736/S0022-4707.17.07012-8
33. Kavanagh T, Mertens DJ, Hamm LF et al (2002) Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. Circulation 106(6):666–671. https://doi.org/10.1161/01.cir.0000024413.15949.ed
34. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE (2002) Exercise Capacity and Mortality among Men Referred for Exercise Testing. N Engl J Med 346(11):793–801. https://doi.org/10.1056/NEJMoa011858
35. Jones LW, Watson D, Herndon JE et al (2010) Peak oxygen consumption and long-term all-cause mortality in nonsmall cell lung cancer. Cancer 116(20):4825–4832. https://doi.org/10.1002/cncr.25396
36. Sietsema K, Sue D, Stringer W, Ward S. Wasserman & whipps principles of exercise testing interpret. 2020.
37. Cullinane EM, Sady SP, Vadeboncoeur L, Burke M, Thompson PD (1986) Cardiac size and VO2max do not decrease after short-term exercise cessation. Med Sci Sports Exerc 18(4):420–424
38. Coyle EF, Martin WH 3rd, Bloomfield SA, Lowry OH, Holloszy JO (1985) Effects of detraining on responses to submaximal exercise. J Appl Physiol 59(3):853–859. https://doi.org/10.1152/jappl.1985.59.3.853
39. Klausen K, Andersen LB, Pelle I (1981) Adaptive changes in work capacity, skeletal muscle capillarization and enzyme levels during training and detraining. Acta Physiol Scand 113(1):9–16. https://doi.org/10.1111/j.1748-1716.1981.tb06854.x
40. Herrero F, San Juan AF, Fleck SJ, Foster C, Lucia A (2007) Effects of detraining on the functional capacity of previously trained breast cancer survivors. Int J Sports Med 28(3):257–264. https://doi.org/10.1055/s-2006-924348
41. Mujika I, Padilla S (2000) Detraining: loss of training-induced physiological and performance adaptations Part I short term insufficient training stimulus. Sports Med 30(2):79–87. https://doi.org/10.2165/00007256-200030020-00002
42. Mujika I, Padilla S (2000) Detraining: loss of training-induced physiological and performance adaptations Part II: Long term insufficient training stimulus. Sports Med 30(3):145–154. https://doi.org/10.2165/00007256-200030030-00001
43. Fearon K, Strasser F, Anker SD et al (2011) Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 12(5):489–495. https://doi.org/10.1016/S1470-2045(10)70218-7
44. Montalvo RN, Hardee JP, Vanderveen BN, Carson JA (2018) Resistance exercise's ability to reverse cancer-induced anabolic resistance. Exerc Sport Sci Rev 46(4):247–253. https://doi.org/10.1249/JES.0000000000000159
45. Cruz Bermudez HF, Moreno Collazos JE, Angarita FA (2013) Medición de la calidad de vida por el cuestionario QLQ-C30 en sujetos con diversos tipos de cáncer de la ciudad de Bucaramanga-Colombia. Enfermería Glob 12:294–303
46. Pareja-Galeano H, Garatachea N, Lucia A (2015) Exercise as a polypill for chronic diseases. Prog Mol Biol Transl Sci 135:497–526. https://doi.org/10.1016/bs.pmbts.2015.07.019

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Artículo dos

Association between PhA and Physical Performance Variables in Cancer Patients

RESUMEN

Antecedentes

El mantenimiento del rendimiento físico de los pacientes con cáncer se tiene cada vez más en cuenta debido al creciente número de enfermos de cáncer y a la agresividad de los tratamientos. Por este motivo la bioimpedancia se utiliza actualmente para registrar la composición corporal de los pacientes mediante la obtención del ángulo de fase (PhA). Aunque existe una relación directa entre el PhA, la edad, el sexo y el pronóstico de la enfermedad, éste no se ha medido como análisis del rendimiento físico en pacientes oncológicos y es una herramienta válida herramienta válida en el seguimiento de pacientes oncológicos.

Métodos

Se evaluaron 311 pacientes de cáncer a los cuales se les realizó tanto el análisis de impedancia bioeléctrica (BIA) como mediciones del rendimiento físico.

Resultados

Se observó que la modificación de los resultados relativos al AF era altamente relacional, ya que una variación en una de las variables afectaba a la otra. Se concluyó que cada grado de aumento del PhA modificaba 22,57 s [27,58; 17,53] en la prueba de marcha de 400 m (400 mWT); 13,25 kg [10,13; 16,35] en la fuerza de la parte superior del cuerpo (UBS); 6,3 [4,95; 7,65] en la fuerza de la parte inferior del cuerpo (LBS); 1,55 mL/kg/min [0,98; 2,12] en el VO_{2pico}; 6,53 vatios [3,83; 9,20] en el umbral ventilatorio 1 (VT1); 10,36 vatios [7,02; 13,64] en el umbral ventilatorio 2 (VT2). También se observó que la edad era un factor que afectaba a la relación entre PhA y 400 mWT; cuanto mayor era la edad, mayor era la relación.

Conclusión

Se ha demostrado que los datos de PhA están correlación con el rendimiento físico. Esto es de gran importancia en la práctica clínica porque los niveles de pacientes oncológicos pueden evaluarse durante el tratamiento.

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Article

Association between PhA and Physical Performance Variables in Cancer Patients

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Abstract: Maintaining the physical performance of cancer patients is increasingly considered due to the growing number of cancer patients and the aggressiveness of the treatments. For this reason, bioimpedance is now being used to record patients' body composition by obtaining the phase angle (PhA). Although there is a direct relationship between PhA, age, sex and disease prognosis, it has not been measured as an analysis of physical performance in oncology patients and is a valid tool in the follow-up of cancer patients. For this purpose, 311 patients were evaluated, and both bioelectrical impedance analysis (BIA) and physical performance measurements were performed. The modification of the results concerning PhA was found to be highly relational, as a variation in one of the variables affected the other. It was concluded that each degree increase in PhA modified −22.57 s [−27.58; −17.53] in 400-m walking test (400 mWT); 13.25 kg [10.13; 16.35] in upper-body strength (UBS); 6.3 [4.95; 7. 65] in lower-body strength (LBS); 1.55 mL/kg/min [0.98; 2.12] in VO_{2peak}; 6.53 Watts [3.83; 9.20] in ventilatory threshold 1 (VT1); 10.36 Watts [7.02; 13.64] in ventilatory threshold 2 (VT2). It was also noted that age was a factor that affected the relationship between PhA and 400 mWT; the older the age, the higher the relationship. PhA data has been shown to be highly correlated with physical performance. This is of great importance in clinical practice because a cancer patient's physical performance levels can be assessed during treatment.

Keywords: phase angle; bioimpedance; physical performance; cancer

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1. Introduction

The assessment of body composition changes and nutritional status using bioelectrical impedance analysis (BIA) has gained popularity, and one of the parameters measured, the phase angle (PhA), is considered an indicator of cellular health and integrity, and has been used as a prognostic marker in diseases such as cancer, HIV and other comorbidities [1].

PhA is obtained from direct measurements of the BIA, comprising resistance (in ohms), reactance (in ohms) and the derived phase angle (in degrees). The phase angle is calculated as the arc tangent of the bioelectrical impedance, reactance and resistance analysis vectors. These describe the positions of cell membranes, in the case of reactance, with body fluids, in the case of resistance, against an injected alternating electric current. Therefore, PhA is a value obtained from the raw data of the BIA analysis, making it high quality and usable data.

PhA has recently been identified as a predictor of competitive level and has been related to sports performance in athletes because it assesses the quality of cells (in terms of cell membrane improvement because it is the main aspect measured by PhA) directly related to physical performance [2,3]. It has been suggested that since increased PhA can be explained by increased muscle cell volume by intracellular fluid, it may be more sensitive for detecting muscle size and function than lean soft tissue estimates [4]. However, it is not yet known whether PhA can be used as an indicator of muscle quantity and strength and maximal aerobic power in the adult population, who also represent an understudied population, as is the case with cancer-affected populations. Skeletal muscle mass and strength, as well as aerobic fitness level, are relevant fitness parameters underlying physical performance [4].

Although physical performance is not looked for in cancer patients as it can be looked for in athletes, it is necessary to optimize the physical performance of patients to improve both their quality of life and their disease [5,6]. Physical performance in cancer patients is understood as a person's ability to perform activities that require physical actions, ranging from self-care (activities of daily living) to more complex activities that require a combination of skills, often with a social component or within a social context [7].

Previous articles have shown that subjects with lower PhA also had reduced levels of strength and muscle mass, and were even being diagnosed with sarcopenia depending on the severity [8].

Although the evidence on PhA is still limited, it is beginning to be related to physical parameters in different pathologies. In previous articles, the authors hypothesized the relationship of phase angle with cardiovascular values. Phase angle has also been found to be related to maximal strength and fat percentage in adults with obesity [9], as well as with predicting the risk of falls in older adults [10] and type 2 diabetes patients, predicting muscle catabolism [11].

Therefore, and considering the above, this article aims to: (1) evaluate the relationship between PhA and physical fitness; (2) and determine how age and sex affect the relationship between PhA and physical performance in cancer patients.

2. Methods

2.1. Participants

This study was a descriptive cross-sectional study of a convenience sample of patients diagnosed with cancer. Participants were referred by their oncologists or hematologists at the Cruces, Basurto and Galdakao University Hospitals in Bizkaia/Biscay, Basque Country, Spain, as part of the main project called Bizi Orain for which the protocol was published [12]. Bizi Orain is an evidence-based exercise program that adheres to the American College of Sports Medicine guidelines for cancer survivors [13] and is based on the "Life Now" exercise program for people with cancer delivered in Australia [14]. The program is administered by the Primary Care Research Unit of the Bizkaia-Biocruces Bizkaia Research Institute and the University of Deusto, and is delivered in a network of health centers equipped with Bizi Orain exercise laboratories integrated into the public health system of the Basque Country (Osakidetza).

2.2. Procedure

Patients were physically and psychologically evaluated at the University of Deusto, (Vizcaya, Spain) from July 2019 to July 2022. Measurements were taken at the time of study enrolment and after 3, 6 and 12 months at the same times of the day (9:00 to 14:00) and under similar environmental conditions (temperature, ±21 °C; relative humidity, 50–55%; barometric pressure, ±720 mmHg).

2.3. Measurements

The patient physical test evaluation begins with the measurement of body composition, followed by the evaluation of the 400 mWT, and finally, an upper and lower body strength test.

The subject's height was measured using a wall stadiometer (Seca, Hamburg, Germany) and body composition with an Inbody 770 bioimpedance analyzer (In-body, Seoul, Korea), conforming with the measurement protocol [15]. Measurements were taken in a standing position because the position interferes with some of the values from which the PhA is taken [16].

The 400-m walk protocols consisted of a 400-m fast-paced walk administered by trained and certified personnel. The walk was conducted in a long corridor with cones at both ends, separated by 20 m [12,17].

To determine the VO_{2peak} (the maximum VO_2 value in the last seconds of the last stage of the submaximal test performed), a test was performed on a cycloergometer with an electric brake (Ergostik, Geratherm Respiratory, Bad Kissingen, Germany). After a 5-min warm-up with no load, the load was increased by 10 W per minute from an initial load of 20 W. Participants were instructed to maintain a cadence above 65 rpm. Gas exchange was analyzed throughout the test with a gas analyzer (Ergostik, Sanro, Spain). The first and second ventilatory thresholds (VT1 and VT2) were obtained by the first exponential increase in ventilatory oxygen (O_2) equivalent (VE/VO_2). VT2, or respiratory compensation point (RCP), was banished using the ventilatory equivalent ratio (VE/VCO_2) method. The test was performed until confirmation of at least one of the following criteria: (1) The second ventilatory threshold or the so-called "respiratory compensation point" (RCP) is observed from the Wasserman figures (respiratory equivalents, and O_2 and CO_2 partial pressure changes); (2) The respiration exchange ratio (RER) ≥ 1.05 and rating of perceived effort (RPE) > 8 on the 0–10-point Borg scale; 3) Participants exhibit volitional exhaustion without meeting the previous criteria [18,19].

As the assessment and measurement of VO_{2Max} is the most accurate value to know the state of the cardiovascular system and the implication in the prediction of mortality because of any cause [20], it is an expensive and laborious method. For this reason, correlations were sought between this value and others of greater complexity and price at the time of assessment. For example, long-distance walking tests, such as the 400-m walking test (400 mWT), when performed as fast as possible, are widely used to assess cardiorespiratory fitness instead of the VO_{2Max} test [21].

Through the test of five maximum repetitions (5RM) and using strength exercise machines, general muscular strength was evaluated with chest press exercises (L070, BH, Vitoria, Spain) and leg press (L050, BH, Vitoria, Spain) [22].

2.4. Statistical Analysis

The relationship between phase angle and the physical tests was analyzed using mixed linear regression models (SAS: PROC MIXED), which account for the correlations between repeated measurements for each patient. Age and sex were used as adjustment variables, and the best model was chosen following a stepwise backward strategy using likelihood ratio tests (with a significance criterion of $p < 0.05$). We also performed correlation tests between the PhA and the physical variables.

Subgroup analyses were carried out to study whether the relationship between PhA and the outcome variables was different depending on sex or age, testing interaction terms between these covariates and angle phase ($p < 0.01$). All analyses were performed with SAS 9.4 (SAS Institue Inc., Cary, NC, USA) and R.4.2.2 (The R Foundation, Vienna, Austria).

3. Results

Of the 311 patients included in the study, 309 had at least one PhA measurement, 239 had at least two, 201 had at least three and 94 had four measurements, respectively. Therefore, the total data were 843 PhA measurements. Table 1 shows the characteristics of the sample according to the main descriptive variables.

Table 1. Characteristics of the sample. Data is shown as mean ± standard deviation (SD) or percentage (%).

Variable	n (%)	Mean ± SD
Age (years)	311 (100)	55.54 ± 10.98
Sex		
Female	225 (712.3)	
Male	86 (27.7)	
Height (cm)		164.7 ± 8.7
Weight (kg)		70.93 ± 14.52
BMI (kg/m^2)		26.1 ± 4.9
PhA (°)		4.88 ± 0.68
400 mWT (seg.)		278.73 ± 53.37
VO_{2peak} (mL/kg/min)		15.31 ± 4
VT1		54.09 ± 16.81
VT2		80.97 ± 23.17
UBS		61.70 ± 23.17
LBS		33.26 ± 13.37
Surgery	164 (52.9)	
Metastatic	50 (19.6)	
Cancer stage		
I	48 (15.4)	
II	80 (25.7)	
III	62 (19.9)	
IV	121 (38.9)	

BMI: body mass index; PhA: phase angle; 400 mWT: 400 m walking test; VO_{2peak}: peak consumption of VO_2; VT1: first ventilatory threshold; VT2: second ventilatory threshold; UBS: upper-body strength; LBS: Lower-Body strength.

Firstly, and according to Figure 1, a descending pattern of the phase angle in relation to age is observed in both sexes, being higher in men with respect to women in all age ranges.

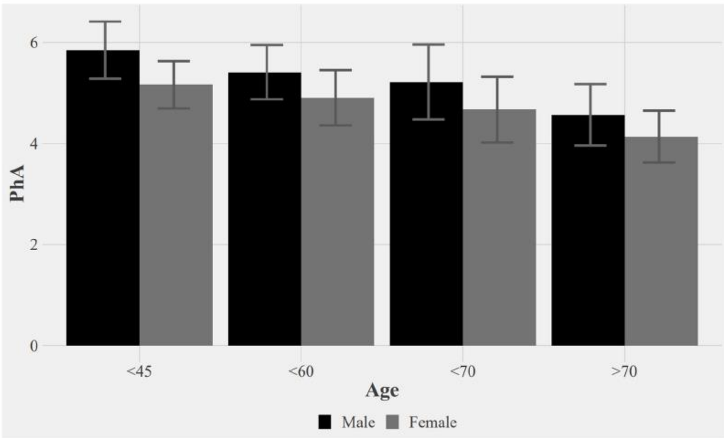

Figure 1. PhA values according to the age and sex of subjects.

Regarding the relationship values shown in Table 2, a statistically significant relationship is observed when comparing the PhA value against the 400 mWT having a reduction of 22.57 s (CI = −27.58 to −17.53) for each one-degree increase in the PhA.

Table 2. Relationship of physical performance and the PhA.

Variable	Mixed Linear Regression Estimate [95% CI]	Mixed Linear Regression *p*-Value	Pearson Correlation [95% CI]	*p*-Value
400 mWT (sec)	−22.57 [−27.58; −17.53]	<0.001	−0.36 [−0.42; −0.3]	<0.001
UBS (kg)	6.3 [4.95; 7.65]	<0.001	0.54 [0.48; 0.59]	<0.001
LBS (kg)	13.25 [10.13; 16.35]	<0.001	0.47 [0.42; 0.53]	<0.001
VO_{2peak} (mL/kg/min)	1.55 [0.98; 2.12]	<0.001	0.25 [0.18; 0.32]	<0.001
VT1 (W)	6.53 [3.83; 9.20]	<0.001	0.35 [0.28; 0.42]	<0.001
VT2 (W)	10.36 [7.02; 13.64]	<0.001	0.42 [0.36; 0.49]	<0.001

Sec: seconds; kg: kilograms; W: watts; UBS: upper-body strength; LBS: Lower-Body strength. Statistical significance set at $p < 0.05$.

Looking at the behavior of PhA compared to strength, we can see how the comparison of PhA with both upper and lower body strength is statistically significant. We see an increase of 13.25 kg (CI = 10.13 to 16.35) in lower body strength for each one-degree increase in PhA. Likewise, an increase of 6.3 kg (CI = 4.95 to 7.65) in lower body strength for each grade increase in PhA.

When observing the behavior of PhA compared to VO_{2peak}, we can determine that there is a significant comparison between the two values observing an increase of 1.55 mL/kg/min (CI = 0.98 to 2.12) for each one-degree increase in PhA. Similarly, watts (W) increases of 6.53 W (CI = 3.83 to 9.2) and 10.36 W (CI = 7.02 to 13.64) are also shown in VT1 and VT2, respectively, for each one-degree increase in PhA.

Model results, including the effect of sex and age, are shown in Supplementary Table S1.

The effect of phase angle on any of the variables was not significantly modified by age or sex except the 400 mWT by age. Estimates from this model can be observed in Figure 2; although, for all patients, an increase in PhA implies a decrease in the time required to perform the 400 mWT, and this decrease is significantly greater for the older group of patients. Results for this model and the rest of the subgroup analysis are shown in Supplementary Table S2.

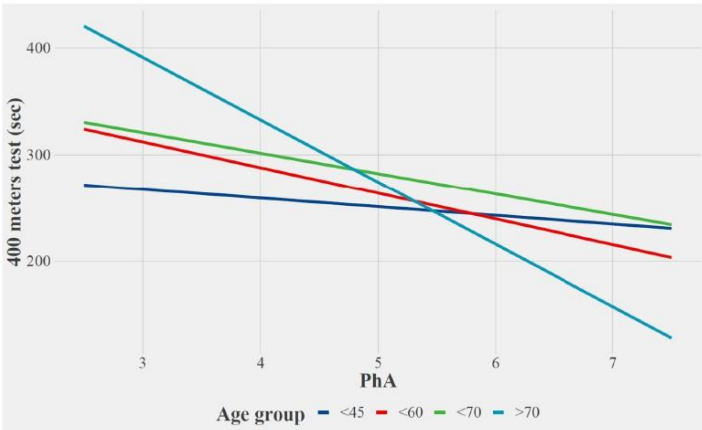

Figure 2. Estimated relationship between PhA and 400 mWT by age group.

4. Discussion

In this research, PhA was used as a predictor of physical performance, considering that it is a non-invasive, cheap and fast method with a high correlation with 400 m WT, UBS, LBS, VO_2 peak, VT1 and VT2. Thus, it fulfills the objectives of studying the relationship between PhA values and physical performance, and analyzing if this relationship is affected by differences in age and sex.

A high PhA represents good cell quality (from the point of view of the cell membrane because it is the parameter analyzed by PhA), and a low PhA represents a decreased cell quality or even a cell death. PhA usually ranges from 4 to 9 in healthy individuals and decreases in females, as well as with increasing age, lower for females, high body mass index and various disease states, such as cancer [23]. In our study, as in previous research, this pattern of change in PhA according to age and sex has been observed.

The mean PhA of our sample is 4.88°, being lower than the values collected in a healthy reference population with normal BMI (18.5–25) and mean age between 50–59 years (referring to the mean age of our sample) that showed a PhA of 5.73 ± 0.68, about one degree higher than the cancer sample studied. Moreover, our sample, even has lower PhA than healthy people with obesity (BMI > 40) aged between 50–59 years (referring to the mean age of our sample) with a PhA of 5.81± 0.7 and even people older than 70 years with BMI > 40 with PhA mean of 5.07 ± 0.72 [24].

Sex and age were the main determinants of PhA in adults, with males and younger subjects having higher PhA [24]. Other studies show similar results in adults. The phase angle was significantly lower in women than in men and was lower at older ages [25]. As can be seen in Figures 1 and 2, our study sample behaves in the same way, which corroborates the results of previous research on the change in PhA according to age and sex. This is an important characteristic to consider when evaluating the PhA value. Due to these results obtained in other research studies, and as our sample behaves in the same way, it was proposed to analyze the data, considering these two variables of important relevance for the interpretation of the data.

Continuing with the functional capacity assessments, it has been observed in other studies that breast cancer patients, divided into two groups by PhA ≤ 5.6 or >5.6 degrees, do not show significant differences in the 6 min walking test (p = 0.678) [26]. This research was carried out in a small population sample of n = 25 divided into two groups of n = 12 men and n = 13 women, much smaller than the sample of our study (n = 311). Specifically, in our research, considering the results of 311 cancer patients, we can observe that the 400 mWT values can be predicted with great accuracy and significance by measuring the PhA, so it could be a useful tool to predict the improvement of functional capacity in a clinical setting where it may not be possible to perform functional capacity measurements such as the 6 min walking test or the 400 mWT. In these results, two different tests are being compared (6-min walking test and 400 mWT), but, due to lack of scientific evidence on the relationship of PhA and 400 mWT, and taking into account that the nature of the tests is similar, we accept the comparison without the same test being used in each case [27].

On the other hand, a reduction in muscle mass and strength is part of the symptomatology of sarcopenia, even more in cancer patients [28]. Previous review articles have shown a relationship between phase angle and sarcopenia [8]. It shows how PhA is decreased in sarcopenic subjects leading to reduced strength in these patients. It was also evidenced that the prevalence of sarcopenia is higher in subjects with low PhA, although further studies are needed to determine to what extent PhA may be valuable in detecting low muscle quality and/or identifying sarcopenia [8]. In our study we have seen increases in strength levels as PhA increases. This shows how the strength value is strongly related to PhA and is, therefore, a parameter that provides information on strength levels without the need for a specific strength test, which facilitates the follow-up of the cancer patient. Many studies have reported the clinical relevance of decreased phase angle or sarcopenia as a predictor of shorter cancer survival [29–32]. Given the importance of phase angle as a predictor of sarcopenia and poor muscle quality, our finding of the association of PhA with an increase in both upper and lower body strength levels may be a key element in improving quality of life. If this increase in strength is maintained over time, it will lead to an increase in muscle mass and a reversal or delay in the onset of sarcopenia.

It is well known that when these events occur, the prognosis against any disease is worse, and this has an important clinical relevance since knowing this relationship. Special attention can be paid to patients at risk of sarcopenia to reduce, slow down and even reverse the disease to improve the patient's functionality, and thus their prognosis against the disease, since sarcopenia is an adverse effector in cancer patients. This is associated with reduced performance status, complications, and overall survival [33,34]. It has also been observed that as a result of the treatments, patients' nutrition worsens and leads to cases of sarcopenia. Before treatment, 69.1% of patients were well-nourished, 16.4% were malnourished, and 14.5% were cachectic/sarcopenic; post-treatment proportions were 16.4%, 45.4% and 38.2%, respectively [32]. Therefore, cancer patients should pay particular attention to nutrition, especially protein levels consumed [35], and to specific physical exercise aimed at building or maintaining muscle mass in order to increase strength levels [36] and thus PhA.

Regarding the VO_{2peak} values (which represent the gold standard in the representation of the level of functional capacity), the significance shown by the value when predicted by the PhA can be observed. The observed values appear not to be significantly relevant due to their small magnitude (1.55 each PhA angle), but it can be determined that slight increases in patients with a low VO_{2peak} (mean of 15.3 $\pm$ 4) may be significant as a health improvement. The slight beneficial changes observed in VO_{2peak} are clinically relevant because VO_{2peak} is an important predictor of all-cause mortality [37,38]. Our results, combined with previous findings of VO_{2peak} impairment among cancer patients with observed values ranging from 15.75 $\pm$ 5.52 to 29.82 $\pm$ 5.08 [39–43], emphasize the clinical importance of increasing or maintaining VO_{2peak} at this stage of the cancer trajectory. Therefore, although changes in VO_{2peak} that in the normal population would be slightly low (changes of 1.55 per each degree of PhA) are observed, in cancer patients, they could be decisive in maintaining functionality in activities of daily living

VO_{2peak} alone only represents the organism's capacity to capture, transport and consume oxygen during exercise [44]. It is, therefore advisable to also observe the improvement in VT1 and VT2 since these are the thresholds at which modifications in the individual's physiology occur and are used to prescribe physical exercise in athletes [45] and in cancer patients [46]. Therefore, the significant relationship between increases in VT1 and VT2 with PhA makes it a predictor of improvement in both VO_{2peak} and VT1 and VT2, representing an improvement in the functional capacity of cancer patients. As the assessment and measurement of VO_{2Max} is the most accurate value to know the state of the cardiovascular system and the implication in the prediction of mortality because of any cause [37], it is an expensive and laborious method, which is why sometimes, this methodology is unavailable. For this reason, correlations were sought between this value and others of greater complexity and price at the time of assessment. Long-distance walk tests like the 400 mWT, when performed as fast as possible, are widely used to assess cardiorespiratory fitness [47]. Through this study, we are giving another alternative to expensive laboratory VO_{2peak} tests, by means of PhA knowing that they are closely related, we could know, with its limitations in terms of accuracy, at what VO_{2peak} levels the cancer patient could be at, knowing that if PhA values increase, most likely their VO_{2peak} values will also increase.

As for the relationship between 400 mWT performance, PhA and age, it can be observed that the older the age, the greater the relationship between these variables. This may be because the 400 mWT is used at older ages to determine the function of that older person [48]. Therefore, what we can determine, is that the older, the better the relationship between PhA and 400 mWT. That is why it is an important fact to consider when making this prediction of performance.

5. Conclusions

BIA is a popular method because it is non-invasive, inexpensive and fast for monitoring changes in body composition in cancer patients.

It has been shown that PhA data directly obtained from the BIA test is highly related to physical performance, and thus provides information on patient changes during treatment. In particular, the relationship with the 400 mWT has been shown to be a very valid test for predicting sarcopenia problems and estimating the VO_{2Max} of patients, especially in older adults, and even to be related to death from any cause. This is of great importance in clinical practice because, without the need to carry out long and costly laboratory tests, the physical performance levels of a cancer patient during treatment can be assessed

6. Future Research Lines

More research is needed to confirm the hypothesis, and it would be convenient to know PhA values in which the oncologist would have information that could be a red flag and be able to pay special attention to this patient to maintain the physical performance in order to not deteriorate his quality of life.

7. Limitations

It should be known that there is evidence that the phase angle measurement can vary according to the measuring device and body position at the time of measurement, being different to measure standing to supine [16]. During the research carried out in this investigation, all the measurements were made in a standing position, so that any other position could not recreate the same results.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ijerph20021145/s1. Table S1: Relationship of physical performance and the PhA; Table S2: Subgroups analysis.

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Institutional Review Board Statement: This study complies with the Declaration of Helsinki and its revisions and good clinical practice. The Ethics Committee of the Basque Country approved the study in the health centers ensuring it would be implemented in compliance with the established regulations (Code: PI2019016). Regarding data confidentiality, only the study researchers have access to the data of individuals who agree to participate in the study, in compliance with the Organic Act 15/1999 of December 2013, on the protection of personal data and its 2011 revision.

Informed Consent Statement: The project is part of a wider project on recovery stress balance and injury in sports that has been approved by the IRB, and participants provided informed consent.

Data Availability Statement: All available data can be obtained by contacting the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Norman, K.; Stobäus, N.; Pirlich, M.; Bosy-Westphal, A. Bioelectrical phase angle and impedance vector analysis–Clinical relevance and applicability of impedance parameters. *Clin. Nutr.* **2012**, *31*, 854–861. [CrossRef] [PubMed]
2. Micheli, M.L.; Pagani, L.; Marella, M.; Gulisano, M.; Piccoli, A.; Angelini, F.; Burtscher, M.; Gatterer, H. Bioimpedance and impedance vector patterns as predictors of league level in male soccer players. *Int. J. Sport Physiol. Perform.* **2014**, *9*, 532–539. [CrossRef] [PubMed]
3. Nabuco, H.C.G.; Silva, A.M.; Sardinha, L.B.; Rodrigues, F.B.; Tomeleri, C.M.; Ravagnani, F.C.P.; Cyrino, E.S.; Ravagnani, C.F.C. Phase Angle is Moderately Associated with Short-term Maximal Intensity Efforts in Soccer Players. *Int. J. Sport. Med.* **2019**, *40*, 739–743. [CrossRef] [PubMed]
4. Lukaski, H.; Raymond-Pope, C.J. New Frontiers of Body Composition in Sport. *Int. J. Sport Med.* **2021**, *42*, 588–601. [CrossRef]
5. Schmitz, K.H.; Courneya, K.S.; Matthews, C.; Demark-Wahnefried, W.; Galvão, D.A.; Pinto, B.M.; Irwin, M.L.; Wolin, K.Y.; Segal, R.J.; Lucia, A.; et al. American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Med. Sci. Sport Exerc.* **2010**, *42*, 1409–1426. [CrossRef]
6. Wolin, K.Y.; Schwartz, A.L.; Matthews, C.E.; Courneya, K.S.; Schmitz, K.H. Implementing the exercise guidelines for cancer survivors. *J. Support. Oncol.* **2012**, *10*, 171–177. [CrossRef]
7. PROMIS. Dynamic Tools to Measure Health Outcomes from the Patient Perspective. Available online: https://www.healthmeasures.net/ (accessed on 17 August 2022).
8. Di Vincenzo, O.; Marra, M.; Di Gregorio, A.; Pasanisi, F.; Scalfi, L. Bioelectrical impedance analysis (BIA) -derived phase angle in sarcopenia: A systematic review. *Clin. Nutr.* **2021**, *40*, 3052–3061. [CrossRef]
9. Streb, A.R.; Hansen, F.; Gabiatti, M.P.; Tozetto, W.R.; Del Duca, G.F. Phase angle associated with different indicators of health-related physical fitness in adults with obesity. *Physiol. Behav.* **2020**, *225*, 113104. [CrossRef]
10. Uemura, K.; Yamada, M.; Okamoto, H. Association of bioimpedance phase angle and prospective falls in older adults. *Geriatr. Gerontol. Int.* **2019**, *19*, 503–507. [CrossRef]
11. Dittmar, M.; Reber, H.; Kahaly, G.J. Bioimpedance phase angle indicates catabolism in Type 2 diabetes. *Diabet. Med.* **2015**, *32*, 1177–1185. [CrossRef]
12. Arietaleanizbeaskoa, M.S.; Gil Rey, E.; Mendizabal Gallastegui, N.; García-Álvarez, A.; De La Fuente, I.; Domínguez-Martinez, S.; Pablo, S.; Coca, A.; Gutiérrez Santamaría, B.; Grandes, G. Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial. *JMIR Res. Protoc.* **2021**, *10*, e24835. [CrossRef] [PubMed]
13. Patel, A.V.; Friedenreich, C.M.; Moore, S.C.; Hayes, S.C.; Silver, J.K.; Campbell, K.L.; Winters-Stone, K.; Gerber, L.H.; George, S.M.; Fulton, J.E.; et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med. Sci. Sports Exerc.* **2019**, *51*, 2391–2402. [CrossRef]
14. Cormie, P.; Lamb, S.; Newton, R.U.; Valentine, L.; McKiernan, S.; Spry, N.; Joseph, D.; Taaffe, D.R.; Doran, C.M.; Galvão, D.A. Implementing exercise in cancer care: Study protocol to evaluate a community-based exercise program for people with cancer. *BMC Cancer* **2017**, *17*, 103. [CrossRef] [PubMed]
15. Walter-Kroker, A.; Kroker, A.; Mattiucci-Guehlke, M.; Glaab, T. A practical guide to bioelectrical impedance analysis using the example of chronic obstructive pulmonary disease. *Nutr. J.* **2011**, *10*, 35. [CrossRef] [PubMed]
16. Więch, P.; Wołoszyn, F.; Trojnar, P.; Skórka, M.; Bazaliński, D. Does Body Position Influence Bioelectrical Impedance? An Observational Pilot Study. *Int. J. Environ. Res. Public Health* **2022**, *19*, 9908. [CrossRef]
17. Lange-Maia, B.S.; Newman, A.B.; Strotmeyer, E.S.; Harris, T.B.; Caserotti, P.; Glynn, N.W. Performance on fast- and usual-paced 400-m walk tests in older adults: Are they comparable? *Aging Clin. Exp. Res.* **2015**, *27*, 309–314. [CrossRef]
18. Gil-Rey, E.; Quevedo-Jerez, K.; Maldonado-Martin, S.; Herrero-Roman, F. Exercise Intensity Guidelines for Cancer Survivors: A Comparison with Reference Values. *Int. J. Sports Med.* **2014**, *35*, e1–e9. [CrossRef]
19. Mishra, S.I.; Scherer, R.W.; Geigle, P.M.; Berlanstein, D.R.; Topaloglu, O.; Gotay, C.C.; Snyder, C. Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database Syst. Rev.* **2012**, *2012*, CD007566. [CrossRef]
20. Blair, S.N.; Kampert, J.B.; Kohl, H.W., 3rd; Barlow, C.E.; Macera, C.A.; Paffenbarger, R.S.J.; Gibbons, L.W. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA* **1996**, *276*, 205–210. [CrossRef]
21. Simonsick, E.M.; Fan, E.; Fleg, J.L. Estimating cardiorespiratory fitness in well-functioning older adults: Treadmill validation of the long distance corridor walk. *J. Am. Geriatr. Soc.* **2006**, *54*, 127–132. [CrossRef]
22. Kraemer, W.J.; Fleck, S.J. *Strength Training for Young Athletes*; Human Kinetics: Champaign, IL, USA, 2005.
23. Hui, D.; Moore, J.; Park, M.; Liu, D.; Bruera, E. Phase Angle and the Diagnosis of Impending Death in Patients with Advanced Cancer: Preliminary Findings. *Oncologist* **2019**, *24*, e365–e373. [CrossRef] [PubMed]
24. Bosy-Westphal, A.; Danielzik, S.; Dörhöfer, R.-P.; Later, W.; Wiese, S.; Müller, M.J. Phase angle from bioelectrical impedance analysis: Population reference values by age, sex, and body mass index. *JPEN J. Parenter. Enteral Nutr.* **2006**, *30*, 309–316. [CrossRef] [PubMed]
25. Barbosa-Silva, M.C.G.; Barros, A.J.D.; Wang, J.; Heymsfield, S.B.; Pierson, R.N.J. Bioelectrical impedance analysis: Population reference values for phase angle by age and sex. *Am. J. Clin. Nutr.* **2005**, *82*, 49–52. [CrossRef] [PubMed]
26. Martins, A.D.; Oliveira, R.; Brito, J.P.; Costa, T.; Ramalho, F.; Pimenta, N.; Santos-Rocha, R. Phase angle cutoff value as a marker of the health status and functional capacity in breast cancer survivors. *Physiol. Behav.* **2021**, *235*, 113400. [CrossRef]

27. Schmidt, K.; Vogt, L.; Thiel, C.; Jäger, E.; Banzer, W. Validity of the six-minute walk test in cancer patients. *Int. J. Sport Med.* **2013**, *34*, 631–636. [CrossRef] [PubMed]
28. Sieber, C.C. Malnutrition and sarcopenia. *Aging Clin. Exp. Res.* **2019**, *31*, 793–798. [CrossRef]
29. Hui, D.; Bansal, S.; Morgado, M.; Dev, R.; Chisholm, G.; Bruera, E. Phase angle for prognostication of survival in patients with advanced cancer: Preliminary findings. *Cancer* **2014**, *120*, 2207–2214. [CrossRef] [PubMed]
30. Martin, L.; Birdsell, L.; Macdonald, N.; Reiman, T.; Clandinin, M.T.; McCargar, L.J.; Murphy, R.; Ghosh, S.; Sawyer, M.B.; Baracos, V.E. Cancer cachexia in the age of obesity: Skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J. Clin. Oncol.* **2013**, *31*, 1539–1547. [CrossRef]
31. Paiva, S.I.; Borges, L.R.; Halpern-Silveira, D.; Assunção, M.C.F.; Barros, A.J.D.; Gonzalez, M.C. Standardized phase angle from bioelectrical impedance analysis as prognostic factor for survival in patients with cancer. *Support. Care Cancer* **2010**, *19*, 187–192. [CrossRef]
32. Stegel, P.; Kozjek, N.R.; Brumen, B.A.; Strojan, P. Bioelectrical impedance phase angle as indicator and predictor of cachexia in head and neck cancer patients treated with (chemo)radiotherapy. *Eur. J. Clin. Nutr.* **2016**, *70*, 602–606. [CrossRef]
33. Baracos, V.E.; Reiman, T.; Mourtzakis, M.; Gioulbasanis, I.; Antoun, S. Body composition in patients with non-small cell lung cancer: A contemporary view of cancer cachexia with the use of computed tomography image analysis. *Am. J. Clin. Nutr.* **2010**, *91*, 1133S–1137S. [CrossRef] [PubMed]
34. Janssen, I.; Baumgartner, R.N.; Ross, R.; Rosenberg, I.H.; Roubenoff, R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am. J. Epidemiol.* **2004**, *159*, 413–421. [CrossRef] [PubMed]
35. Ravasco, P. Nutrition in Cancer Patients. *J. Clin. Med.* **2019**, *8*, 1211. [CrossRef] [PubMed]
36. Koeppel, M.; Mathis, K.; Schmitz, K.H.; Wiskemann, J. Muscle hypertrophy in cancer patients and survivors via strength training. A meta-analysis and meta-regression. *Crit. Rev. Oncol. Hematol.* **2021**, *163*, 103371. [CrossRef] [PubMed]
37. Kodama, S.; Saito, K.; Tanaka, S.; Maki, M.; Yachi, Y.; Asumi, M.; Sugawara, A.; Totsuka, K.; Shimano, H.; Ohashi, Y.; et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: A meta-analysis. *JAMA* **2009**, *301*, 2024–2035. [CrossRef]
38. O'Neill, J.O.; Young, J.B.; Pothier, C.E.; Lauer, M.S. Peak oxygen consumption as a predictor of death in patients with heart failure receiving beta-blockers. *Circulation* **2005**, *111*, 2313–2318. [CrossRef]
39. Burnett, D.; Kluding, P.; Porter, C.; Fabian, C.; Klemp, J. Cardiorespiratory fitness in breast cancer survivors. *Springerplus* **2013**, *2*, 68. [CrossRef]
40. Jones, L.W.; Courneya, K.S.; Mackey, J.R.; Muss, H.B.; Pituskin, E.N.; Scott, J.M.; Hornsby, W.E.; Coan, A.D.; Herndon, J.E., 2nd; Douglas, P.S.; et al. Cardiopulmonary function and age-related decline across the breast cancer survivorship continuum. *J. Clin. Oncol.* **2012**, *30*, 2530–2537. [CrossRef]
41. Lakoski, S.G.; Barlow, C.E.; Koelwyn, G.J.; Hornsby, W.E.; Hernandez, J.; Defina, L.F.; Radford, N.B.; Thomas, S.M.; Herndon, J.E., 2nd; Peppercorn, J.; et al. The influence of adjuvant therapy on cardiorespiratory fitness in early-stage breast cancer seven years after diagnosis: The Cooper Center Longitudinal Study. *Breast Cancer Res. Treat.* **2013**, *138*, 909–916. [CrossRef]
42. Peel, A.B.; Thomas, S.M.; Dittus, K.; Jones, L.W.; Lakoski, S.G. Cardiorespiratory fitness in breast cancer patients: A call for normative values. *J. Am. Heart Assoc.* **2014**, *3*, e000432. [CrossRef]
43. Steins Bisschop, C.N.; Velthuis, M.J.; Wittink, H.; Kuiper, K.; Takken, T.; van der Meulen, W.J.T.M.; Lindeman, E.; Peeters, P.H.M.; May, A.M. Cardiopulmonary exercise testing in cancer rehabilitation: A systematic review. *Sports Med.* **2012**, *42*, 367–379. [CrossRef] [PubMed]
44. Lundby, C.; Montero, D.; Joyner, M. Biology of VO(2) max: Looking under the physiology lamp. *Acta Physiol.* **2017**, *220*, 218–228. [CrossRef] [PubMed]
45. Seiler, K.S.; Kjerland, G.Ø. Quantifying training intensity distribution in elite endurance athletes: Is there evidence for an "optimal" distribution? *Scand. J. Med. Sci. Sports* **2006**, *16*, 49–56. [CrossRef] [PubMed]
46. Schneider, J.; Schlüter, K.; Sprave, T.; Wiskemann, J.; Rosenberger, F. Exercise intensity prescription in cancer survivors: Ventilatory and lactate thresholds are useful submaximal alternatives to VO_{2peak}. *Support. Care Cancer* **2020**, *28*, 5521–5528. [CrossRef]
47. Lindemann, U.; Krumpoch, S.; Becker, C.; Sieber, C.C.; Freiberger, E. The course of gait speed during a 400m walk test of mobility limitations in community-dwelling older adults. *Z. Gerontol. Geriatr.* **2021**, *54*, 768–774. [CrossRef] [PubMed]
48. Rolland, Y.M.; Cesari, M.; Miller, M.E.; Penninx, B.W.; Atkinson, H.H.; Pahor, M. Reliability of the 400-m usual-pace walk test as an assessment of mobility limitation in older adults. *J. Am. Geriatr. Soc.* **2004**, *52*, 972–976. [CrossRef]

Artículo tres

Association between Phase Angle and Subjective Perceptions of Health Variables in Cancer Patients

RESUMEN

Antecedentes

El ángulo de fase, una herramienta sanitaria cada vez más estudiada, se estudió para explorar su relación con factores psicológicos en pacientes con cáncer. El objetivo de este estudio era investigar la relación entre el ángulo de fase (PhA), obtenido mediante análisis de bioimpedancia de la composición corporal, y los factores psicológicos medidos mediante cuestionario en pacientes con cáncer.

Métodos

En el estudio participaron 311 pacientes que se sometieron a pruebas de bioimpedancia para determinar su valor de PhA, y sus perfiles psicológicos se evaluaron mediante cuestionarios SF-36, FACIT, QLQ-C30 y GHQ-12. Se utilizaron modelos de regresión lineal mixta para analizar la relación entre el PhA y las pruebas psicológicas.

Resultados

Los resultados mostraron una correlación estadística entre el PhA y los cuestionarios GHQ-12, FACIT y SF-36, con valores de PhA más altos asociados a mejores resultados en los cuestionarios. En el cuestionario QLQ-C30, se observó una correlación entre el PhA y las escalas de funcionamiento ($p<0,001$), excepto en el Funcionamiento Emocional y Cognitivo ($p=0,148$ y $p=0,544$, respectivamente), pero no en la mayoría de las escalas de síntomas.

Conclusión

El PhA es una herramienta útil para evaluar la percepción subjetiva de la salud de los pacientes con cáncer, especialmente en lo que respecta a los factores psicológicos. Aunque existe una correlación estadísticamente significativa, se requiere más investigación antes de aplicarlo con confianza en la práctica clínica. El valor predictivo actual de este predictor para determinados aspectos psicológicos es limitado, lo que subraya la necesidad de investigaciones adicionales.

healthcare

MDPI

Article

Association between Phase Angle and Subjective Perceptions of Health Variables in Cancer Patients

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Abstract: The phase angle, an increasingly studied healthcare tool, was studied to explore its relationship with psychological factors in cancer patients. The aim of this study was to investigate the relationship between the phase angle (PhA), obtained by the bioimpedance analysis of body composition, and psychological factors measured by questionnaire in cancer patients. The study included 311 patients who underwent bioimpedance testing to determine their PhA value; their psychological profiles were assessed using SF-36, FACIT, QLQ-C30, and GHQ-12 questionnaires. Mixed linear regression models were used to analyze the relationship between PhA and the psychological tests. The results showed a statistical correlation between PhA and the GHQ-12, FACIT, and SF-36 questionnaires, with higher PhA values associated with better results on the questionnaires. In the QLQ-C30 questionnaire, a correlation was observed between PhA and the functioning scales ($p < 0.001$), except for emotional and cognitive functioning ($p = 0.148$ and $p = 0.544$, respectively), but not in most of the symptom scales. The PhA is a useful tool for assessing the subjective health perception of cancer patients, especially with regard to psychological factors. While there is a statistically significant correlation, further research is required before confidently applying it in clinical practice. The current predictive value of this predictor for certain psychological aspects is limited, underscoring the need for additional research.

Keywords: GHQ-12; FACIT; SF-36; bioimpedance; phase angle; early diagnosis; physical activity

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1. Introduction

The phase angle (PhA) is used to evaluate nutritional status and is an indicator of cellular health [1]. Clinically, the PhA reflects cell membrane function and body cell mass, which means that the higher the PhA, the better the cell function [2]. The principle behind the PhA concept relies on alterations in both resistance and reactance when alternating current flows through analyzed tissues. As the current traverses cellular membranes, a portion of it is stored within the resistive sections, resulting in a phase shift [2]. As a general rule, it is negatively correlated with the ratios of extra-to-intracellular water, age, and body mass index (BMI) but positively associated with physical activity [3,4].

The PhA's impact has been evaluated in a wide range of malignancies and diseases such as sarcopenia [5–7], acute stroke [8], chronic obstructive pulmonary disease [8,9], liver cirrhosis [10], severe obesity [2], locomotive syndrome [11], cancer [12] and even in outpatient palliative cancer care settings [13]. In cancer patients, the PhA is considered a prognostic factor for survival [14,15], and it can predict postoperative infectious complications [16]. The PhA is frequently lower than normal in disease patients since processes such as inflammation, infection, or disease-specific events may impair the PhA [17]. Such alterations in the PhA can be measured through bioelectrical impedance analysis (BIA), a simple, fast, non-invasive and reproducible tool to assess body composition [18]. Furthermore, it can be performed at the bedside of critical patients to measure body composition [19]. The PhA has also been used as a nutritional status marker because the measured values reflect the amounts of various tissue components and hydration status [2]. The results of previous research suggest that there are some alterations in the electrical properties of tissues with malnutrition that can be detected by BIA, giving alterations in the PhA values. Currently, there are no cut-off points for malnutrition states but there are cut-off points for sarcopenia and frailty patterns in older adults, with a PhA value of $\leq$4.1 degrees being risky values [20].

In the assessment of sarcopenia and frailty in cancer patients, often due to nutritional problems, it is vital to record parameters related to these because, due to the side effects of treatments, many patients suffer from these conditions. The presence of sarcopenia in older adults has been related to increased functional impairment, disability, risk of falls and fractures, loss of independence, and death [21].

Another aspect to consider in cancer patients is their perception of their health. This is usually measured by different questionnaires such as the general health status indicator, which measures eight dimensions of health: physical function, physical role, bodily pain, general health, vitality, social function, emotional role and mental health (SF-36) in primary care [22,23] and in cancer [24,25]. The EORTC QLQ-C30 questionnaire encompasses a set of distinct components designed to evaluate the impact of cancer on individuals. It consists of five functional items, namely physical role, cognitive, emotional, and social functioning. In addition, it includes three symptom items focusing on fatigue, pain, and nausea–vomiting. Furthermore, there is a single item dedicated to assessing the global health status and overall quality of life [26–29]. The states of fatigue in different aspects of life (FACIT) is a specific instrument that objectively assesses health-related quality of life in patients with advanced or life-limiting chronic diseases [26,30]. Finally, the perception of general health (GHQ-12) is a screening instrument that aims to detect psychological morbidity and possible cases of psychiatric disorders in settings such as primary care [31–33]. The questionnaires chosen are all validated and have been used in previous research. They are also widely used by health professionals due to their reliability. Although there is a wide variety of questionnaires, these were chosen according to the criteria of mental health specialists. Some questionnaires are specific to the disease studied.

In previous research, it has been shown that the psychological state of cancer patients is significantly worsened compared to the healthy population. Psychological stressors for the majority of the population, such as COVID-19 [34–36], had no effect on cancer patients, possibly due to the previous psychological impairment of the patients [37].

A previous study by our research group has shown the relationship between the PhA and physical performance [38]. However, to our knowledge, the relationship between PhA and psychological aspects has not been discussed. To fill this gap, this study used the GHQ-12, FACIT, SF-36 and QLQ-C30 items to relate questionnaire results to the PhA values in cancer patients.

Regarding the use of PhA, a recent systematic review with meta-analysis explained that predicting survival in patients with advanced cancer remains a challenge but findings suggest that the PhA may be an important factor in this population [39].

Therefore, and considering the above, this article aims to: (1) evaluate the relationship between PhA and physiological state and (2) be able to use a predictive methodology for psychological state using the PhA as a measured value.

2. Methods

2.1. Study Design

The implementation of the program was overseen by the Primary Care Research Unit, which operates under the Bizkaia-Biocruces Bizkaia Research Institute and the University of Deusto. This initiative is executed through a network of health centers that are equipped with Bizi Orain exercise laboratories. These laboratories are seamlessly integrated into the public health system of the Basque Country, known as Osakidetza. The present study adopted a descriptive cross-sectional design and focused on a sample of individuals who have received a cancer diagnosis. Bizi Orain is an evidence-based exercise program that aligns with the guidelines established by the American College of Sports Medicine for cancer survivors [40]. The study lasted 12 months and was divided into two phases. During the first three months, participants were randomly assigned to a group that received both the Bizi Orain exercise program and a behavioral intervention to promote healthy habits, or to a group that received only the healthy habits prescription. After three months, participants in the second group started the exercise program. During the last six months of the study, participants continued with their daily activities and were evaluated at 6 and 12 months before the end of their participation in the study. During this time, PhA measurements were obtained and used for further data analysis.

Each study participant was informed of all study procedures, signed the consent form about the tests performed, and completed all study procedures.

2.2. Participants

Anyone with a cancer diagnosis currently receiving treatment or diagnosed less than two years earlier was eligible to participate. The participants included in this study were referred by their respective oncologists or hematologists at Cruces, Basurto, and Galdakao University Hospitals, located in Bizkaia, Basque Country, Spain. These referrals were made as part of the main project, which established the study's selection and exclusion criteria in detail [41].

To ensure ethical compliance, this study adheres to the principles outlined in the Declaration of Helsinki and its subsequent revisions, as well as good clinical practice. The Ethics Committee of the Basque Country granted approval for this study to be conducted in the health centers, guaranteeing compliance with all relevant regulations (Code: PI2019016).

Regarding data confidentiality, only the designated study researchers had access to patient data, which was provided voluntarily by the participants. The handling of this data adhered to the requirements outlined in the Organic Act 15/1999 of December 2013, which concerns the protection of personal data, as well as its 2011 revision.

It is important to note that this project is part of a broader initiative focusing on recovery, stress balance, and injury in sports, which received approval from the Institutional Review Board. All participants involved in the study provided informed consent prior to their involvement.

2.3. Measurements

During the period spanning July 2019 to July 2022, patients underwent physical and psychological evaluations at the University of Deusto (Spain). The assessments were conducted at the time of study enrollment and subsequently at 3-, 6-, and 12-month intervals. Consistent with maintaining standardization, these evaluations were conducted within the same time frame each day, specifically from 9:00 to 14:00. Furthermore, the evaluations took place under similar environmental conditions, ensuring that the temperature remained at approximately ± 21 °C, the relative humidity was maintained between 50 and 55%, and the barometric pressure hovered around ± 720 mmHg.

The patients' height was measured utilizing a wall stadiometer (Seca, Hamburg, Germany). In addition, body composition measurements were obtained using an Inbody 770 bioimpedance analyzer (Inbody, Seoul, Korea). These measurement procedures strictly adhered to the established protocol to ensure accuracy and consistency [42]. The use of the Inbody 770 device as a meter is validated against the gold standard DEXA with 98% correlation [43]. The measurements were taken standing up because research has shown that position from which the PhA is taken interferes with some of the values, so the way in which the bioimpedance was measured should always be known [44]. The PhA is compounded by two elements: the reactance (X) and the resistance (R). It should be noted that this measurement is a direct assessment of the cell membrane, and not a calculation based on indirect equations. The formula for the phase angle is:

$$\varphi = \text{arctg } X/R$$

A series of questionnaires with sound psychometric properties were used to assess general health, cancer-specific quality of life, and cancer-related fatigue. These questionnaires were those used in practice by the clinicians in the hospitals involved in the study. The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) is used to assess general health-related quality of life status [23,41], and cancer-specific quality of life is assessed by the Core Quality of Life Questionnaire (QLQ-C-30). The SF-36 consists of eight scaled scores obtained through the weighted sums of the questions in each section. Each scale is directly transformed into a 0–100 scale, assuming that each question carries equal weight. The lower the score, the higher the impediment, the higher the score, the lower the disability [29,41]. The General Health Questionnaire (GHQ-12) assesses psychological morbidity and possible psychiatric disorders [32,41]. Items on the GHQ-12 are rated on a 4-point scale using a timeframe of "the last two weeks." There are three ways of scoring the GHQ-12: the bimodal GHQ scoring method (0-0-1-1), recommended by the test authors for use in clinical settings; the Likert scoring method (0-1-2-3), which is commonly used in research; and the C-GHQ scoring method where positively phrased items are scored (0-0-1-1) and negatively phrased items (0-1-1-1) [45]. The more severe the problem, the higher the score (with a maximum of 9 for each of the subscales). Finally, cancer-related fatigue is assessed using the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue) scale [28,41]. The FACIT-Fatigue Scale is a short, 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue is measured on a four-point Likert scale (4 = not at all fatigued to 0 = very much fatigued), lower test scores indicate greater fatigue [46].

2.4. Statistical Analysis

Mixed linear regression models were employed to examine the association between the PhA and the psychological tests (SAS: PROC MIXED), which accommodate the inherent correlations observed in repeated measurements within each patient. Adjustment variables such as age, sex, cancer type, stage, treatments, smoking status, and comorbidities were incorporated into the analysis. Importantly, none of these variables exhibited any missing values.

A stepwise backward strategy was employed to identify the most appropriate model, guided by likelihood ratio tests. The selection process involved iteratively removing variables that did not significantly contribute to the model's explanatory power, with a significance criterion set at $p < 0.05$. The final model was determined by following this rigorous approach, ensuring a robust and reliable analysis. We reported the proportion of variance explained by the fixed variables in the models using the marginal R square obtained by the Nakagawa method [47]. We also performed correlation tests between the PhA and the psychological variables. All analyses were performed with SAS 9.4 and R.

3. Results

Of the 311 patients included in the study, 309 had at least one PhA measurement, 239 had at least two measurements, 205 had at least three measurements, and 121 had four measurements. Therefore, the total data are 874 PhA measurements; each accepted measurement of PhA had to go with the corresponding results of the questionnaires, thus providing the data of both PhA and the psychological situation at each moment, Within the mixed statistical model, the special feature of these measurements is taken into account. Table 1 shows the sample characteristics according to the main descriptive variables. The results of the questionnaires are presented in Table A2.

Table 1. Characteristics of the sample. The data is shown as mean ± standard deviation (SD) or percentage (%).

Variable	n (%)	Mean ± SD
AGE (years)	311 (100)	55.5 ± 10.9
SEX		
FEMALE	225 (72.3)	-
MALE	86 (27.65)	
HEIGHT (cm)		164.7 ± 8.7
WEIGHT (kg)		70.9 ± 14.5
BMI (kg/m^2)		26.1 ± 4.9
PhA (°)		4.9 ± 0.7
VO_2peak (mL/kg/min)		15.3 ± 4
CHEMOTHERAPY	274 (88.1)	
RADIOTHERAPY	92 (29.6)	
BONE METASTASES	50 (16.1)	
SURGERY	164 (52.9)	
CANCER STAGE		
I	48 (15.4)	
II	80 (25.7)	
III	62 (19.9)	
IV	121 (38.9)	
CANCER TYPE		
Breast	132 (42.4)	
Colorectal	24 (7.7)	
Hematologic	69 (22.2)	
Ovary	14 (4.5)	
Pancreas	17 (5.5)	
Lung	19 (6.1)	
Other	36 (11.6)	
SMOKING		
Never	169 (54.3)	
Ex-smoker	94 (30.2)	
Smoker	48 (15.4)	
COMORBIDITIES		
Diabetes	27 (8.7)	
COPD	16 (5.1)	
Heart failure	8 (2.6)	
Hypertension	68 (21.9)	
Hyperlipidemia	70 (22.5)	

BMI: body mass index; PhA: phase angle; VO2peak: peak consume of VO_2; COPD: chronic obstructive pulmonary disease.

With regard to the results shown in Table 2, we appreciate the significant relationship that exists between GHQ-12 and FACIT values and PhA. It is known that the lower the score in the GHQ-12-questionnaire values, the better the general state of health of the patient and the higher the PhA, all with a high significance. Furthermore, observing the FACIT questionnaire, the higher the score, the lower the fatigue perceived by the questionnaire. A relationship was also observed between the FACIT questionnaire score and the PhA value.

Table 2. Relationship between PhA and questionnaires.

Questionnaire	Mixed Linear Regression Estimate (95% CI) Size Effect	Mixed Linear Regression *p*-Value	R^2	Pearson Coefficient Correlation (95%CI)	Correlation *p*-Value
GHQ-12	−0.72 (−1.16; −0.27)	0.002 *	0.05 (0.01; 0.12)	−0.05 (−0.12; 0.02)	0.132
FACIT	3.2 (1.99; 4.41)	<0.001 *	0.08 (0.04; 0.16)	0.16 (0.09; 0.22)	<0.001 *
SF-36					
Physical functioning	7.99 (5.54; 10.44)	<0.001 *	0.14 (0.09; 0.21)	0.23 (0.17; 0.3)	<0.001 *
Social functioning	9.13 (5.67; 12.54)	<0.001 *	0.06 (0.03; 0.12)	0.11 (0.04; 0.17)	<0.001 *
Physical role	13.03 (7.4; 18.59)	<0.001 *	0.08 (0.03; 0.14)	0.09 (0.02; 0.15)	0.009 *
Emotional role	1.88 (−3.91; 7.62)	0.525	0.04 (0.02; 0.11)	−0.01 (−0.07; 0.06)	0.829
Mental health	4.34 (1.76; 6.9)	<0.001 *	0.10 (0.04; 0.20)	0.11 (0.05; 0.18)	<0.001 *
Energy/vitality	8.2 (5.38; 11)	<0.001 *	0.12 (0.07; 0.22)	0.18 (0.12; 0.25)	<0.001 *
Pain index	1.75 (−1.55; 5.03)	0.296	0.08 (0.04; 0.16)	0.05 (−0.02; 0.11)	0.176
General health perception	5.17 (2.78; 7.55)	<0.001 *	0.07 (0.04; 0.16)	0.12 (0.05; 0.18)	<0.001 *
Standardized physical comp.	3.02 (1.79; 4.22)	<0.001 *	0.10 (0.08; 0.20)	0.16 (0.1; 0.23)	<0.001 *
Standardized mental comp.	2.31 (0.68; 3.92)	0.006 *	0.06 (0.02; 0.14)	0.05 (−0.01; 0.12)	0.120
QLQ-C30					
Functioning scales					
Global health status	5.63 (2.91; 8.33)	<0.001 *	0.06 (0.02; 0.11)	0.1 (0.04; 0.17)	0.003 *
Physical functioning	5.22 (3.34; 7.09)	<0.001 *	0.11 (0.07; 0.18)	0.22 (0.15; 0.28)	<0.001 *
Role functioning	7.86 (4.64; 11.05)	<0.001 *	0.11 (0.08; 0.20)	0.14 (0.07; 0.2)	<0.001 *
Emotional functioning	2.06 (−0.73; 4.84)	0.148	0.08 (0.03; 0.15)	0.02 (−0.05; 0.09)	0.538
Cognitive functioning	1.62 (−1.12; 4.36)	0.248	0.05 (0.02; 0.13)	0.07 (0.01; 0.14)	0.030 *
Social functioning	8.23 (4.66; 11.75)	<0.001 *	0.10 (0.05; 0.20)	0.08 (0.01; 0.14)	0.021 *
Symptom scale/items					
Fatigue	−6.37 (−9.34; −3.36)	<0.001 *	0.09 (0.04; 0.18)	−0.12 (−0.19; −0.06)	<0.001 *
Nausea and vomiting	−2.15 (−3.81; −0.49)	0.012 *	0.02 (0.01; 0.06)	−0.06 (−0.13; 0)	0.057
Pain	−1.07 (−4.19; 2.06)	0.504	0.07 (0.03; 0.14)	−0.03 (−0.1; 0.03)	0.310
Dyspnoea	−1.58 (−4.8; 1.69)	0.341	0.08 (0.05; 0.18)	−0.05 (−0.11; 0.02)	0.152
Insomnia	0.58 (−3.56; 4.73)	0.786	0.03 (0.01; 0.10)	−0.01 (−0.07; 0.06)	0.819
Appetite loss	−3.73 (−6.38; −1.08)	0.006 *	0.07 (0.04; 0.18)	−0.1 (−0.16; −0.03)	0.004 *
Constipation	−2.79 (−6; 0.41)	0.089	0.05 (0.02; 0.13)	−0.05 (−0.12; 0.02)	0.142
Diarrhoea	−2.62 (−5.34; 0.1)	0.061	0.09 (0.05; 0.18)	−0.02 (−0.08; 0.05)	0.606
Financial difficulties	0.44 (−2.99; 3.87)	0.803	0.06 (0.03; 0.13)	0.06 (−0.01; 0.12)	0.101

* statistically significant.

Continuing with the results obtained, a high significance can also be seen between the SF-36 questionnaire and the PhA. Specifically, in the subclassification made by the questionnaire, a high relationship can be seen, except in the subclassification of the emotional role and pain index, where a relationship with the PhA cannot be seen. This questionnaire is interpreted as meaning that the lower the score, the greater the patient's limitation in each of the subclassifications.

The QLQ-C30 questionnaire interprets higher scale scores as higher response levels. It is divided into two main scales, the functioning scale and the symptom scale. In the functioning scale, we can appreciate the relationship with the PhA except in the emotional and cognitive functioning parameters, which are not related to the PhA. In the symptom scale, only the parameters of fatigue, nausea and vomiting, and loss of appetite are related to PhA, with no clear relationship in the rest of the subclassifications. Further analysis and supplementary results can be found in Table A1.

Finally, we can see how the pain scale is measured using different questionnaires, SF-36 and QLQ-C30, and the relationship between this parameter and PhA was not significant in either case.

Further statistical analyses not relevant to the research have been added in Table A1.

4. Discussion

This study analyzed the possible associations between the PhA and the cancer patients' subjective perception of several health parameters. Among the most relevant results, we found that while the relationship with PhA was high in the GHQ-12, FACIT, and SF-36 questionnaires, with higher PhA being associated with better results, a relationship with PhA was found in the functioning scale assessment items of the QLQ-C30 but not in most of its symptom scales.

Regarding the patient's subjective assessment, the GHQ-12 questionnaire measures possible affective disorders in different populations [31]. Thus, as a valid tool, finding a high relationship with the PhA could help us predict affective disorders with other tools, such as the PhA. The results obtained in our research show how the two values, both the GHQ-12 score and the PhA, are closely correlated, with higher GHQ-12 values leading to higher PhA values.

In the same way that previous research has shown a relationship between PhA and better physical profiles [38], it is not uncommon to observe the same trend of higher PhA values with better psychological profiles. The relationship that PhA has with physical and psychological aspects could lead to the hypothesis that the better the physical health, the better the psychological health [48] and, therefore, the higher the PhA. Another possible hypothesis for this relationship between GHQ-12 values and PhA could be cellular integrity since patients with a better psychological profile could be those with more favorable cellular integrity [49].

Cancer-related fatigue is a common side effect of cancer treatment, so the fatigue questionnaire (FACIT) has long been used to assess and monitor this side effect [50], especially as a part of physical exercise programs. Our research has shown a close relationship between the values of this questionnaire and the PhA values measured, showing that higher PhA levels would result in lower fatigue as measured by the questionnaire. This result was discussed in previous research where a relationship between fatigue and PhA was observed, especially in cancer patients with PhA <4, but when adjusted for hydration parameters (intracellular and extracellular water), the association was reduced [51]. The relationship between these two parameters, fatigue and PhA, has an important relevance given that PhA values can be related to the fatigue questionnaire (FACIT) value, knowing that, in our study, for each one-grade increase in PhA, an improvement of 3.2 (1.99; 4.41) points in FACIT scores could be seen with a high relationship. This relationship between fatigue and PhA could be explained by the fact that PhA is an indicator of physical health in cancer patients [38], so lower PhA values indicate poorer physical condition, which could easily be associated with higher fatigue.

Looking at the SF-36 questionnaire results, which measured health-related quality of life, we observed a high relationship with the values obtained in PhA values. It is known that on most occasions, a better quality of life is preceded by lifestyle changes, and this positively affects PhA. It has been seen that improving nutritional status by improving diet [52], practicing planned physical exercise or improving body composition [53,54] can lead to an improved quality of life and PHA. Therefore, improvement in any aspect that aids quality of life positively affects both SF-36 and PhA values.

The subsections measured by this SF-36 questionnaire are highly related to PhA with values of $p < 0.05$, except for the parameters of emotional role and pain, which have not been found to have a significant relationship. Emotional role measures the degree to which emotional problems interfere with work or other daily activities, so it can be extrapolated that there is no relationship between PhA and this measure, possibly because, in many cases, psychological problems do not affect their daily activities, although a large proportion report episodes of depression and anxiety [55]. These results may also be biased by possible psychiatric medication to control these depression and anxiety problems because at least 25–30% of cancer patients and an even higher percentage of those with advanced disease meet the criteria for a psychiatric diagnosis, including depression, anxiety, stress-related syndromes, adjustment disorders, sleep disorders, and delirium [56]. Previous studies showed that emotional role and one's physical state negatively influenced each other, while fatigue and pain positively influenced each other. These results suggest that mind and body interact in a direct way [57], with differences in the results in our research.

The results obtained in the QLQ-C30, specifically those corresponding to the measurement of functioning scales, show how emotional functioning is unrelated to PhA. It should be noted that this same section was assessed in the SF-36 questionnaire, giving similar data regarding the non-significance of the relationship with PhA, confirming the non-significance of the relationship with PhA with two different tools. This could be because, as we have previously stated, the better or worse value of PhA is independent of the problems that the illness may cause in work or daily activities. Nutrition plays a fundamental role in the quality of life [52] and in the possibility of modifying PhA values. Therefore, a parameter related to nutrition could be the item that speaks of appetite loss measured with the QLQ-C30, which has a significant relationship with PhA. Thus, patients with low PhA have a significant loss of appetite.

The PhA's relationship with pain is not significant for the results in the QLQ-C30 and the SF-36 questionnaires. The same parameter, measured with two different instruments, provided us with the important information that it does not have a relationship with the PhA.

Due to the novelty of the analyzed parameters and the relative association between the parameters, more and better research is needed to be able to apply this knowledge in daily practice although this research lays the foundation for further research regarding PhA in the management of cancer patients.

It is important to note that bioimpedance measurements obtained from single and multifrequency devices should not be treated as interchangeable. When evaluating highly active populations, there was a notable lack of consensus between devices when determining individual values such as R, Xc, Z, and PhA [58]. This discrepancy could be attributed to various methodological and biological factors. Consequently, if this methodology is to be applied in clinical practice, it is strongly advised to consistently use the same device, conduct measurements under as similar conditions as possible, and refrain from comparing results with data obtained from different devices or methodologies.

4.1. Limitations

There is evidence that PhA measurements can vary according to the measuring device and body position at the time of assessment (standing vs. supine) [44]. During this research, all measurements were made standing to avoid variance.

The sample was taken from a larger project that included cancer patients of all types and stages, so in order to have a good sample it was decided to include all patients knowing the limitation of the heterogeneity of the sample and its possible relationship to the results.

Mixed linear regression models may have limitations in interpretation and more research is needed to apply these regressions to everyday practice to obtain the desired uses.

4.2. Practical Applications

This research opens up a new possibility of having the tools to monitor fatigue in patients whose PhA drops. That is, FACIT questionnaires may be used to assess patient fatigue.

The relationship between most of the items in the questionnaire and the PhA opens up the possibility of carrying out a quick screening, knowing which patients would need more research into their subjective perception of health.

5. Conclusions

This study analyzed the possible associations between the PhA and cancer patients' subjective perception of different health parameters. It could be seen that while in the GHQ-12, FACIT and SF-36 questionnaires, there was a correlation with PhA, with higher PhA being seen with better results in the questionnaires; in other questionnaires, such as the QLQ-C30, a relationship with PhA was seen in the functioning scale assessment items but not in the majority of the symptom scales. Therefore, the PhA is a good tool to assess the subjective health perception of a cancer patient and due to the regressions can make predictions of outcomes except for some items where the association is not significant. It should be noted that the correlation is low, despite being statistically significant, so the actual predictive value is limited.

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Institutional Review Board Statement: This study complies with the Declaration of Helsinki, its revisions, and good clinical practice. The Ethics Committee of the Basque Country approved the study in the health centers ensuring it would be implemented in compliance with the established regulations (Code: PI2019016).

Informed Consent Statement: The project is part of a wider project on recovery, stress balance and injury in sports that has been approved by the IRB, and the participants provided informed consent.

Data Availability Statement: Regarding data confidentiality, only the study researchers have access to the data of individuals who agreed to participate in the study, in compliance with the Organic Act 15/1999 of December 2013 on the protection of personal data and its 2011 revision.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. Supplementary analysis.

Questionnaire				Estimate	95%CI	*p*-Value
SF36	**Physical Functioning**					
		Intercept		47.26	(33.64; 61.08)	<0.001
		PhA		7.08	(4.62; 9.51)	<0.001
		Sex				0.079
			Male	Ref		
			Female	−4.07	(−8.54; 0.41)	
		Smoking				0.018
			Never	Ref		
			Ex-smoker	−6.2	(−10.48; −1.92)	
			Smoker	−3.13	(−8.55; 2.29)	
		Bone metastases		−6.27	(−11.43; −1.09)	0.019
		Hypertension		−7.85	(−13; −2.71)	0.003
		Hyperlipidemia		−4.53	(−9.57; 0.53)	0.083

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	*p*-Value
Physical Role					
	Intercept		−2.51	(−37.87; 33.59)	0.890
	PhA		10.89	(5.2; 16.45)	<0.001
	Age				<0.001
		<45	Ref		
		<60	−2.89	(−18.21; 12.37)	
		<70	20.85	(2.97; 38.68)	
		70+	42.33	(0.64; 84.03)	
	Sex				0.034
		Male	Ref		
		Female	−9.66	(−18.52; −0.85)	
	Hypertension		−16.73	(−26.2; −7.29)	<0.001
Pain Index					
	Intercept		55.64	(33.86; 77.81)	<0.001
	PhA		3.25	(−0.17; 6.61)	0.062
	Age				0.01
		<45	Ref		
		<60	−2.87	(−12.7; 6.92)	
		<70	7.21	(−4.26; 18.67)	
		70+	21.13	(−5.47; 47.84)	
	Sex				<0.001
		Male	Ref		
		Female	−10.55	(−16.21; −4.91)	
	Smoking				0.047
		Never	Ref		
		Ex-smoker	−6.38	(−11.63; −1.11)	
		Smoker	0.26	(−6.43; 6.98)	
	Hypertension		−7.47	(−13.53; −1.45)	0.017
General Health					
	Intercept		34.02	(21.88; 46.22)	<0.001
	PhA		4.25	(1.98; 6.5)	<0.001
	Stage				0.001
		I	Ref		
		II	0.93	(−5.16; 7.01)	
		III	−0.83	(−7.31; 5.66)	
		IV	−7.64	(−13.38; −1.89)	
	Diabetes		9.08	(2.2; 15.96)	0.011
	COPD		−7.39	(−16.03; 1.24)	0.097
Vitality					
	Intercept		14.77	(−2.85; 32.64)	0.106
	PhA		7.74	(5; 10.43)	<0.001
	Age				0.003
		<45	Ref		
		<60	3.92	(−4.27; 12.11)	
		<70	13.14	(3.68; 22.61)	
		70+	20.66	(−0.99; 42.39)	
	Sex				0.027
		Male	Ref		
		Female	−5.34	(−10.02; −0.69)	
	Smoking				0.023
		Never	Ref		
		Ex-smoker	−5.64	(−10.04; −1.23)	
		Smoker	1.21	(−4.56; 6.99)	
	COPD		−10.4	(−19.62; −1.2)	0.029

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	*p*-Value
Social Functioning					
	Intercept		21.33	(1.58; 41.36)	0.035
	PhA		8.96	(5.58; 12.27)	<0.001
	Age				<0.001
		<45	Ref		
		<60	4.86	(−5.34; 15.05)	
		<70	17.38	(5.67; 29.07)	
		70+	26.31	(−1.01; 53.65)	
	Hyperlipidemia		−5.96	(−12.03; 0.11)	0.057
Emotional Role					
	Intercept		62.26	(26.66; 98.22)	<0.001
	PhA		0.86	(−4.75; 6.42)	0.764
	Age				0.024
		<45	Ref		
		<60	9.7	(−6.23; 25.59)	
		<70	24.22	(5.89; 42.48)	
		70+	14.73	(−27.63; 57.06)	
	Sex				0.062
		Male	Ref		
		Female	−8.76	(−17.87; 0.31)	
	COPD		−19.64	(−37.41; −1.93)	0.032
Mental Health					
	Intercept		43.61	(26.19; 61.32)	<0.001
	PhA		4.03	(1.5; 6.52)	0.002
	Age				0.012
		<45	Ref		
		<60	2.42	(−5.6; 10.42)	
		<70	10.82	(1.65; 19.98)	
		70+	10.99	(−10.28; 32.26)	
	Sex				0.007
		Male	Ref		
		Female	−6.62	(−11.34; −1.94)	
	Stage				0.032
		I	Ref		
		II	9.19	(3.02; 15.35)	
		III	4.12	(−2.48; 10.72)	
		IV	5.65	(−0.27; 11.56)	
	COPD		−9.76	(−18.64; −0.91)	0.034
Standarized Physical Component					
	Intercept		28.31	(21.85; 34.9)	<0.001
	PhA		3.17	(2.07; 4.25)	<0.001
	Age				0.054
		<45	Ref		
		<60	−1.35	(−4.71; 2.01)	
		<70	1.51	(−2.36; 5.38)	
		70+	4.11	(−5.01; 13.23)	
	Smoking				0.068
		Never	Ref		
		Ex-smoker	−1.92	(−3.73; −0.11)	
		Smoker	0.53	(−1.76; 2.82)	
	Bone metastases		−2.1	(−4.29; 0.09)	0.064
	Hypertension		−3.96	(−6.02; −1.91)	<0.001

Table A1. *Cont.*

Questionnaire				Estimate	95%CI	*p*-Value
	Standarized Mental Component					
		Intercept		28.05	(18.94; 37.21)	<0.001
		PhA		2.51	(0.99; 4.02)	0.001
		Age				<0.001
			<45	Ref		
			<60	3.85	(−1.06; 8.76)	
			<70	9.77	(4.21; 15.34)	
			70+	8.98	(−4.24; 22.22)	
		Diabetes		4.19	(−0.15; 8.52)	0.061
		COPD		−5.69	(−11.14; −0.26)	0.043
EORT QLQ-30						
	Global Health Status/QoL					
		Intercept		32.54	(17.73; 47.4)	<0.001
		PhA		5.56	(3.06; 8.05)	<0.001
		Age				<0.001
			<45	Ref		
			<60	1.4	(−6.18; 8.97)	
			<70	12.13	(3.57; 20.7)	
			70+	8.98	(−11.1; 29.1)	
		COPD		−8.83	(−17.24; −0.43)	0.042
	Physical functioning					
		Intercept		67.11	(57.64; 76.68)	<0.001
		PhA		4.72	(3; 6.43)	<0.001
		Sex				0.019
			Male	Ref		
			Female	−3.8	(−6.95; −0.66)	
		Bone metastases		−4.76	(−8.44; −1.07)	0.013
		COPD		−6.53	(−12.77; −0.3)	0.042
		Hyperlipidemia		−4.46	(−7.72; −1.2)	0.008
	Role functioning					
		Intercept		50.65	(29.75; 72.08)	<0.001
		PhA		6.7	(3.55; 9.78)	<0.001
		Age				<0.001
			<45	Ref		
			<60	−0.18	(−8.62; 8.19)	
			<70	13.89	(4.05; 23.67)	
			70+	31.91	(9.15; 54.64)	
		Sex				0.044
			Male	Ref		
			Female	−6.19	(−12.09; −0.36)	
		Cancer type				0.034
			Breast	Ref		
			Colorectal	−4.95	(−12.86; 2.97)	
			Hematologic	−3.22	(−9; 2.54)	
			Ovary	−4.65	(−13.74; 4.4)	
			Pancreas	−10.53	(−20.7; −0.5)	
			Lung	9.66	(0.35; 18.85)	
			Other	−4.15	(−11.74; 3.45)	
		Bone metastases		−5.84	(−11.33; −0.3)	0.043
		COPD		−14.17	(−23.88; −4.53)	0.005
		Hypertension		−4.61	(−9.82; 0.55)	0.09

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	p-Value
Emotional functioning					
	Intercept		67.18	(49.51; 84.98)	<0.001
	PhA		1.86	(−0.87; 4.57)	0.181
	Age				0.002
		<45	Ref		
		<60	4.75	(−3.64; 13.14)	
		<70	14.21	(4.65; 23.76)	
		70+	18.54	(−3.69; 40.77)	
	Sex				<0.001
		Male	Ref		
		Female	−8.33	(−13.1; −3.57)	
Cognitive functioning					
	Intercept		88.44	(74.3; 102.62)	<0.001
	PhA		0.52	(−2.06; 3.09)	0.693
	Sex				<0.001
		Male	Ref		
		Female	−9.69	(−14.57; −4.81)	
	COPD		−8.29	(−17.94; 1.37)	0.094
Social functioning					
	Intercept		21.45	(2.12; 40.98)	0.032
	PhA		7.16	(3.88; 10.41)	<0.001
	Age				<0.001
		<45	Ref		
		<60	16.87	(6.88; 26.85)	
		<70	31.68	(20.4; 42.94)	
		70+	26.44	(−0.49; 53.39)	
	Bone metastases		−7.87	(−14.43; −1.31)	0.02
	Diabetes		7.86	(−0.99; 16.69)	0.085
Fatigue					
	Intercept		55.77	(36.81; 74.41)	<0.001
	PhA		−5.65	(−8.5; −2.75)	<0.001
	Age				0.048
		<45	Ref		
		<60	−1.36	(−10.02; 7.32)	
		<70	−9.29	(−19.28; 0.68)	
		70+	−7.64	(−30.26; 15.05)	
	Sex				0.015
		Male	Ref		
		Female	6.12	(1.27; 11)	
	Smoking				0.039
		Never	Ref		
		Ex-smoker	5.89	(1.3; 10.48)	
		Smoker	0.6	(−5.45; 6.63)	
	COPD		13.16	(3.58; 22.8)	0.008
Nausea and vomiting					
	Intercept		12.1	(3.79; 20.36)	0.005
	PhA		−1.61	(−3.18; −0.02)	0.047
	Stage				0.041
		I	Ref		
		II	−0.16	(−3.78; 3.46)	
		III	4.24	(0.4; 8.07)	
		IV	1.99	(−1.43; 5.41)	

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	*p*-Value
Pain					
	Intercept		20.28	(0.93; 39.57)	0.042
	PhA		−1	(−4.01; 2.01)	0.516
	Age				0.021
		<45	Ref		
		<60	4.69	(−4.05; 13.43)	
		<70	−2.54	(−12.76; 7.65)	
		70+	−18.71	(−42.47; 4.98)	
	Sex				<0.001
		Male	Ref		
		Female	10.98	(5.96; 16.01)	
	COPD		9.12	(−0.56; 18.84)	0.069
	Hypertension		5.23	(−0.16; 10.63)	0.061
Dyspnoea					
	Intercept		10.32	(−5.88; 26.26)	0.21
	PhA		−1.32	(−4.19; 1.6)	0.373
	Sex				<0.001
		Male	Ref		
		Female	9.61	(4.66; 14.56)	
	Smoking				0.008
		Never	Ref		
		Ex-smoker	7.28	(2.59; 11.95)	
		Smoker	4.71	(−1.38; 10.78)	
	COPD		15.08	(5.32; 24.85)	0.003
	Hypertension		8.54	(3.35; 13.76)	0.002
Insomnia					
	Intercept		18.28	(−2.5; 39.05)	0.085
	PhA		1.2	(−2.63; 5.02)	0.54
	Sex				<0.001
		Male	Ref		
		Female	13.09	(6.44; 19.73)	
Appetite loss					
	Intercept		12.55	(−4.63; 29.61)	0.157
	PhA		−2.39	(−5.15; 0.42)	0.098
	Sex				0.001
		Male	Ref		
		Female	9.39	(3.83; 14.94)	
	Cancer type				0.002
		Breast	Ref		
		Colorectal	10.61	(2.67; 18.52)	
		Hematologic	0.67	(−4.98; 6.35)	
		Ovary	−5.77	(−14.99; 3.47)	
		Pancreas	18.05	(8.1; 28.02)	
		Lung	6.64	(−2.17; 15.46)	
		Other	5.87	(−1.7; 13.47)	
	Stage				0.042
		I	Ref		
		II	−0.73	(−6.88; 5.39)	
		III	7.62	(0.74; 14.42)	
		IV	2.29	(−4.01; 8.53)	

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	*p*-Value
Constipation					
	Intercept		30.48	(14.37; 46.39)	<0.001
	PhA		−3.25	(−6.38; −0.08)	0.046
	Smoking				0.042
		Never	Ref		
		Ex-smoker	6.96	(1.58; 12.35)	
		Smoker	1.33	(−5.44; 8.09)	
	Cancer type				0.023
		Breast	Ref		
		Colorectal	−1.46	(−10.42; 7.52)	
		Hematologic	−5.04	(−11.14; 1.04)	
		Ovary	17.05	(5.92; 28.2)	
		Pancreas	3.07	(−8.14; 14.24)	
		Lung	3.69	(−6.38; 13.78)	
		Other	1.52	(−6.54; 9.53)	
Diarrhoea					
	Intercept		26.21	(10.07; 42.18)	0.002
	PhA		−1.7	(−4.21; 0.87)	0.201
	Age				0.006
		<45	Ref		
		<60	−11	(−18.26; −3.86)	
		<70	−14.35	(−22.69; −6.15)	
		70+	−24.68	(−44.46; −5.07)	
	Smoking				0.038
		Never	Ref		
		Ex-smoker	4.93	(0.94; 8.93)	
		Smoker	−0.67	(−5.61; 4.31)	
	Cancer type				0.003
		Breast	Ref		
		Colorectal	9.92	(3.19; 16.44)	
		Hematologic	−3.35	(−8.9; 2.13)	
		Ovary	−4.7	(−12.75; 3.36)	
		Pancreas	7.51	(−1.11; 16.09)	
		Lung	−4.55	(−12.06; 3.01)	
		Other	0.5	(−5.65; 6.65)	
	Surgery		−4.47	(−8.64; −0.3)	0.043
	Chemotherapy		5.11	(−0.35; 10.61)	0.077
	Diabetes		9.8	(3.31; 16.51)	0.005
Financial difficulties					
	Intercept		18.26	(−1.62; 38.09)	0.074
	PhA		0.5	(−2.71; 3.71)	0.763
	Age				0.002
		<45	Ref		
		<60	−3.48	(−14.73; 7.79)	
		<70	−16.66	(−29.39; −3.91)	
		70+	−20.17	(−49.84; 9.52)	
	Radiotherapy		−5.25	(−11.15; 0.66)	0.085
	COPD		13.4	(0.97; 25.84)	0.037

Table A1. *Cont.*

Questionnaire			Estimate	95%CI	*p*-Value
Golberg [GHQ-12]					
	Intercept		8.14	(5.4; 10.86)	<0.001
	PhA		−0.62	(−1.06; −0.18)	0.006
	Age				<0.001
		<45	Ref		
		<60	−1	(−2.37; 0.37)	
		<70	−2.52	(−4.06; −0.98)	
		70+	−3.67	(−7.32; −0.03)	
	Stage				0.062
		I	Ref		
		II	−1.42	(−2.47; −0.36)	
		III	−0.79	(−1.91; 0.33)	
		IV	−1.1	(−2.1; −0.11)	
FACIT					
	Intercept		26.96	(19; 35.01)	<0.001
	PhA		2.65	(1.41; 3.88)	<0.001
	Age				0.04
		<45	Ref		
		<60	−0.03	(−3.77; 3.7)	
		<70	3.5	(−0.78; 7.77)	
		70+	3.42	(−6.46; 13.32)	
	Sex				0.04
		Male	Ref		
		Female	−2.26	(−4.39; −0.14)	
	Bone metastases		−2.54	(−4.98; −0.1)	0.044
	COPD		−5.81	(−9.96; −1.67)	0.007

Table A2. General questionnaire original data.

Questionnaire	Mean (SD)
GHQ-12	3.36 (3.63)
FACIT	37.33 (9.53)
SF-36	
Physical functioning	70.92 (20.91)
Social functioning	66.68 (27.58)
Physical role	70.92 (20.91)
Emotional role	67.85 (43.61)
Mental health	66.1 (19.69)
Energy/vitality	50.13 (21.13)
Pain index	58.47 (26.24)
General health perception	51.19 (17.77)
Standardized physical comp.	40.32 (8.28)
Standardized mental comp.	44.21 (12.38)
QLQ-C30	
Functioning scales	
Global health status	60.77 (19.62)
Physical functioning	84.69 (14.72)
Role functioning	74.65 (25.57)
Emotional functioning	75.54 (20.18)
Cognitive functioning	82.85 (22.33)
Social functioning	70.98 (27.77)

Table A2. *Cont.*

Questionnaire	Mean (SD)
Symptom scale/items	
Fatigue	33.64 (22.41)
Nausea and vomiting	7.2 (15.87)
Pain	27.33 (22.79)
Dyspnoea	15.86 (23.34)
Insomnia	35.6 (31.42)
Appetite loss	13.59 (22.68)
Constipation	18.23 (27.3)
Diarrhoea	12.19 (23.24)
Financial difficulties	13.03 (26.75)

References

1. Langer, R.D.; da Costa, K.G.; Bortolotti, H.; Fernandes, G.A.; de Jesus, R.S.; Gonçalves, E.M. Phase angle is associated with cardiorespiratory fitness and body composition in children aged between 9 and 11 years. *Physiol. Behav.* **2020**, *215*, 112772. [CrossRef]
2. Gonzalez, M.C.; Barbosa-Silva, T.G.; Bielemann, R.M.; Gallagher, D.; Heymsfield, S.B. Phase angle and its determinants in healthy subjects: Influence of body composition. *Am. J. Clin. Nutr* **2016**, *103*, 712–716. [CrossRef]
3. Genton, L.; Mareschal, J.; Norman, K.; Karsegard, V.L.; Delsoglio, M.; Pichard, C.; Graf, C.; Herrmann, F.R. Association of phase angle and running performance. *Clin. Nutr. ESPEN* **2020**, *37*, 65–68. [CrossRef]
4. Mundstock, E.; Amaral, M.A.; Baptista, R.R.; Sarria, E.E.; Dos Santos, R.R.G.; Filho, A.D.; Rodrigues, C.A.S.; Forte, G.C.; Castro, L.; Padoin, A.V.; et al. Association between phase angle from bioelectrical impedance analysis and level of physical activity: Systematic review and meta-analysis. *Clin. Nutr.* **2019**, *38*, 1504–1510. [CrossRef]
5. Di Vincenzo, O.; Marra, M.; Di Gregorio, A.; Pasanisi, F.; Scalfi, L. Bioelectrical impedance analysis (BIA)-derived phase angle in sarcopenia: A systematic review. *Clin. Nutr.* **2021**, *40*, 3052–3061. [CrossRef]
6. Pérez Camargo, D.A.; Allende Pérez, S.R.; Verastegui Avilés, E.; Rivera Franco, M.M.; Meneses García, A.; Herrera Gómez, Á.; Ceniceros, V.I.U. Assessment and Impact of Phase Angle and Sarcopenia in Palliative Cancer Patients. *Nutr. Cancer* **2017**, *69*, 1227–1233. [CrossRef]
7. Valentino, N.P.; Gomes, T.L.N.; Barreto, C.S.; Borges, T.C.; Soares, J.D.P.; Pichard, C.; Laviano, A.; Pimentel, G.D. Low phase angle is associated with the risk for sarcopenia in unselected patients with cancer: Effects of hydration. *Nutrition* **2021**, *84*, 111122. [CrossRef]
8. Abe, T.; Yoshimura, Y.; Imai, R.; Yoneoka, Y.; Tsubaki, A.; Sato, Y. Impact of Phase Angle on Physical Function in Patients with Acute Stroke. *J. Stroke Cereb. Dis. Off. J. Natl. Stroke Assoc.* **2021**, *30*, 105941. [CrossRef]
9. Maddocks, M.; Kon, S.S.C.; Jones, S.E.; Canavan, J.L.; Nolan, C.M.; Higginson, I.J.; Gao, W.; Polkey, M.I.; Man, W.D.-C. Bioelectrical impedance phase angle relates to function, disease severity and prognosis in stable chronic obstructive pulmonary disease. *Clin. Nutr.* **2015**, *34*, 1245–1250. [CrossRef]
10. Selberg, O.; Selberg, D. Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. *Eur. J. Appl. Physiol.* **2002**, *86*, 509–516. [CrossRef]
11. Tanaka, S.; Ando, K.; Kobayashi, K.; Seki, T.; Hamada, T.; Machino, M.; Ota, K.; Morozumi, M.; Kanbara, S.; Ito, S.; et al. The decreasing phase angles of the entire body and trunk during bioelectrical impedance analysis are related to locomotive syndrome. *J. Orthop. Sci.* **2019**, *24*, 720–724. [CrossRef]
12. Matias, C.N.; Cavaco-Silva, J.; Reis, M.; Campa, F.; Toselli, S.; Sardinha, L.; Silva, A.M. Phase Angle as a Marker of Muscular Strength in Breast Cancer Survivors. *Int. J. Environ. Res. Public Health* **2020**, *17*, 4452. [CrossRef]
13. Hui, D.; Dev, R.; Pimental, L.; Park, M.; Cerana, M.A.; Liu, D.; Bruera, E. Association Between Multi-frequency Phase Angle and Survival in Patients With Advanced Cancer. *J. Pain Symptom. Manag.* **2017**, *53*, 571–577. [CrossRef]
14. Axelsson, L.; Silander, E.; Bosaeus, I.; Hammerlid, E. Bioelectrical phase angle at diagnosis as a prognostic factor for survival in advanced head and neck cancer. *Eur. Arch. Oto-Rhino-Laryngol.* **2018**, *275*, 2379–2386. [CrossRef]
15. Paiva, S.I.; Borges, L.R.; Halpern-Silveira, D.; Assunção, M.C.F.; Barros, A.J.D.; Gonzalez, M.C. Standardized phase angle from bioelectrical impedance analysis as prognostic factor for survival in patients with cancer. *Support. Care Cancer* **2010**, *19*, 187–192. [CrossRef]
16. Pena, N.F.; Mauricio, S.F.; Rodrigues, A.M.S.; Carmo, A.S.; Coury, N.C.; Correia, M.I.; Generoso, S.V. Association Between Standardized Phase Angle, Nutrition Status, and Clinical Outcomes in Surgical Cancer Patients. *Nutr. Clin. Pract.* **2019**, *34*, 381–386. [CrossRef]
17. Norman, K.; Stobäus, N.; Pirlich, M.; Bosy-Westphal, A. Bioelectrical phase angle and impedance vector analysis—Clinical relevance and applicability of impedance parameters. *Clin. Nutr.* **2012**, *31*, 854–861. [CrossRef]
18. Andreoli, A.; Scalzo, G.; Masala, S.; Tarantino, U.; Guglielmi, G. Body composition assessment by dual-energy X-ray absorptiometry (DXA). *Radiol. Med.* **2009**, *114*, 286–300. [CrossRef]

19. Reis de Lima e Silva, R.; Porto Sabino Pinho, C.; Galvão Rodrigues, I.; Gildo de Moura Monteiro Júnior, J. Phase angle as an indicator of nutritional status and prognosis in critically ill patients. *Nutr. Hosp.* **2014**, *31*, 1278–1285.
20. Rosas-Carrasco, O.; Ruiz-Valenzuela, R.E.; López-Teros, M.T. Phase Angle Cut-Off Points and Their Association With Sarcopenia and Frailty in Adults of 50-64 Years Old and Older Adults in Mexico City. *Front. Med.* **2021**, *8*, 617126. [CrossRef]
21. Visser, M.; Goodpaster, B.H.; Kritchevsky, S.B.; Newman, A.B.; Nevitt, M.; Rubin, S.M.; Simonsick, E.M.; Harris, T.B. Muscle Mass, Muscle Strength, and Muscle Fat Infiltration as Predictors of Incident Mobility Limitations in Well-Functioning Older Persons. *J. Gerontol. Ser. A* **2005**, *60*, 324–333. [CrossRef]
22. Brazier, J.E.; Harper, R.; Jones, N.M.; O'Cathain, A.; Thomas, K.J.; Usherwood, T.; Westlake, L. Validating the SF-36 health survey questionnaire: New outcome measure for primary care. *BMJ* **1992**, *305*, 160–164. [CrossRef]
23. Ware Jr, J.E.; Sherbourne, C.D. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Med. Care* **1992**, *30*, 473–483. [CrossRef]
24. Bunevicius, A. Reliability and validity of the SF-36 Health Survey Questionnaire in patients with brain tumors: A cross-sectional study. *Health Qual. Life Outcomes* **2017**, *15*, 92. [CrossRef]
25. Treanor, C.; Donnelly, M. A methodological review of the Short Form Health Survey 36 (SF-36) and its derivatives among breast cancer survivors. *Qual. Life Res.* **2015**, *24*, 339–362. [CrossRef]
26. Penttinen, H.; Utriainen, M.; Kellokumpu-Lehtinen, P.-L.; Raitanen, J.; Sievänen, H.; Nikander, R.; Blomqvist, C.; Huovinen, R.; Vehmanen, L.; Saarto, T. Effectiveness of a 12-month Exercise Intervention on Physical Activity and Quality of Life of Breast Cancer Survivors; Five-year Results of the BREX-study. *Vivo* **2019**, *33*, 881–888. [CrossRef]
27. Fayers, P.M.; Aaronson, N.K.; Bjordal, K.; Groenvold, M.; Curran, D.; Bottomley, A.; on behalf of the EORTC Quality of Life Group. EORTC QLQ-C30 Scoring Manual The EORTC QLQ-C30 Introduction. *EORTC QLQ-C30 Scoring Man* **2001**, *30*, 1–67. Available online: http://www.eortc.be/qol/files/scmanualqlq-c30.pdf (accessed on 1 January 2002).
28. Cella, D.; Nowinski, C.J. Measuring quality of life in chronic illness: The functional assessment of chronic illness therapy measurement system. *Arch. Phys. Med. Rehabil.* **2002**, *83*, S10–S17. [CrossRef]
29. Aaronson, N.K.; Ahmedzai, S.; Bergman, B.; Bullinger, M.; Cull, A.; Duez, N.J.; Filiberti, A.; Flechtner, H.; Fleishman, S.B.; De Haes, J.C.J.M.; et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *J. Natl. Cancer Inst.* **1993**, *85*, 365–376. [CrossRef]
30. Webster, K.; Cella, D.; Yost, K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: Properties, applications, and interpretation. *Health Qual. Life Outcomes*. **2003**, *1*, 79. [CrossRef]
31. Goldberg, D.P.; Hillier, V.F. A scaled version of the General Health Questionnaire. *Psychol. Med.* **1979**, *9*, 139–145. [CrossRef]
32. Sánchez-López M del, P.; Dresch, V. The 12-Item General Health Questionnaire (GHQ-12): Reliability, external validity and factor structure in the Spanish population. *Psicothema* **2008**, *20*, 839–843.
33. Goldberg, D.P.; Gater, R.; Sartorius, N.; Ustun, T.B.; Piccinelli, M.; Gureje, O.; Rutter, C. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychol. Med.* **1997**, *27*, 191–197. [CrossRef]
34. Khatatbeh, M.; Khasawneh, A.; Hussein, H.; Altahat, O.; Alhalaiqa, F. Psychological Impact of COVID-19 Pandemic Among the General Population in Jordan. *Front. Psychiatry* **2021**, *12*, 618993. [CrossRef]
35. Serafini, G.; Parmigiani, B.; Amerio, A.; Aguglia, A.; Sher, L.; Amore, M. The psychological impact of COVID-19 on the mental health in the general population. *QJM* **2020**, *113*, 531–537. [CrossRef]
36. Saladino, V.; Algeri, D.; Auriemma, V. The Psychological and Social Impact of COVID-19: New Perspectives of Well-Being. *Front Psychol.* **2020**, *11*, 2550. Available online: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.577684 (accessed on 1 January 2002). [CrossRef]
37. Gutiérrez-Santamaría, B.; Castañeda-Babarro, A.; Arietaleanizbeaskoa, M.S.; Mendizabal-Gallastegui, N.; Grandes, G.; Coca, A. Physiological and mental health changes in cancer patients during the COVID-19 state of emergency. *Sport Sci. Health* **2022**, *19*, 123–130. [CrossRef]
38. Gutiérrez-Santamaría, B.; Martinez Aguirre-Betolaza, A.; García-Álvarez, A.; Arietaleanizbeaskoa, M.S.; Mendizabal-Gallastegui, N.; Grandes, G.; Castañeda-Babarro, A.; Coca, A. Association between PhA and Physical Performance Variables in Cancer Patients. *Int. J. Environ. Res. Public Health* **2023**, *20*, 1145. [CrossRef]
39. Arab, A.; Karimi, E.; Vingrys, K.; Shirani, F. Is phase angle a valuable prognostic tool in cancer patients' survival? A systematic review and meta-analysis of available literature. *Clin. Nutr.* **2021**, *40*, 3182–3190. [CrossRef]
40. Patel, A.V.; Friedenreich, C.M.; Moore, S.C.; Hayes, S.C.; Silver, J.K.; Campbell, K.L.; Winters-Stone, K.; Gerber, L.H.; George, S.M.; Fulton, J.E.; et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med. Sci. Sport. Exerc.* **2019**, *51*, 2391–2402. Available online: http://europepmc.org/abstract/MED/31626056 (accessed on 1 January 2002). [CrossRef]
41. Arietaleanizbeaskoa, M.S.; Gil Rey, E.; Mendizabal Gallastegui, N.; García-Álvarez, A.; De La Fuente, I.; Domínguez-Martinez, S.; Pablo, S.; Coca, A.; Santamaría, B.G.; Grandes, G. Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial. *JMIR Res. Protoc.* **2021**, *10*, e24835. [CrossRef]
42. Walter-Kroker, A.; Kroker, A.; Mattiucci-Guehlke, M.; Glaab, T. A practical guide to bioelectrical impedance analysis using the example of chronic obstructive pulmonary disease. *Nutr. J.* **2011**, *10*, 35. [CrossRef]

43. McLester, C.N.; Nickerson, B.S.; Kliszczewicz, B.M.; McLester, J.R. Reliability and Agreement of Various InBody Body Composition Analyzers as Compared to Dual-Energy X-Ray Absorptiometry in Healthy Men and Women. *J. Clin. Densitom.* **2020**, *23*, 443–450. [CrossRef]
44. Więch, P.; Wołoszyn, F.; Trojnar, P.; Skórka, M.; Bazaliński, D. Does Body Position Influence Bioelectrical Impedance? An Observational Pilot Study. *Int. J. Environ. Res. Public Health* **2022**, *19*, 9908. [CrossRef]
45. Anjara, S.G.; Bonetto, C.; Van Bortel, T.; Brayne, C. Using the GHQ-12 to screen for mental health problems among primary care patients: Psychometrics and practical considerations. *Int. J. Ment. Health Syst.* **2020**, *14*, 62. [CrossRef]
46. Al-shair, K.; Muellerova, H.; Yorke, J.; Rennard, S.I.; Wouters, E.F.M.; Hanania, N.A.; Sharafkhaneh, A.; Vestbo, J. Examining fatigue in COPD: Development, validity and reliability of a modified version of FACIT-F scale. *Health Qual. Life Outcomes* **2012**, *10*, 100. [CrossRef]
47. Nakagawa, S.; Johnson, P.C.D.; Schielzeth, H. The coefficient of determination R2 and intra-class correlation coefficient from generalized linear mixed-effects models revisited and expanded. *J. R Soc. Interface* **2017**, *14*, 20170213. [CrossRef]
48. Ohrnberger, J.; Fichera, E.; Sutton, M. The relationship between physical and mental health: A mediation analysis. *Soc. Sci. Med.* **2017**, *195*, 42–49. Available online: https://www.sciencedirect.com/science/article/pii/S0277953617306639 (accessed on 1 January 2002). [CrossRef]
49. Hui, D.; Moore, J.; Park, M.; Liu, D.; Bruera, E. Phase Angle and the Diagnosis of Impending Death in Patients with Advanced Cancer: Preliminary Findings. *Oncologist* **2019**, *24*, e365–e373. [CrossRef]
50. Hauth, F.; De-Colle, C.; Weidner, N.; Heinrich, V.; Zips, D.; Gani, C. Quality of life and fatigue before and after radiotherapy in breast cancer patients. *Strahlenther. Und Onkol.* **2021**, *197*, 281–287. [CrossRef]
51. Gomes, T.L.N.; Soares, J.D.P.; Borges, T.C.; Pichard, C.; Pimentel, G.D. Phase angle is not associated with fatigue in cancer patients: The hydration impact. *Eur. J. Clin. Nutr.* **2020**, *74*, 1369–1373. [CrossRef]
52. Gupta, D.; Lis, C.G.; Dahlk, S.L.; King, J.; Vashi, P.G.; Grutsch, J.F.; Lammersfeld, C.A. The relationship between bioelectrical impedance phase angle and subjective global assessment in advanced colorectal cancer. *Nutr. J.* **2008**, *7*, 19. [CrossRef]
53. Campa, F.; Silva, A.M.; Toselli, S. Changes in Phase Angle and Handgrip Strength Induced by Suspension Training in Older Women. *Int. J. Sport Med.* **2018**, *39*, 442–449. [CrossRef]
54. dos Santos, L.; Cyrino, E.S.; Antunes, M.; Santos, D.A.; Sardinha, L.B. Changes in phase angle and body composition induced by resistance training in older women. *Eur. J. Clin. Nutr.* **2016**, *70*, 1408–1413. [CrossRef]
55. Gregurek, R.; Braš, M.; Đorđević, V.; Ratković, A.-S.; Brajković, L. Psychological problems of patients with cancer. *Psychiatr. Danub.* **2010**, *22*, 227–230.
56. Grassi, L.; Caruso, R.; Hammelef, K.; Nanni, M.G.; Riba, M. Efficacy and safety of pharmacotherapy in cancer-related psychiatric disorders across the trajectory of cancer care: A review. *Int. Rev. Psychiatry* **2014**, *26*, 44–62. [CrossRef]
57. Lee, Y.-S.; Jung, W.-M.; Jang, H.; Kim, S.; Chung, S.-Y.; Chae, Y. The dynamic relationship between emotional and physical states: An observational study of personal health records. *Neuropsychiatr. Dis. Treat* **2017**, *13*, 411–419. [CrossRef]
58. Silva, A.M.; Matias, C.N.; Nunes, C.L.; Santos, D.A.; Marini, E.; Lukaski, H.C.; Sardinha, L.B. Lack of agreement of in vivo raw bioimpedance measurements obtained from two single and multi-frequency bioelectrical impedance devices. *Eur. J. Clin. Nutr.* **2019**, *73*, 1077–1083. [CrossRef]

CAPÍTULO 5

RESUMEN DE RESULTADOS Y DISCUSIÓN

Capítulo 5. Resumen de Resultados y Discusión

Cada vez es mayor la evidencia existente sobre los beneficios del ejercicio físico para la mejora de la salud (Pedersen & Saltin, 2015) y esto se aprecia en un aumento del interes por parte de los sanitarios que recomiendan ejercicio físico como parte del tratamiento de diferentes patologías o como soporte para mejorar la eficacia de tratamientos convencionales(Luan et al., 2019). En 2013, un equipo de investigación español acuñó al ejercicio físico el término de "polipíldora" debido a que podría mimetizar el efecto de una gran cantidad de medicamentos en cuanto a la salud se refiere(Fiuza-Luces et al., 2013).

Cuando entramos en el ejercicio físico y el cáncer, autores relevantes en el campo hablan de los beneficios que tiene el EF bien planificado e individualizado, en el manejo de los efectos secundarios del tratamiento tanto a nivel físico como psicológico(Rezende et al., 2018; Schmitz et al., 2010; Wolin et al., 2012). En la actualidad, cada vez es mayor el número de sanitarios que recomiendan la práctica de ejercicio físico debido al creciente número de evidencias a favor de la práctica y la creación de guías claras de actuación al igual que programas de intervención(Campbell et al., 2019; Orange et al., 2021).

Del mismo modo, la inactividad física y el tiempo de sedentarismo se asocia a un incremento en las probabilidades de padecer cáncer de cualquier tipo(Schmid & Leitzmann, 2014) y a padecer mayor cantidad de efectos secundarios en comparación con el grupo que realizaba EF durante el tratamiento(Mustian et al., 2009; Piraux et al., 2020). Estos estudios muestran la importancia de evitar el sedentarismo y la inactividad física, lo que está relacionado con el primer artículo de la presente tesis doctoral. Debido a una privación forzada de la libertad de salir al exterior debido a un estado de alarma producido por el COVID-19, los niveles de actividad física y ejercicio físico se vieron reducidos de manera drástica durante este confinamiento. Conociendo la actual evidencia que existe sobre la inactividad física y los problemas que acarrea, queríamos conocer en profundidad el declive que esto produjo en los pacientes de cáncer.

Un aspecto importante a la hora del manejo del paciente de cáncer es el seguimiento clínico tras el tratamiento con el objetivo de controlar los efectos secundarios, detectar precozmente las posibles recaídas y ofrecer al enfermo una relación más continua en el tiempo. Sin embargo, por las características del manejo de estos enfermos (multidisciplinaria), el seguimiento puede hacerse de forma engorrosa, redundante e ineficaz por lo que es necesario tener herramientas fáciles de utilizar y que proporcionen la mayor cantidad de información posible al equipo médico con el fin de tomar las mejores decisiones(Chu et al., 2022; Expósito Hernández & Dadet, 2004)

Resumen de resultados y discusión del artículo 1:

En cuanto a los resultados más relevantes, se observa una reducción significativa en WT and ST. También se observa una reducción significativa de fuerza tanto en tren superior como inferior. En cuanto a los aspectos psicológicos, no se aprecian diferencias significativas en ninguno los parámetros analizados.

TABLA 9: *Niveles de composición corporal y parámetros físicos y fisiológicos antes y después de la interrupción de la AF debido al estado de emergencia.*

Variable	Pre (Mean±SD)	Post (Mean±SD)	p-value	d-Cohen
Musculoskeletal mass (kg)	23.8±5.4	23.8±5.6	0.934	0
Fat mass (%)	37.1±8.4	35.5±10.7	0.354	0.16
Visceral fat (cm^2)	134.2±54.2	132.4±55.3	0.791	0.03
VO_{2peak} (mL·min·kg−1)	17.03±5.08	15.42±3.98	0.023*	0.35
WMAX (W)	90.34±28.85	86.55±27.03	0.078	0.14
WVT2 (W)	88.57±26.06	85±26.60	0.106	0.13
Lower body strength (kg)	61.96±22.10	52.86±23.18	0.012*	0.40
Upper body strength (kg)	30.39±14.46	24.95±14.27	0.009*	0.38

Notes: *=p<0.05; WMAX: Watts maximun ; WVT2: Watts at ventilatory threshold 2.

En cuanto a la composición corporal, no se aprecian modificaciones en cuanto a valores pre y post el estado de alarma. Esto puede ser debido a que los pacientes ya tenían una composición corporal modificada debido a la enfermedad en la que se aprecian aumentos en la masa grasa y reducciones en la cantidad de masa muscular (Brown et al., 2018).

Cada vez hay más evidencia sobre la reducción de actividad física durante un estado de alarma con restricciones de movilidad como el que está suponiendo el COVID-19 y debido a esta creciente evidencia, actualmente existen revisiones sistemáticas sobre el comportamiento de la cantidad de actividad física durante el estado de emergencia por COVID-19 en población general (Stockwell et al., 2021) apreciándose en los artículos revisados una reducción en los niveles de actividad física y aumento de tiempo sentado.

En la muestra estudiada, no se aprecian diferencias significativas en VPA, posiblemente debido a los bajos niveles de actividad que realizan a esta intensidad debido a la patología, dado que la propia patología induce un estado de fatiga crónica que podría impedir la práctica de ejercicio físico (Cramp & Daniel, 2008) pero a su vez, romper con este círculo vicioso y empezar a realizar ejercicio físico es una buena estrategia para combatir la fatiga relacionada con el cáncer (Lucía et al., 2003).

TABLA 10: *Variaciones en los niveles de AF y tiempo sentado durante y después del estado de emergencia debido a COVID-19. (*=p<0.05)*

Variable	During	Post	p-value	d-Cohen
VPA (min/week)	1.88±10.61	0	0.325	<0.01
MPA (min/week)	117.50±160.02	91.56±124.24	0.349	0.18
WALKING TIME (min/week)	76±113.08	327.50±206.92	<0.001*	1.51
SITTING TIME (hours/day)	7.53±2.66	6.63±5	0.014*	0.47

Notes: VPA: vigorous physical activity; MPV: Moderate physical activity

Se debe apreciar que nuestra muestra no realiza los niveles mínimos de actividad física vigorosa recomendados por la WHO de >75 minutos/semana que, aunque estas recomendaciones son para población sana, se ha visto que la realización de estos mínimos de PA tanto en VPA como MPA en personas con patologías y en concreto en cáncer, tiene efectos positivos en el pronóstico de la enfermedad (McTiernan et al., 2019; Rezende et al., 2018). La realización de este tipo de actividades intensas o alta intensidad sería recomendada debido a que produce adaptaciones similares a las producidas por ejercicio prolongado de intensidad moderada pero en menor tiempo (-40% de tiempo) por lo que se podría hablar de que el ejercicio de intensidad vigorosa es más eficiente en la producción de adaptaciones fisiológicas beneficiosas y saludables y una práctica segura (McTiernan et al., 2019; Wallen et al., 2020; Wewege et al., 2017).

En cuanto a los niveles de MPA se observa que los valores en la práctica de actividad física a dicha intensidad son mayores y esto representa que este colectivo realiza más MPA que VPA aunque tampoco llegan a las recomendaciones mínimas de la WHO de >150 minutos/semanales de MPA (Bull et al., 2020). El tiempo de andar, por otra parte, se ve reducido durante el estado de emergencia debido posiblemente a la imposibilidad de salir de sus domicilios (durante un periodo del estado de alarma) o restricciones de movilidad entre territorios, pero una vez finalizado el periodo restricciones de movilidad, se observa un brusco incremento en el tiempo de andar posiblemente debido a ser una actividad al aire libre y por ello libre de posibles riesgos de contagio por COVID-19. Del mismo modo, al reducirse el tiempo de andar, aumenta el tiempo de sentado, observándose también una reducción cuando el tiempo de andar aumenta.

Aunque la muestra estudiada es una población la cual recibió o está recibiendo tratamiento para el cáncer, en la población general se observan unas reducciones/aumentos similares como se ha podido observar en el estudio llevado a cabo por investigadores españoles con una muestra de 3800 sujetos sanos antes y durante el state of emergency, observándose reducciones en VPA, MPA y tiempo de andar pero un aumento en el tiempo sentado (Castañeda-Babarro, Arbillaga-Etxarri, et al., 2020b). Este patrón de comportamiento en cuanto a los tiempos de actividad se corroboran con revisiones de artículos sobre el efecto del confinamiento en la práctica de actividad física (Stockwell et al., 2021).

La reducción en actividad física lleva a unas adaptaciones fisiológicas negativas en niveles cardiovasculares y fuerza como las más destacadas llegando a perder la autonomía del propio paciente según la edad y pronóstico de la enfermedad (Dias Reis et al., 2017). El consumo de oxigeno pico (VO_{2pico}) es un predictor de supervivencia en población general (Kavanagh et al., 2002; Myers et al., 2002) y en población afectada de cáncer (Jones et al., 2010; Schmitz et al., 2010). En la muestra estudiada se aprecia una reducción significativa del VO_{2pico} durante el periodo estudiado. El VO_{2pico} depende de tres componentes principales, la captación de oxígeno, la distribución del mismo hasta el músculo vía arterial y por la utilización en la generación de energía por parte de las mitocondrias (Sietsema et al., 2020). Si observamos los efectos del desentrenamiento en estos componentes del VO_{2pico}, podemos ver como en dos días de no entrenamiento se reduce los niveles plasmáticos entre 5-12% (Cullinane et al., 1986). También en cuanto al trasporte del oxígeno, se aprecia una reducción del 8% del fracción de eyección cardiaca en 21 días de desentrenamiento juntos con otras adaptaciones cardiacas (Coyle et al., 1985). También la capilarización muscular se reduce hasta niveles previos al entrenamiento en tan solo 4 semanas (Klausen et al., 1981). Por último, en el uso del oxígeno (O2), se observan reducciones en la producción de ATP por las mitocondrias en un 12-28% en 3 semanas de cesión del entrenamiento (Klausen et al., 1981). En pacientes de cáncer de mama se ha visto cómo un desentrenamiento de 8 semanas posterior a un entrenamiento combinado de 8 semanas produjo reducciones en niveles cardiovasculares en torno a un 8% en VO_{2max}. (Herrero et al., 2007).

A su vez, debido a la reducción en la práctica de PA, los niveles de fuerza se ven reducidos significativamente durante el estado de alarma por COVID-19. En los artículos de Mújika y Padilla (Mujika & Padilla, 2000a, 2000b) se explica cómo los niveles de fuerza pueden verse reducidos entre un 7-12% en un periodo de inactividad de entre 8-12 semanas, en estos pacientes, aun no siendo una inactividad total, los niveles de fuerza se vieron reducido (14,68% en fuerza de tren inferior y 17,9% en tren superior) en mayor medida que en lo esperado por inactividad total en población deportista posiblemente debido a su tratamiento pero a su vez no se ven pérdidas de masa muscular como cabría esperar en base a las características de estos pacientes y sus tratamientos (Fearon et al., 2011; Montalvo et al., 2018). De acuerdo con esta evidencia, en nuestra muestra se aprecian reducciones de fuerza de en torno a un 14-15% por lo que se asemejan a las perdidas en población sana deportista. En el estudio previamente citado (Herrero et al., 2007) se obtuvo una reducción de fuerza tanto en tren superior como inferior que van en la misma tendencia con los datos encontrados en nuestra muestra de pacientes de cáncer. Se puede hablar de que ha existido una reducción de fuerza debido a desadaptaciones neuronales por falta de entrenamiento de fuerza dado que las adaptaciones periféricas (cantidad de masa muscular) no se ha visto modificada.

TABLA 11: *Diferencias psicológicas entre antes y después del estado de emergencia debido al COVID.*

Variable	Pre	Post	P value	d-Cohen
EORTC QLQ30				
Global health status	4.74±1.15	4.83±1.19	0.684	0.08
Emotion role	1.56±0.63	1.55±0.56	0.798	0.02
Social function	1.56±0.83	1.67±0.92	0.408	0.12
Cognitive function	1.53±0.71	1.54±0.75	0.851	0.01
SF-36				
Emotional role	1.77±0.39	1.87±0.38	0.096	0.26
Mental health	4.26±0.82	4.14±0.75	0.568	0.15

Notes: EORTC QLQ-C-30: European Organization for Research and Treatment of Cancer; SF-36: Short-Form Health Survey.

En cuanto a los resultados en psicología presentados en la tabla 11, no se aprecian diferencias significativas en ninguna de las variables medidas con los cuestionarios SF-36 y EORTC QLQ-30. Esto podría deberse a los resultados negativos que tienen estos pacientes en este tipo de cuestionario que mide calidad de vida debido a la mala percepción de la calidad de vida de estos pacientes debido a su grave problema de salud

(Cruz Bermudez et al., 2013). En estudios realizados en pacientes de cáncer, se vio cómo el ejercicio físico tiene efectos significativos en la mejora de global health status medido mediante el cuestionario EORTC QLQ30 pero no se aprecian diferencias significativas cuando se comparan los valores previos a la intervención y los valores durante el periodo de estado de emergencia. Además, no se aprecian diferencias significativas en ninguno de los items cuando se comparan los datos pre entrenamiento (sin haber empezado el programa de ejercicio) y los obtenidos después de un periodo de estado de excepción por lo que se puede concluir que después de un periodo de estado de excepción, se volvería a un punto inicial en cuanto a valores subjetivos de calidad de vida (Herrero et al., 2007). Cuando observamos el ítem de emotional role, se aprecia una tendencia a la significancia. Debido al periodo de estado de alarma, puede darse una reducción en la valoración subjetiva del estado emocional habiéndose perjudicado a las restricciones como se vio en personas sanas un aumento en ansiedad, depresión e impacto emocional (Pérez-Fuentes et al., 2020).

Resumen de resultados y discusión del artículo 2:

En esta investigación se utilizó el PhA como predictor del rendimiento físico, considerando que es un método no invasivo, barato y rápido, con una alta correlación con 400 m WT, UBS, LBS, $VO_{2\ pico}$, VT1 y VT2. Por lo tanto, cumple los objetivos de estudiar la relación entre los valores de PhA y el rendimiento físico, y analizar si esta relación se ve afectada por las diferencias de edad y sexo.

Un PhA alto representa una buena calidad celular (desde el punto de vista de la membrana celular porque es el parámetro analizado por el PhA), y un PhA bajo representa una calidad celular disminuida o incluso una muerte celular. El PhA suele oscilar entre 4 y 9 en individuos sanos y disminuye en las mujeres, así como con el aumento de la edad, siendo más bajo en las mujeres, un índice de masa corporal elevado y diversos estados patológicos, como el cáncer (Hui et al., 2019). En nuestro estudio, al igual que en investigaciones anteriores, se ha observado este patrón de cambio en el PhA en función de la edad y el sexo.

TABLA 12: *Relación entre rendimiento físico y el PhA.*

Variable	Mixed linear Regression Estimate [95% CI]	Mixed Linear Regression p-Value	Pearson Correlation [95%CI]	p-Value
400 mWT(sec)	−22.57 [−27.58; −17.53]	<0.001	−0.36 [−0.42; −0.3]	<0.001
UBS (kg)	6.3 [4.95; 7.65]	<0.001	0.54 [0.48;0.59]	<0.001
LBS (kg)	13.25 [10.13; 16.35]	<0.001	0.47 [0.42;0.53]	<0.001
VO_{2peak} (ml/kg/min)	1.55 [0.98; 2.12]	<0.001	0.25 [0.18;0.32]	<0.001
VT1 (W)	6.53 [3.83; 9.20]	<0.001	0.35 [0.28;0.42]	<0.001
VT2 (W)	10.36 [7.02; 13.64]	<0.001	0.42 [0.36;0.49]	<0.001

Note: Sec: seconds; kg: kilograms; W: watts; UBS: upper-body strength; LBS: Lower-Body strength. Statistical significance set at $p < 0.05$.

El PhA medio de nuestra muestra es de 4,88º, siendo inferior a los valores recogidos en una población sana de referencia con IMC normal (18,5-25) y edad media entre 50-59 años (referida a la edad media de nuestra muestra) que mostró un PhA de 5,73 ± 0,68, aproximadamente un grado superior a la muestra de cáncer estudiada. Además, nuestra muestra, incluso tiene un PhA más bajo que las personas sanas con obesidad (IMC > 40) con edades comprendidas entre 50-59 años (refiriéndose a la edad media de nuestra muestra) con un PhA de 5,81± 0,7 e incluso las personas mayores de 70 años con IMC > 40 con un PhA medio de 5,07 ± 0,72 (Bosy-Westphal et al., 2006).

El sexo y la edad fueron los principales determinantes del PhA en adultos, siendo los varones y los sujetos más jóvenes los que presentaron un PhA más elevado (Bosy-Westphal et al., 2006). Otros estudios muestran resultados similares en adultos. El ángulo de fase fue significativamente menor en las mujeres que en los hombres y fue menor a edades más avanzadas (Barbosa-Silva et al., 2005). Como puede observarse en las figuras 1 y 2, la muestra de nuestro estudio se comporta de la misma manera, lo que corrobora los resultados de investigaciones anteriores sobre el cambio del PhA en función de la edad y el sexo. Esta es una característica importante a tener en cuenta a la hora de evaluar el valor del PhA. Debido a estos resultados obtenidos en otras investigaciones, y como nuestra muestra se comporta de la misma manera, se propuso analizar los datos, considerando estas dos variables de importante relevancia para la interpretación de los datos.

Siguiendo con las valoraciones de la capacidad funcional, se ha observado en otros estudios que las pacientes con cáncer de mama, divididas en dos grupos por PhA ≤ 5,6 o >5,6 grados, no muestran diferencias significativas en la prueba de marcha de 6 min (p = 0,678) (Alexandre D Martins et al., 2021). Esta investigación se realizó en una pequeña muestra poblacional de n = 25 dividida en dos grupos de n = 12 hombres y n = 13 mujeres, mucho menor que la muestra de nuestro estudio (n = 311). Concretamente, en nuestra investigación, considerando los resultados de 311 pacientes con cáncer, podemos observar que los valores de 400 mWT pueden predecirse con gran exactitud y significación mediante la medición de la PhA, por lo que podría ser una herramienta útil para predecir la mejora de la capacidad funcional en un entorno clínico en el que quizá no sea posible realizar mediciones de la capacidad funcional como la prueba de marcha de 6 min o la de 400 mWT. En estos resultados se están comparando dos pruebas diferentes (test de marcha de 6 min y 400 mWT), pero, debido a la falta de evidencia científica sobre la relación del PhA y 400 mWT, y teniendo en cuenta que la naturaleza de las pruebas es similar, aceptamos la comparación sin que se utilice la misma prueba en cada caso (Schmidt et al., 2013).

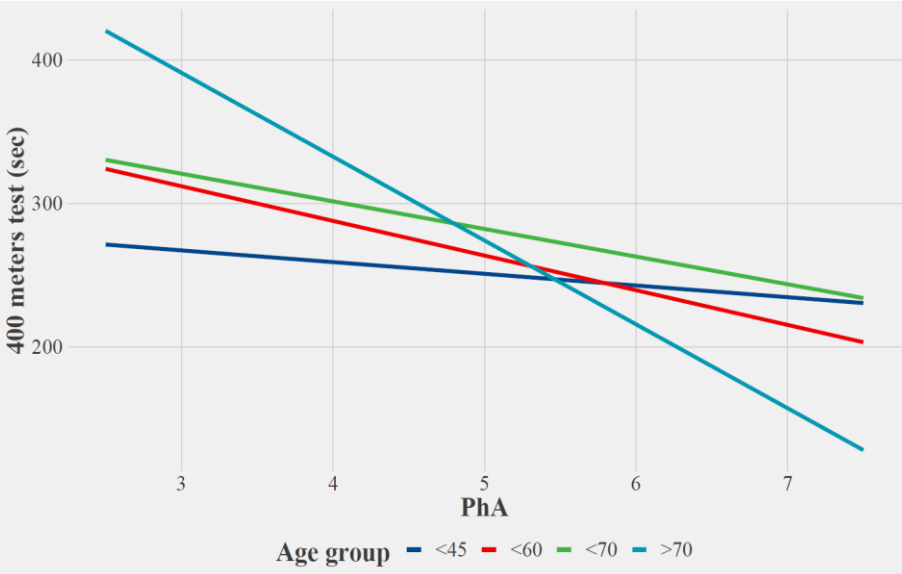
Por otra parte, la reducción de la masa y la fuerza musculares forma parte de la sintomatología de la sarcopenia, más aún en los pacientes con cáncer (Sieber, 2019). Artículos de revisión anteriores han mostrado una relación entre el ángulo de fase y la sarcopenia(Di Vincenzo et al., 2021). Se muestra cómo el PhA está disminuido en sujetos sarcopénicos, lo que conduce a una reducción de la fuerza en estos pacientes. También se evidenció que la prevalencia de sarcopenia es mayor en sujetos con bajo PhA, aunque se necesitan más estudios para determinar hasta qué punto el PhA puede ser valioso para detectar baja calidad muscular y/o identificar sarcopenia (Di Vincenzo et al., 2021). En nuestro estudio hemos observado aumentos en los niveles de fuerza a medida que aumenta el PhA. Esto demuestra cómo el valor de la fuerza está fuertemente relacionado con el PhA y es, por tanto, un parámetro que proporciona información sobre los niveles de fuerza sin necesidad de realizar una prueba de fuerza específica, lo que facilita el seguimiento del paciente oncológico. Muchos estudios han informado de la relevancia clínica de la disminución del ángulo de fase o sarcopenia como predictor de una menor supervivencia al cáncer (Hui et al., 2014; Martin et al., 2013; Paiva et al., 2010; Stegel et al., 2016). Dada la importancia del ángulo de fase como predictor de sarcopenia y mala calidad muscular, nuestro hallazgo de la asociación de PhA con un aumento de los niveles de fuerza tanto en la parte superior como inferior del cuerpo puede ser un elemento clave para mejorar la calidad de vida. Si este aumento de la fuerza se mantiene en el tiempo, conducirá a un aumento de la masa muscular y a una inversión o retraso de la aparición de la sarcopenia.

Es bien sabido que cuando estos eventos ocurren, el pronóstico frente a cualquier enfermedad es peor, y esto tiene una importante relevancia clínica desde que se conoce esta relación. Se puede prestar especial atención a los pacientes con riesgo de sarcopenia para reducir, ralentizar e incluso revertir la enfermedad para mejorar la funcionalidad del paciente, y por tanto su pronóstico frente a la enfermedad, ya que la sarcopenia es un efector adverso en pacientes con cáncer. Ésta se asocia a una reducción del estado funcional, de las complicaciones y de la supervivencia global (Baracos et al., 2010; Janssen et al., 2004). También se ha observado que, como consecuencia de los tratamientos, la nutrición de los pacientes empeora y da lugar a casos de sarcopenia. Antes del tratamiento, el 69,1% de los pacientes estaban bien nutridos, el 16,4% desnutridos y el 14,5% caquéxicos/sarcopénicos; las proporciones después del tratamiento fueron del 16,4%, el 45,4% y el 38,2%, respectivamente (Stegel et al., 2016). Por lo tanto, los pacientes con cáncer deben prestar especial atención a la nutrición, especialmente a los niveles de proteínas consumidas (Ravasco, 2019), y al ejercicio físico específico dirigido a aumentar o mantener la masa muscular con el fin de aumentar los niveles de fuerza (Koeppel et al., 2021) y, por lo tanto, PhA.

En cuanto a los valores del VO_{2pico} (que representan el patrón oro en la representación del nivel de capacidad funcional), puede observarse la significación que muestra el valor cuando es predicho por el PhA. Los valores observados no parecen ser significativamente relevantes debido a su pequeña magnitud (1,55 cada ángulo del PhA), pero puede determinarse que los ligeros aumentos en pacientes con un VO_{2pico} bajo (media de 15,3 ± 4) pueden ser significativos como mejora de la salud. Los ligeros cambios beneficiosos observados en el VO_{2pico} son clínicamente relevantes porque el VO_{2pico} es un importante predictor de la mortalidad por cualquier causa [37,38]. Nuestros resultados, combinados con hallazgos previos de deterioro del VO_{2pico} entre pacientes con cáncer con valores observados que oscilan entre 15,75 ± 5,52 y 29,82 ± 5,08 (Kodama et al., 2009; O'Neill et al., 2005), enfatizan la importancia clínica de aumentar o mantener el VO_{2pico} en esta etapa de la trayectoria del cáncer. Por tanto, aunque se observan cambios en el VO_{2pico} que en la población normal serían ligeramente bajos (cambios de 1,55 por cada grado de PhA), en los pacientes con cáncer podrían ser decisivos para mantener la funcionalidad en las actividades de la vida diaria el VO_{2pico} por sí solo sólo representa la capacidad del organismo para captar, transportar y consumir oxígeno durante el ejercicio (Lundby et al., 2017). Por lo tanto, es aconsejable observar también la mejora en VT1 y VT2, ya que estos son los umbrales en los que se producen modificaciones en la fisiología del individuo y se utilizan para prescribir ejercicio físico en atletas (Seiler & Kjerland, 2006) y en pacientes con cáncer (Schneider et al., 2020). Por lo tanto, la relación significativa entre los aumentos del VT1 y VT2 con el PhA lo convierte en un predictor de la mejora tanto del VO_{2pico} como del VT1 y VT2, lo que representa una mejora de la capacidad funcional de los pacientes oncológicos. Siendo la valoración y medición del $VO_{2Máx}$ el valor más preciso para conocer el estado del sistema cardiovascular y la implicación en la predicción de mortalidad por cualquier causa (Kodama et al., 2009), es un método caro y laborioso, por lo que en ocasiones, no se dispone de esta metodología. Por esta razón, se buscaron correlaciones entre este valor y otros de mayor complejidad y precio en el momento de la evaluación. Las pruebas de marcha de larga distancia como la de 400 mWT, cuando se realizan lo más rápido posible, se utilizan ampliamente para evaluar la aptitud cardiorrespiratoria (Lindemann et al., 2021). A través de este estudio, estamos dando otra alternativa a las costosas pruebas de VO_{2pico} de laboratorio, mediante la PhA sabiendo que están estrechamente relacionadas, podríamos saber, con sus limitaciones en cuanto a precisión, en qué niveles de VO_{2pico} podría estar el paciente con cáncer, sabiendo que si los valores de PhA aumentan, lo más probable es que sus valores de VO_{2pico} también aumenten.

En cuanto a la relación entre el rendimiento de 400 mWT, el PhA y la edad, se observa que cuanto mayor es la edad, mayor es la relación entre estas variables. Esto puede deberse a que el 400 mWT se utiliza a edades más avanzadas para determinar la función de esa persona mayor (Rolland et al., 2004). Por lo tanto, lo que podemos determinar, es que a mayor edad, mejor es la relación entre PhA y 400 mWT. Por eso es un dato importante a tener en cuenta a la hora de hacer esta predicción del rendimiento.

Figura 2: *Estimated relationship between PhA and 400 mWT by age group.*



. ***Resumen de resultados y discusión del artículo 3:***

En esta investigación se analizó la relación existente entre el PhA y los cuestionarios GHQ-12, FACIT, SF-36 y QLQ-C30. Se encontraron relaciones significativas entre los valores del cuestionario GHQ-12 y los valores de PhA, lo que indica que a menor puntuación en el GHQ-12, mejor es el estado de salud general del paciente y mayor es la PhA. Del mismo modo, se observó una relación entre los puntajes del cuestionario FACIT y el valor de PhA, donde a mayor puntaje en el FACIT, menor era la fatiga percibida.

Además, se encontró una relación significativa entre el cuestionario SF-36 y la PhA, excepto en las subclasificaciones de "rol emocional" e "índice de dolor". El SF-36 indica que a menor puntuación en estas subclasificaciones, mayor es la limitación del paciente.

El cuestionario QLQ-C30 se divide en dos escalas principales: la escala de funcionamiento y la escala de síntomas. En la escala de funcionamiento, se encontró una relación con la PhA, excepto en los parámetros de "funcionamiento emocional" y "funcionamiento cognitivo". En la escala de síntomas, solo los parámetros de fatiga, náuseas y vómitos, y pérdida de apetito estuvieron relacionados con la PhA.

Este estudio analizó las posibles asociaciones entre la actividad física (PhA, por sus siglas en inglés) y la percepción subjetiva de varios parámetros de salud en pacientes con cáncer. Entre los resultados más relevantes, encontramos que mientras la relación con la PhA es alta en los cuestionarios GHQ-12, FACIT y SF-36, donde una mayor PhA se asocia con mejores resultados, se encontró una relación con la PhA en los ítems de evaluación de la escala de funcionamiento del QLQ-C30 pero no en la mayoría de sus escalas de síntomas.

En cuanto a la evaluación subjetiva del paciente, el cuestionario GHQ-12 mide posibles trastornos afectivos en diferentes poblaciones (Aaronson et al., 1993). Por lo tanto, como herramienta válida, encontrar una alta relación con la PhA podría ayudarnos a predecir trastornos afectivos con otras herramientas, como la PhA. Los resultados obtenidos en nuestra investigación muestran cómo los dos valores, tanto la puntuación del GHQ-12 como la PhA, están estrechamente correlacionados, con valores más altos en el GHQ-12 que conducen a valores más altos en la PhA.

De la misma manera que investigaciones anteriores han mostrado una relación entre la actividad física (PhA) y perfiles físicos mejorados (Saladino et al., 2020), no es infrecuente observar la misma tendencia de valores más altos de PhA con perfiles psicológicos mejorados. La relación que la PhA tiene con aspectos físicos y psicológicos podría llevar a la hipótesis de que cuanto mejor sea la salud física, mejor será la salud psicológica y, por lo tanto, más alta será la PhA. Otra posible hipótesis para esta relación entre los valores del GHQ-12 y la PhA podría ser la integridad celular, ya que los pacientes con un perfil psicológico mejorado podrían ser aquellos con una integridad celular más favorable (Więch et al., 2022).

La fatiga relacionada con el cáncer es un efecto secundario común del tratamiento contra el cáncer, por lo que desde hace tiempo se ha utilizado el cuestionario de fatiga (FACIT) para evaluar y monitorear este efecto secundario (Anjara et al., 2020), especialmente como parte de programas de ejercicio físico. Nuestra investigación ha mostrado una estrecha relación entre los valores de este cuestionario y los valores de PhA medidos, demostrando que niveles más altos de PhA se traducirían en una menor fatiga según lo medido por el cuestionario. Este resultado se discute en investigaciones anteriores donde se observa una relación entre la fatiga y la PhA, especialmente en pacientes con cáncer con PhA <4, pero cuando se ajusta por parámetros de hidratación (agua intracelular y extracelular), la asociación se reduce (Al-shair et al., 2012). La relación entre estos dos parámetros, fatiga y PhA, tiene una relevancia importante dado que los valores de PhA pueden estar relacionados con el valor del cuestionario de fatiga (FACIT), sabiendo que, en nuestro estudio, por cada aumento de una unidad en la PhA, se puede observar una mejora de 3,2 (1,99; 4,41) puntos en las puntuaciones del FACIT con una relación alta. Esta relación entre la fatiga y la PhA podría explicarse por el hecho de que la PhA es un indicador de la salud física en pacientes con cáncer (Saladino et al., 2020), por lo que valores más bajos de PhA indican una peor condición física, lo cual fácilmente se puede asociar con una mayor fatiga.

Al analizar los resultados del cuestionario SF-36, que mide la calidad de vida relacionada con la salud, observamos una alta relación con los valores obtenidos en la PhA. Se sabe que en la mayoría de las ocasiones, una mejor calidad de vida es precedida por cambios en el estilo de vida, lo cual afecta positivamente a la PhA. Se ha visto que mejorar el estado nutricional mediante una mejor dieta practicar ejercicio físico planificado o mejorar la composición corporal (Hui et al., 2019; Ohrnberger et al., 2017) puede llevar a una mejor calidad de vida y PhA. Por lo tanto, la mejora en cualquier aspecto que favorezca la calidad de vida afecta positivamente tanto a los valores del SF-36 como a la PhA.

Las subsecciones medidas por este cuestionario SF-36 están altamente relacionadas con la PhA con valores de $p<0,05$, excepto para los parámetros de rol emocional y dolor, que no se ha encontrado que tengan una relación significativa. El rol emocional mide el grado en que los problemas emocionales interfieren con el trabajo u otras actividades diarias, por lo que se puede inferir que no hay relación entre la PhA y esta medida, posiblemente porque, en muchos casos, los problemas psicológicos no afectan sus actividades diarias, aunque una gran proporción reporta episodios de depresión y ansiedad (Hauth et al., 2021). Además, estos resultados pueden estar sesgados por la posible medicación psiquiátrica para controlar estos problemas de depresión y ansiedad, ya que al menos el 25-30% de los pacientes con cáncer e incluso un mayor porcentaje de aquellos con enfermedad avanzada cumplen los criterios para un diagnóstico psiquiátrico, incluyendo depresión, ansiedad, síndromes relacionados con el estrés, trastornos de adaptación, trastornos del sueño y delirio (Gomes et al., 2020). Estudios anteriores mostraron que el rol emocional y el estado físico se influenciaban negativamente entre sí, mientras que la fatiga y el dolor se influenciaban positivamente entre sí. Estos resultados sugieren que la mente y el cuerpo interactúan de manera directa (Gupta et al., 2008), con diferencias en los resultados en nuestra investigación.

Los resultados obtenidos en el QLQ-C30, específicamente los correspondientes a la medición de las escalas de funcionamiento, muestran que el funcionamiento emocional no está relacionado con la PhA. Cabe destacar que esta misma sección fue evaluada en el cuestionario SF-36, arrojando datos similares en cuanto a la falta de significancia de la relación con la PhA, lo cual confirma la falta de significancia de la relación con la PhA utilizando dos herramientas diferentes. Esto podría ser porque, como hemos mencionado anteriormente, el valor mejor o peor de la PhA es independiente de los problemas que la enfermedad pueda causar en el trabajo o las actividades diarias. La nutrición juega un papel fundamental en la calidad de vida y en la posibilidad de modificar los valores de PhA. Por lo tanto, un parámetro relacionado con la nutrición podría ser el ítem que habla de la pérdida de apetito medido con el QLQ-C30, el cual tiene una relación significativa con la PhA. Así, los pacientes con baja PhA tienen una pérdida de apetito significativa.

La relación de la PhA con el dolor no es significativa según los resultados de los cuestionarios QLQ-C30 y SF-36. El mismo parámetro, medido con dos instrumentos diferentes, nos proporciona información importante de que no tiene relación con la PhA.

Debido a la novedad de los parámetros analizados y la asociación relativa entre los parámetros, se necesita más y mejor investigación para poder aplicar este conocimiento en la práctica diaria, aunque esta investigación sienta las bases para futuras investigaciones sobre la PhA en el manejo de pacientes con cáncer.

Es importante tener en cuenta que las mediciones de bioimpedancia obtenidas de dispositivos de frecuencia única y multifrecuencia no deben tratarse como intercambiables. Al evaluar poblaciones altamente activas, se observó una notable falta de consenso entre los dispositivos al determinar valores individuales como R, Xc, Z y PhA(Lee et al., 2017). Esta discrepancia podría atribuirse a diversos factores metodológicos y biológicos. En consecuencia, si se va a aplicar esta metodología en la práctica clínica, se recomienda encarecidamente utilizar de manera consistente el mismo dispositivo, realizar las mediciones en condiciones lo más similares posibles y abstenerse de comparar los resultados con datos obtenidos de diferentes dispositivos o metodologías.

CAPÍTULO 6

CONCLUSIONES, LIMITACIONES Y FUTURAS LÍNEAS DE INVESTIGACIÓN

Capítulo 6. Conclusiones, Limitaciones, Futuras Líneas de Investigación

Conclusiones

There is an increasing amount of data on the population affected by cancer, and expectations for the coming years indicate a rising trend in the number of new diagnoses. One of the most important factors in managing both the disease and the side effects of treatment is the practice of physical activity and individually tailored exercise. Engaging in the minimum recommended levels of physical activity by the World Health Organization (WHO) is sufficient to obtain most of the benefits of this practice. Therefore, one of the recommendations that doctors are increasingly adding when notifying a cancer diagnosis is education on physical exercise, the elimination of toxic habits, and the practice of a healthy lifestyle as a fundamental part of pharmacological treatment.

With the arrival of COVID-19, the hours of physical activity practice were greatly reduced in the general population. At the same time, maintaining a relationship with the general population, cancer-affected individuals were also negatively impacted due to public health restrictions aimed at containing the pandemic, which limited outdoor activities. Due to these restrictions, cancer patients experienced physical limitations during the lockdown. However, their psychological capacities were not as affected, likely due to the psychological stress that cancer patients are exposed to because of their illness.

Cancer is a disease that affects both the physical and emotional aspects of a person. During times of confinement, when access to outdoor activities and exercise spaces may be limited, staying active is more important than ever for cancer patients. From a physical perspective, staying active during confinement can help improve physical fitness and the quality of life for cancer patients. Physical activity can enhance cardiovascular function and muscular strength. Furthermore, exercise can also help reduce the risk of cancer and treatment-related side effects, such as fatigue, muscle loss, pain, etc.

From a psychological standpoint, physical activity is also beneficial for cancer patients during confinement. Cancer and its treatment can be very stressful and cause anxiety and depression. Physical activity can help reduce these symptoms by releasing endorphins that can improve mood and reduce stress.

Additionally, exercise can provide a sense of accomplishment and a feeling of control over one's own body, which can be especially important for cancer patients who may feel they have lost control over their health.

It is important to note that the type and amount of physical activity that is appropriate for each cancer patient may vary depending on their health status, the type of cancer, and the treatment they are receiving. Therefore, it is always important to consult with your doctor before starting any exercise program and, if possible, engage in physical exercise under the guidance of specialized personnel trained in cancer patient care, addressing their potential needs in the best possible way.

When it comes to managing cancer patients and determining the best exercise dose for each patient based on their disease status, it is vital to have objective data on both physical and psychological health. There are various tools such as physical and psychological tests that correlate with the disease's status. The more tools available for evaluating a patient, the better and more precise the physical exercise intervention can be. Therefore, this doctoral thesis aimed to assess the possibility of using a new parameter that can help us better understand the patient. This parameter is novel and has incalculable potential due to its ease, speed, and precision.

The phase angle is a measure of the relationship between body mass and total body water and can be a useful tool for evaluating the health and nutrition of a cancer patient. Moreover, the phase angle can be affected by multiple factors associated with cancer, such as cancer stage and the type of treatment received.

The phase angle is determined by measuring a patient's electrical impedance. Electrical impedance is the resistance that the body offers to electric current and is related to the amount of body water present. The phase angle is calculated from the phase difference between the electric current and voltage measured in the body. A low phase angle indicates a decrease in body water relative to body mass, which can indicate dehydration, malnutrition, or a chronic illness.

In cancer patients, the phase angle can be affected by various factors. The cancer stage is one of the factors that can influence the phase angle. Patients with advanced-stage cancer may have a low phase angle due to the loss of muscle mass and dehydration associated with cancer and its treatment. Muscle loss and dehydration are common in advanced-stage cancer patients due to a lack of appetite, nausea, and treatment side effects.

The type of treatment received can also influence the phase angle. Patients undergoing chemotherapy or radiation therapy may experience nausea, vomiting, and diarrhea, which can affect body hydration and nutrition. Chemotherapy and radiation therapy can also lead to a decrease in muscle mass and an increase in inflammation, which can impact the phase angle.

Regular physical exercise can have a positive impact on the phase angle in cancer patients. Exercise can help improve muscle mass and hydration, which can increase the phase angle. Additionally, exercise can help reduce inflammation and enhance the immune response, which can have a positive impact on overall health.

In conclusion, the phase angle is a useful measure for assessing the health and nutrition of cancer patients. The cancer stage and the type of treatment received can influence the phase angle. Regular physical exercise can have a positive impact on the phase angle and improve muscle mass, hydration, and immune response.

Limitaciones

Hay que reconocer y tener en cuenta algunas limitaciones a la hora de interpretar los resultados. En primer lugar, hay que conocer la naturaleza de la muestra, se ha obtenido una muestra muy heterogénea por lo que los datos pueden haber sido en ocasiones confusos, se ha intentado en todo momento realizar el análisis de datos de la manera más correcta posible. También, se debe tener en cuenta que, aunque la medición de PhA es un valor muy fiable, todavía queda mucha investigación por hacer para conocer verdaderamente qué factores modifican el PhA y conocer mejor la relación que existe entre este valor y los de rendimiento físico y psicológico.

Futuras líneas de investigación

El presente estudio doctoral ha sentado las bases para un campo de investigación en constante evolución que involucra la exploración profunda del ángulo de fase en el contexto de la oncología, así como su intrincada interacción con aspectos físicos, psicológicos y socioemocionales de pacientes aquejados por esta enfermedad. A raíz de los hallazgos y conclusiones obtenidos en esta investigación, se desprenden diversas direcciones prometedoras para futuros estudios que podrían ampliar y enriquecer nuestro entendimiento de estos fenómenos de vital importancia clínica.

1. Exploración de la Influencia del Ángulo de Fase en la Respuesta al Tratamiento Oncológico

Una vía fundamental para la investigación futura consiste en discernir más a fondo la contribución precisa del ángulo de fase en la respuesta terapéutica de los pacientes oncológicos. Esta línea de investigación podría involucrar la realización de investigaciones translacionales que exploren las implicaciones biológicas de las variaciones en el ángulo de fase en entornos in vitro y en modelos animales. De manera complementaria, se insta a la ejecución de ensayos clínicos prospectivos en cohortes de pacientes que permitan discernir la relación entre los valores del ángulo de fase y la eficacia, tolerabilidad y supervivencia tras distintos tratamientos oncológicos.

2. Validación del Ángulo de Fase como Biomarcador Pronóstico en Pacientes Oncológicos

Una senda intrigante y de gran relevancia clínica es la validación del ángulo de fase como un biomarcador pronóstico en pacientes con diagnóstico de cáncer. Esta línea de investigación precisa de estudios clínicos rigurosos y longitudinalmente extensos que examinen la asociación entre los valores del ángulo de fase y la progresión de la enfermedad, la respuesta al tratamiento y la supervivencia en diferentes tipos de cáncer. La identificación de patrones consistentes y significativos podría conllevar la integración del ángulo de fase como una herramienta de estratificación de pacientes, enriqueciendo la toma de decisiones médicas y posiblemente mejorando los resultados clínicos.

3. Evaluación de Estrategias de Educación y Comunicación en la Promoción de la Práctica de Actividad Física en Pacientes Oncológicos

Un ámbito fundamental y en creciente demanda en la práctica clínica es la exploración de estrategias efectivas de educación y comunicación que fomenten la adopción de la actividad física en pacientes oncológicos. La investigación futura podría centrarse en el diseño y la evaluación de intervenciones que incorporen enfoques pedagógicos y de promoción de la salud adaptados al contexto de la oncología. La implementación de estudios que analicen cómo estos enfoques afectan las actitudes, las percepciones y los comportamientos de los pacientes hacia la actividad física, podría generar valiosas recomendaciones prácticas para los profesionales de la salud y contribuir al mejoramiento de la calidad de vida de los pacientes oncológicos.

REFERENCIAS BIBLIOGRÁFICAS

Referencias Bibliográficas

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., & de Haes, J. C. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, *85*(5), 365–376. https://doi.org/10.1093/jnci/85.5.365

Al-shair, K., Muellerova, H., Yorke, J., Rennard, S. I., Wouters, E. F. M., Hanania, N. A., Sharafkhaneh, A., & Vestbo, J. (2012). Examining fatigue in COPD: development, validity and reliability of a modified version of FACIT-F scale. *Health and Quality of Life Outcomes*, *10*(30). https://doi.org/10.1186/1477-7525-10-100

Anjara, S. G., Bonetto, C., Van Bortel, T., & Brayne, C. (2020). Using the GHQ-12 to screen for mental health problems among primary care patients: psychometrics and practical considerations. *International Journal of Mental Health Systems*, *14*, 62. https://doi.org/10.1186/s13033-020-00397-0

Arietaleanizbeaskoa, M. S., Gil Rey, E., Mendizabal Gallastegui, N., García-Álvarez, A., De La Fuente, I., Domínguez-Martinez, S., Pablo, S., Coca, A., Gutiérrez Santamaría, B., & Grandes, G. (2021). Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial. *JMIR Research Protocols*, *10*(8), e24835. https://doi.org/10.2196/24835

Baracos, V. E., Reiman, T., Mourtzakis, M., Gioulbasanis, I., & Antoun, S. (2010). Body composition in patients with non-small cell lung cancer: a contemporary view of cancer cachexia with the use of computed tomography image analysis. *The American Journal of Clinical Nutrition*, *91*(4), 1133S-1137S. https://doi.org/10.3945/ajcn.2010.28608C

Barbosa-Silva, M. C. G., Barros, A. J. D., Wang, J., Heymsfield, S. B., & Pierson, R. N. J. (2005). Bioelectrical impedance analysis: population reference values for phase angle by age and sex. *The American Journal of Clinical Nutrition*, *82*(1), 49–52. https://doi.org/10.1093/ajcn.82.1.49

Bosy-Westphal, A., Danielzik, S., Dörhöfer, R.-P., Later, W., Wiese, S., & Müller, M. J. (2006). Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. *JPEN. Journal of Parenteral and Enteral Nutrition*, *30*(4), 309–316. https://doi.org/10.1177/0148607106030004309

Brazier, J. E., Harper, R., Jones, N. M., O'Cathain, A., Thomas, K. J., Usherwood, T., & Westlake, L. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ (Clinical Research Ed.)*, *305*(6846), 160–164. https://doi.org/10.1136/bmj.305.6846.160

Brown, J. C., Cespedes Feliciano, E. M., & Caan, B. J. (2018). The evolution of body composition in oncology-epidemiology, clinical trials, and the future of patient care: facts and numbers. *Journal of Cachexia, Sarcopenia and Muscle*, *9*(7), 1200–1208. https://doi.org/10.1002/jcsm.12379

Bull, F. C., Al-Ansari, S. S., Biddle, S., Borodulin, K., Buman, M. P., Cardon, G., Carty, C., Chaput, J.-P., Chastin, S., Chou, R., Dempsey, P. C., DiPietro, L., Ekelund, U., Firth, J., Friedenreich, C. M., Garcia, L., Gichu, M., Jago, R., Katzmarzyk, P. T., … Willumsen, J. F. (2020). World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine*, *54*(24), 1451 LP – 1462. https://doi.org/10.1136/bjsports-2020-102955

Bunevicius, A. (2017). Reliability and validity of the SF-36 Health Survey Questionnaire in patients with brain tumors: a cross-sectional study. *Health and Quality of Life Outcomes*, *15*(1), 92. https://doi.org/10.1186/s12955-017-0665-1

Campbell, K. L., Winters-Stone, K. M., Wiskemann, J., May, A. M., Schwartz, A. L., Courneya, K. S., Zucker, D. S., Matthews, C. E., Ligibel, J. A., Gerber, L. H., Morris, G. S., Patel, A. V, Hue, T. F., Perna, F. M., & Schmitz, K. H. (2019). Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. *Medicine and Science in Sports and Exercise*, *51*(11), 2375–2390. https://doi.org/10.1249/MSS.0000000000002116

Castañeda-Babarro, A., Arbillaga-Etxarri, A., Gutiérrez-Santamaría, B., & Coca, A. (2020a). *Impact of COVID-19 confinement on the time and intensity of physical activity in the Spanish population*. https://api.semanticscholar.org/CorpusID:234972524

Castañeda-Babarro, A., Arbillaga-Etxarri, A., Gutiérrez-Santamaría, B., & Coca, A. (2020b). Physical Activity Change during COVID-19 Confinement. In *International Journal of Environmental Research and Public Health* (Vol. 17, Issue 18). https://doi.org/10.3390/ijerph17186878

Castañeda-Babarro, A., Santamaría, B. G., Coca, A., Calleja-González, J., & Cayero, R. (2021). Assessment of Tug of War pullers competition intensity and physiological response at the 2019 European Championship. *Retos*. https://api.semanticscholar.org/CorpusID:244912151

Castañeda-Babarro, A., Santos-Concejero, J., Viribay, A., Gutiérrez-Santamaría, B., & Mielgo-Ayuso, J. (2020). The Effect of Different Cadence on Paddling Gross Efficiency and Economy in Stand-Up Paddle Boarding. *International Journal of Environmental Research and Public Health*, *17*(13). https://doi.org/10.3390/ijerph17134893

Chu, A. K., Mutsaers, B., & Lebel, S. (2022). The Association between Survivorship Care Plans and Patient-Reported Satisfaction and Confidence with Follow-Up Cancer Care Provided by Primary Care Providers. *Current Oncology (Toronto, Ont.)*, *29*(10), 7343–7354. https://doi.org/10.3390/curroncol29100577

Coyle, E. F., Martin, W. H. 3rd, Bloomfield, S. A., Lowry, O. H., & Holloszy, J. O. (1985). Effects of detraining on responses to submaximal exercise. *Journal of Applied Physiology (Bethesda, Md. : 1985)*, *59*(3), 853–859. https://doi.org/10.1152/jappl.1985.59.3.853

Cramp, F., & Daniel, J. (2008). Exercise for the management of cancer-related fatigue in adults. *The Cochrane Database of Systematic Reviews*, *2*, CD006145. https://doi.org/10.1002/14651858.CD006145.pub2

Cruz Bermudez, H. F., Moreno Collazos, J. E., & Angarita Fonseca, A. (2013). Medición de la calidad de vida por el cuestionario QLQ-C30 en sujetos con diversos tipos de cáncer de la ciudad de Bucaramanga-Colombia . In *Enfermería Global* (Vol. 12, pp. 294–303). scieloes .

Cullinane, E. M., Sady, S. P., Vadeboncoeur, L., Burke, M., & Thompson, P. D. (1986). Cardiac size and VO2max do not decrease after short-term exercise cessation. *Medicine and Science in Sports and Exercise*, *18*(4), 420–424.

Di Vincenzo, O., Marra, M., Di Gregorio, A., Pasanisi, F., & Scalfi, L. (2021). Bioelectrical impedance analysis (BIA) -derived phase angle in sarcopenia: A systematic review. *Clinical Nutrition (Edinburgh, Scotland)*, *40*(5), 3052–3061. https://doi.org/10.1016/j.clnu.2020.10.048

Dias Reis, A., Silva Garcia, J. B., Rodrigues Diniz, R., Silva-Filho, A. C., Dias, C. J., Leite, R. D., & Mostarda, C. (2017). Effect of exercise training and detraining in autonomic modulation and cardiorespiratory fitness in breast cancer survivors. *The Journal of Sports Medicine and Physical Fitness*, *57*(7–8), 1062–1068. https://doi.org/10.23736/S0022-4707.17.07012-8

Expósito Hernández, J., & Dadet, A. (2004). Para qué sirve y quién debe hacer el seguimiento después del tratamiento del paciente con cáncer . In *Oncología (Barcelona)* (Vol. 27, pp. 38–41). scieloes .

Fayers P, Aaronson N, Bjordal K, S. M. (2001). The EORTC QLQ-C30 Scoring Manual. *European Organisation for Research and Treatment of Cancer*.

Fayers P. M. et al. (2001). EORTC QLQ-C30 Scoring Manual The EORTC QLQ-C30 Introduction. *EORTC QLQ-C30 Scoring Manual*, *30*, 1–67. http://www.eortc.be/qol/files/scmanualqlq-c30.pdf

Fearon, K., Strasser, F., Anker, S. D., Bosaeus, I., Bruera, E., Fainsinger, R. L., Jatoi, A., Loprinzi, C., MacDonald, N., Mantovani, G., Davis, M., Muscaritoli, M., Ottery, F., Radbruch, L., Ravasco, P., Walsh, D., Wilcock, A., Kaasa, S., & Baracos, V. E. (2011). Definition and classification of cancer cachexia: an international consensus. *The Lancet. Oncology*, *12*(5), 489–495. https://doi.org/10.1016/S1470-2045(10)70218-7

Fiuza-Luces, C., Garatachea, N., Berger, N. A., & Lucia, A. (2013). Exercise is the real polypill. *Physiology (Bethesda, Md.)*, *28*(5), 330–358. https://doi.org/10.1152/physiol.00019.2013

Galvão, D. A., Taaffe, D. R., Spry, N., Joseph, D., Turner, D., & Newton, R. U. (2009). Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. *Prostate Cancer and Prostatic Diseases*, *12*(2), 198–203. https://doi.org/10.1038/pcan.2008.51

Goldberg, D. P., Gater, R., Sartorius, N., Ustun, T. B., Piccinelli, M., Gureje, O., & Rutter, C. (1997). The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychological Medicine*, *27*(1), 191–197. https://doi.org/10.1017/s0033291796004242

Gomes, T. L. N., Soares, J. D. P., Borges, T. C., Pichard, C., & Pimentel, G. D. (2020). Phase angle is not associated with fatigue in cancer patients: the hydration impact. *European Journal of Clinical Nutrition*, *74*(9), 1369–1373. https://doi.org/10.1038/s41430-020-0597-4

Gupta, D., Lis, C. G., Dahlk, S. L., King, J., Vashi, P. G., Grutsch, J. F., & Lammersfeld, C. A. (2008). The relationship between bioelectrical impedance phase angle and subjective global assessment in advanced colorectal cancer.

Nutrition Journal, *7*(1), 19. https://doi.org/10.1186/1475-2891-7-19

Hauth, F., De-Colle, C., Weidner, N., Heinrich, V., Zips, D., & Gani, C. (2021). Quality of life and fatigue before and after radiotherapy in breast cancer patients. *Strahlentherapie Und Onkologie : Organ Der Deutschen Rontgengesellschaft ... [et Al]*, *197*(4), 281–287. https://doi.org/10.1007/s00066-020-01700-1

Herrero, F., San Juan, A. F., Fleck, S. J., Foster, C., & Lucia, A. (2007). Effects of detraining on the functional capacity of previously trained breast cancer survivors. *International Journal of Sports Medicine*, *28*(3), 257–264. https://doi.org/10.1055/s-2006-924348

Hui, D., Bansal, S., Morgado, M., Dev, R., Chisholm, G., & Bruera, E. (2014). Phase angle for prognostication of survival in patients with advanced cancer: preliminary findings. *Cancer*, *120*(14), 2207–2214. https://doi.org/10.1002/cncr.28624

Hui, D., Moore, J., Park, M., Liu, D., & Bruera, E. (2019). Phase Angle and the Diagnosis of Impending Death in Patients with Advanced Cancer: Preliminary Findings. *The Oncologist*, *24*(6), e365–e373. https://doi.org/10.1634/theoncologist.2018-0288

Janssen, I., Baumgartner, R. N., Ross, R., Rosenberg, I. H., & Roubenoff, R. (2004). Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *American Journal of Epidemiology*, *159*(4), 413–421. https://doi.org/10.1093/aje/kwh058

Jones, L. W., Watson, D., Herndon, J. E., Eves, N. D., Haithcock, B. E., Loewen, G., & Kohman, L. (2010). Peak oxygen consumption and long-term all-cause mortality in nonsmall cell lung cancer. *Cancer*, *116*(20), 4825–4832. https://doi.org/10.1002/cncr.25396

Kavanagh, T., Mertens, D. J., Hamm, L. F., Beyene, J., Kennedy, J., Corey, P., & Shephard, R. J. (2002). Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. *Circulation*, *106*(6), 666–671. https://doi.org/10.1161/01.cir.0000024413.15949.ed

Klausen, K., Andersen, L. B., & Pelle, I. (1981). Adaptive changes in work capacity, skeletal muscle capillarization and enzyme levels during training and detraining. *Acta Physiologica Scandinavica*, *113*(1), 9–16. https://doi.org/10.1111/j.1748-1716.1981.tb06854.x

Kodama, S., Saito, K., Tanaka, S., Maki, M., Yachi, Y., Asumi, M., Sugawara, A., Totsuka, K., Shimano, H., Ohashi, Y., Yamada, N., & Sone, H. (2009). Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*, *301*(19), 2024–2035. https://doi.org/10.1001/jama.2009.681

Koeppel, M., Mathis, K., Schmitz, K. H., & Wiskemann, J. (2021). Muscle hypertrophy in cancer patients and survivors via strength training. A meta-analysis and meta-regression. *Critical Reviews in Oncology/Hematology*, *163*, 103371. https://doi.org/10.1016/j.critrevonc.2021.103371

Lee, Y.-S., Jung, W.-M., Jang, H., Kim, S., Chung, S.-Y., & Chae, Y. (2017). The dynamic relationship between emotional and physical states: an observational study of personal health records. *Neuropsychiatric Disease and Treatment*, *13*, 411–419. https://doi.org/10.2147/NDT.S120995

Lindemann, U., Krumpoch, S., Becker, C., Sieber, C. C., & Freiberger, E. (2021). The course of gait speed during a 400m walk test of mobility limitations in community-dwelling older adults. *Zeitschrift Fur Gerontologie Und Geriatrie*, *54*(8), 768–774. https://doi.org/10.1007/s00391-021-01908-5

Lopez de Munain, A., & Audicana, C. (2023). *Cáncer en la Comunidad Autónoma de Euskadi 2001-2021*. https://www.euskadi.eus/contenidos/informacion/registros_cancer/es_def/adjuntos/Cancer-CAE-2001-2021.pdf

Luan, X., Tian, X., Zhang, H., Huang, R., Li, N., Chen, P., & Wang, R. (2019). Exercise as a prescription for patients with various diseases. *Journal of Sport and Health Science*, *8*(5), 422–441. https://doi.org/10.1016/j.jshs.2019.04.002

Lucía, A., Earnest, C., & Pérez, M. (2003). Cancer-related fatigue: can exercise physiology assist oncologists? *The Lancet. Oncology*, *4*(10), 616–625. https://doi.org/10.1016/s1470-2045(03)01221-x

Lundby, C., Montero, D., & Joyner, M. (2017). Biology of VO(2) max: looking under the physiology lamp. *Acta Physiologica (Oxford, England)*, *220*(2), 218–228. https://doi.org/10.1111/apha.12827

Machado, P., Morgado, M., Raposo, J., Mendes, M., Silva, C. G., & Morais, N. (2022). Effectiveness of exercise training on cancer-related fatigue in colorectal cancer survivors: a systematic review and meta-analysis of randomized controlled trials. *Supportive Care in Cancer : Official Journal of the Multinational Association of Supportive Care in Cancer*, *30*(7), 5601–5613. https://doi.org/10.1007/s00520-022-06856-3

Martin, L., Birdsell, L., Macdonald, N., Reiman, T., Clandinin, M. T., McCargar, L. J., Murphy, R., Ghosh, S., Sawyer, M. B., & Baracos, V. E. (2013). Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, *31*(12), 1539–1547. https://doi.org/10.1200/JCO.2012.45.2722

Martins, Alexandre D, Oliveira, R., Brito, J. P., Costa, T., Ramalho, F., Pimenta, N., & Santos-Rocha, R. (2021). Phase angle cutoff value as a marker of the health status and functional capacity in breast cancer survivors. *Physiology & Behavior*, *235*, 113400. https://doi.org/10.1016/j.physbeh.2021.113400

Martins, Alexandre Duarte, Fernandes, O., Oliveira, R., Bilro, V., Lopes, G., Rego, A. M., Parraça, J. A., Raimundo, A. M. M., & Brito, J. P. (2022). Effects of exercise programs on phase angle in older adults: A systematic review and meta-analysis. *Archives of Gerontology and Geriatrics*, *103*, 104787. https://doi.org/https://doi.org/10.1016/j.archger.2022.104787

McTiernan, A., Friedenreich, C. M., Katzmarzyk, P. T., Powell, K. E., Macko, R., Buchner, D., Pescatello, L. S., Bloodgood, B., Tennant, B., Vaux-Bjerke, A., George, S. M., Troiano, R. P., Piercy, K. L., & COMMITTEE*, 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY. (2019). Physical Activity in Cancer Prevention and Survival: A Systematic Review. *Medicine and Science in Sports and Exercise*, *51*(6), 1252–1261. https://doi.org/10.1249/MSS.0000000000001937

Minnella, E. M., Awasthi, R., Loiselle, S.-E., Agnihotram, R. V, Ferri, L. E., & Carli, F. (2018). Effect of Exercise and Nutrition Prehabilitation on Functional Capacity in

Esophagogastric Cancer Surgery: A Randomized Clinical Trial. *JAMA Surgery*, *153*(12), 1081–1089. https://doi.org/10.1001/jamasurg.2018.1645

Montalvo, R. N., Hardee, J. P., Vanderveen, B. N., & Carson, J. A. (2018). Resistance Exercise's Ability to Reverse Cancer-Induced Anabolic Resistance. *Exercise and Sport Sciences Reviews*, *46*(4), 247–253. https://doi.org/10.1249/JES.0000000000000159

Mujika, I., & Padilla, S. (2000a). Detraining: loss of training-induced physiological and performance adaptations. Part I: short term insufficient training stimulus. *Sports Medicine (Auckland, N.Z.)*, *30*(2), 79–87. https://doi.org/10.2165/00007256-200030020-00002

Mujika, I., & Padilla, S. (2000b). Detraining: loss of training-induced physiological and performance adaptations. Part II: Long term insufficient training stimulus. *Sports Medicine (Auckland, N.Z.)*, *30*(3), 145–154. https://doi.org/10.2165/00007256-200030030-00001

Mustian, K. M., Sprod, L. K., Palesh, O. G., Peppone, L. J., Janelsins, M. C., Mohile, S. G., & Carroll, J. (2009). Exercise for the management of side effects and quality of life among cancer survivors. *Current Sports Medicine Reports*, *8*(6), 325–330. https://doi.org/10.1249/JSR.0b013e3181c22324

Myers, J., Prakash, M., Froelicher, V., Do, D., Partington, S., & Atwood, J. E. (2002). Exercise Capacity and Mortality among Men Referred for Exercise Testing. *New England Journal of Medicine*, *346*(11), 793–801. https://doi.org/10.1056/NEJMoa011858

O'Neill, J. O., Young, J. B., Pothier, C. E., & Lauer, M. S. (2005). Peak oxygen consumption as a predictor of death in patients with heart failure receiving beta-blockers. *Circulation*, *111*(18), 2313–2318. https://doi.org/10.1161/01.CIR.0000164270.72123.18

Ohrnberger, J., Fichera, E., & Sutton, M. (2017). The relationship between physical and mental health: A mediation analysis. *Social Science & Medicine*, *195*, 42–49. https://doi.org/https://doi.org/10.1016/j.socscimed.2017.11.008

Orange, S. T., Gilbert, S. E., Brown, M. C., & Saxton, J. M. (2021). Recall, perceptions and determinants of receiving physical activity advice amongst cancer survivors: a mixed-methods survey. *Supportive Care in Cancer*, *29*(11), 6369–6378. https://doi.org/10.1007/s00520-021-06221-w

Paiva, S. I., Borges, L. R., Halpern-Silveira, D., Assunção, M. C. F., Barros, A. J. D., & Gonzalez, M. C. (2010). Standardized phase angle from bioelectrical impedance analysis as prognostic factor for survival in patients with cancer. *Supportive Care in Cancer : Official Journal of the Multinational Association of Supportive Care in Cancer*, *19*(2), 187–192. https://doi.org/10.1007/s00520-009-0798-9

Pedersen, B. K., & Saltin, B. (2015). Exercise as medicine – evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scandinavian Journal of Medicine & Science in Sports*, *25*(S3), 1–72. https://doi.org/10.1111/sms.12581

Pérez-Fuentes, M. D. C., Molero Jurado, M. D. M., Martos Martínez, Á., & Gázquez Linares, J. J. (2020). Threat of COVID-19 and emotional state during quarantine: Positive and negative affect as mediators in a cross-sectional study of the Spanish population. *PloS One*, *15*(6), e0235305.

https://doi.org/10.1371/journal.pone.0235305

Piraux, E., Caty, G., Aboubakar Nana, F., & Reychler, G. (2020). Effects of exercise therapy in cancer patients undergoing radiotherapy treatment: a narrative review. *SAGE Open Medicine*, *8*, 2050312120922657. https://doi.org/10.1177/2050312120922657

Prado, C. M. M., Baracos, V. E., McCargar, L. J., Reiman, T., Mourtzakis, M., Tonkin, K., Mackey, J. R., Koski, S., Pituskin, E., & Sawyer, M. B. (2009). Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. *Clinical Cancer Research : An Official Journal of the American Association for Cancer Research*, *15*(8), 2920–2926. https://doi.org/10.1158/1078-0432.CCR-08-2242

Prado, C. M. M., Lieffers, J. R., McCargar, L. J., Reiman, T., Sawyer, M. B., Martin, L., & Baracos, V. E. (2008). Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *The Lancet. Oncology*, *9*(7), 629–635. https://doi.org/10.1016/S1470-2045(08)70153-0

Quinn, T. D., Gutiérrez-Santamaría, B., Sáez, I., Santisteban, A., Lee, J.-Y., Kim, J.-H., & Coca, A. (2021). Comparison of three internationally certified firefighter protective ensembles: Physiological responses, mobility, and comfort. *International Journal of Industrial Ergonomics*, *86*, 103232. https://doi.org/https://doi.org/10.1016/j.ergon.2021.103232

Ravasco, P. (2019). Nutrition in Cancer Patients. *Journal of Clinical Medicine*, *8*(8). https://doi.org/10.3390/jcm8081211

Rezende, L. F. M. de, Sá, T. H. de, Markozannes, G., Rey-López, J. P., Lee, I. M., Tsilidis, K. K., Ioannidis, J. P. A., & Eluf-Neto, J. (2018). Physical activity and cancer: an umbrella review of the literature including 22 major anatomical sites and 770 000 cancer cases. *British Journal of Sports Medicine*, *52*(13), 826–833. https://doi.org/10.1136/bjsports-2017-098391

Rodriguez-Arietaleanizbeaskoa, M., Ereño, E. M., Arietaleanizbeaskoa, M. S., Grandes, G., Sanchez, A. R., Urquijo, V., Alday, I. H., Dublang, M., Angulo-Garay, G., Cacicedo, J., del Rodriguez-Arietaleanizbeaskoa Mojas Ereño Arietale, M. E. M. S. G. A. A. N. O., Rodriguez-Arietaleanizbeaskoa, M., Ereño, E. M., Arietaleanizbeaskoa, M. S., Grandes, G., García-Álvarez, A., Coca, A., Mendizábal, N., del Hoyo, O., … Cacicedo, J. (2023). Protocol for the SEHNeCa randomised clinical trial assesing Supervised Exercise for Head and Neck Cancer patients. *BMC Cancer*, *23*. https://api.semanticscholar.org/CorpusID:257698035

Rolland, Y. M., Cesari, M., Miller, M. E., Penninx, B. W., Atkinson, H. H., & Pahor, M. (2004). Reliability of the 400-m usual-pace walk test as an assessment of mobility limitation in older adults. *Journal of the American Geriatrics Society*, *52*(6), 972–976. https://doi.org/10.1111/j.1532-5415.2004.52267.x

Saladino, V., Algeri, D., & Auriemma, V. (2020). The Psychological and Social Impact of Covid-19: New Perspectives of Well-Being. *Frontiers in Psychology*, *11*. https://doi.org/10.3389/fpsyg.2020.577684

Sánchez-López, M. del P., & Dresch, V. (2008). The 12-Item General Health Questionnaire (GHQ-12): reliability, external validity and factor structure in the Spanish population. *Psicothema*, *20*(4), 839–843.

Schmid, D., & Leitzmann, M. F. (2014). Television Viewing and Time Spent Sedentary in Relation to Cancer Risk: A Meta-Analysis. *JNCI: Journal of the National Cancer Institute*, *106*(7), dju098. https://doi.org/10.1093/jnci/dju098

Schmidt, K., Vogt, L., Thiel, C., Jäger, E., & Banzer, W. (2013). Validity of the six-minute walk test in cancer patients. *International Journal of Sports Medicine*, *34*(7), 631–636. https://doi.org/10.1055/s-0032-1323746

Schmitz, K. H., Courneya, K. S., Matthews, C., Demark-Wahnefried, W., Galvão, D. A., Pinto, B. M., Irwin, M. L., Wolin, K. Y., Segal, R. J., Lucia, A., Schneider, C. M., Von Gruenigen, V. E., & Schwartz, A. L. (2010). American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Medicine and Science in Sports and Exercise*, *42*(7), 1409–1426. https://doi.org/10.1249/MSS.0b013e3181e0c112

Schneider, J., Schlüter, K., Sprave, T., Wiskemann, J., & Rosenberger, F. (2020). Exercise intensity prescription in cancer survivors: ventilatory and lactate thresholds are useful submaximal alternatives to VO(2peak). *Supportive Care in Cancer : Official Journal of the Multinational Association of Supportive Care in Cancer*, *28*(11), 5521–5528. https://doi.org/10.1007/s00520-020-05407-y

Seiler, K. S., & Kjerland, G. Ø. (2006). Quantifying training intensity distribution in elite endurance athletes: is there evidence for an “optimal” distribution? *Scandinavian Journal of Medicine & Science in Sports*, *16*(1), 49–56. https://doi.org/10.1111/j.1600-0838.2004.00418.x

Short, T., Teranishi-Hashimoto, C., & Yamada, P. (2022). Exercise-Based Cancer Rehabilitation Program Improves Phase Angle in Breast Cancer Survivors. *International Journal of Exercise Science*, *15*(3), 1444–1456.

Sieber, C. C. (2019). Malnutrition and sarcopenia. *Aging Clinical and Experimental Research*, *31*(6), 793–798. https://doi.org/10.1007/s40520-019-01170-1

Sietsema, K., Sue, D., Stringer, W., & Ward, S. (2020). *WASSERMAN & WHIPPS PRINCIPLES OF EXERCISE TESTING INTERPRET*.

Stegel, P., Kozjek, N. R., Brumen, B. A., & Strojan, P. (2016). Bioelectrical impedance phase angle as indicator and predictor of cachexia in head and neck cancer patients treated with (chemo)radiotherapy. *European Journal of Clinical Nutrition*, *70*(5), 602–606. https://doi.org/10.1038/ejcn.2016.13

Stockwell, S., Trott, M., Tully, M., Shin, J., Barnett, Y., Butler, L., McDermott, D., Schuch, F., & Smith, L. (2021). Changes in physical activity and sedentary behaviours from before to during the COVID-19 pandemic lockdown: a systematic review. *BMJ Open Sport &Amp; Exercise Medicine*, *7*(1), e000960. https://doi.org/10.1136/bmjsem-2020-000960

Virto, N., Etayo-Urtasun, P., Isla, J. R. S., Arietanizbeaskoa, M. S., Gallastegui, N. M., Grandes, G., Gutiérrez, B. R., Coca, A., & Río, X. (2023). Efectos de una intervención de 12 semanas de ejercicio en los niveles de hemoglobina glicada (HbA1c) en pacientes con cáncer (Effects of a 12-week exercise intervention on glycated hemoglobin (HbA1c) levels in cancer patients). *Retos*. https://api.semanticscholar.org/CorpusID:256772496

Wallen, M. P., Hennessy, D., Brown, S., Evans, L., Rawstorn, J. C., Wong Shee, A., & Hall, A. (2020). High-intensity interval training improves cardiorespiratory fitness in cancer patients and survivors: A meta-analysis. *European Journal of Cancer Care*, *29*(4), e13267. https://doi.org/10.1111/ecc.13267

Ware Jr, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, 473–483.

Wewege, M., van den Berg, R., Ward, R. E., & Keech, A. (2017). The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, *18*(6), 635–646. https://doi.org/10.1111/obr.12532

Więch, P., Wołoszyn, F., Trojnar, P., Skórka, M., & Bazaliński, D. (2022). Does Body Position Influence Bioelectrical Impedance? An Observational Pilot Study. *International Journal of Environmental Research and Public Health*, *19*(16). https://doi.org/10.3390/ijerph19169908

Williams, G. R., Chen, Y., Kenzik, K. M., McDonald, A., Shachar, S. S., Klepin, H. D., Kritchevsky, S., & Bhatia, S. (2020). Assessment of Sarcopenia Measures, Survival, and Disability in Older Adults Before and After Diagnosis With Cancer. *JAMA Network Open*, *3*(5), e204783–e204783. https://doi.org/10.1001/jamanetworkopen.2020.4783

Wolin, K. Y., Schwartz, A. L., Matthews, C. E., Courneya, K. S., & Schmitz, K. H. (2012). Implementing the exercise guidelines for cancer survivors. *The Journal of Supportive Oncology*, *10*(5), 171–177. https://doi.org/10.1016/j.suponc.2012.02.001

ANEXOS

Anexos

Anexo 1. Protocolo Bizi Orain (Artículo publicado)

JMIR RESEARCH PROTOCOLS Arietaleanizbeaskoa et al

Protocol

Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial

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Abstract

Background: Despite the established benefits of regular exercise for patients with cancer to counteract the deleterious effects of the disease itself and treatment-related adverse effects, most of them do not engage in sufficient levels of physical activity and there is a paucity of data on the integration of efficacious exercise programs that are accessible and generalizable to a large proportion of patients with cancer into routine cancer care.

Objective: We intend to examine the effects attributable to the implementation of a community-based exercise program on cardiorespiratory functional capacity and quality of life for patients with cancer.

Methods: This will be a hybrid study. In the first experimental phase, patients diagnosed with any type of cancer will be randomized into two parallel groups. One group immediately performs Bizi Orain, a 3-month supervised exercise program (3 times a week), in addition to behavioral counseling in a primary health care setting; the other is a reference group that starts the exercise program 3 months later (delayed treatment). In the second observational phase, the entire cohort of participants will be followed-up for 5 years. Any person diagnosed with cancer in the previous 2 years is eligible for the program. The program evaluation involves the uptake, safety, adherence, and effectiveness assessed after completion of the program and with follow-ups at 3, 6, 12, 24, 36, 48, and 60 months. The primary outcomes of the experimental study, to be compared between groups, are improved physical function and quality of life, whereas overall survival is the main objective of the prospective study. To analyze the association between changes in physical activity levels and overall survival, longitudinal mixed-effects models will be used for repeated follow-up measures.

Results: A total of 265 patients have been enrolled into the study since January 2019, with 42 patients from the hematology service and 223 from the oncology service.

Conclusions: Bizi Orain is the first population-based exercise program in Spain that will offer more insight into the implementation of feasible, generalizable, and sustainable supportive care services involving structured exercise to extend survival of patients with cancer, improve their physical function and quality of life, and reverse the adverse effects of their disease and related treatments, thereby reducing the clinical burden.

Trial Registration: ClinicalTrials.gov NCT03819595; http://clinicaltrials.gov/ct2/show/NCT03819595

International Registered Report Identifier (IRRID): DERR1-10.2196/24835

(JMIR Res Protoc 2021;10(8):e24835) doi: 10.2196/24835

KEYWORDS

patients with cancer; physical activity; primary care; behavioral change; randomized controlled trial; overall survival

Anexo 2. Otra producción científica durante el proceso de doctorado.

Arietaleanizbeaskoa, M. S., Gil Rey, E., Mendizabal Gallastegui, N., García-Álvarez, A., De La Fuente, I., Domínguez-Martinez, S., Pablo, S., Coca, A., Gutiérrez Santamaría, B., & Grandes, G. (2021). Implementing Exercise in Standard Cancer Care (Bizi Orain Hybrid Exercise Program): Protocol for a Randomized Controlled Trial. JMIR Research Protocols, 10(8), e24835. https://doi.org/10.2196/24835

Castañeda-Babarro, A., Arbillaga-Etxarri, A., Gutiérrez-Santamaría, B., & Coca, A. (2020a). Impact of COVID-19 confinement on the time and intensity of physical activity in the Spanish population. https://api.semanticscholar.org/CorpusID:234972524

Castañeda-Babarro, A., Arbillaga-Etxarri, A., Gutiérrez-Santamaría, B., & Coca, A. (2020b). Physical Activity Change during COVID-19 Confinement. In International Journal of Environmental Research and Public Health (Vol. 17, Issue 18). https://doi.org/10.3390/ijerph17186878

Castañeda-Babarro, A., Santamaría, B. G., Coca, A., Calleja-González, J., & Cayero, R. (2021). Assessment of Tug of War pullers competition intensity and physiological response at the 2019 European Championship. Retos. https://api.semanticscholar.org/CorpusID:244912151

Castañeda-Babarro, A., Santos-Concejero, J., Viribay, A., Gutiérrez-Santamaría, B., & Mielgo-Ayuso, J. (2020). The Effect of Different Cadence on Paddling Gross Efficiency and Economy in Stand-Up Paddle Boarding. International Journal of Environmental Research and Public Health, 17(13). https://doi.org/10.3390/ijerph17134893

Quinn, T. D., Gutiérrez-Santamaría, B., Sáez, I., Santisteban, A., Lee, J.-Y., Kim, J.-H., & Coca, A. (2021). Comparison of three internationally certified firefighter protective ensembles: Physiological responses, mobility, and comfort. International Journal of Industrial Ergonomics, 86, 103232. https://doi.org/https://doi.org/10.1016/j.ergon.2021.103232

Rodriguez-Arietaleanizbeaskoa, M., Ereño, E. M., Arietaleanizbeaskoa, M. S., Grandes, G., Sanchez, A. R., Urquijo, V., Alday, I. H., Dublang, M., Angulo-Garay, G., Cacicedo, J., del Rodriguez-Arietaleanizbeaskoa Mojas Ereño Arietale, M. E. M. S. G. A. A. N. O., Rodriguez-Arietaleanizbeaskoa, M., Ereño, E. M., Arietaleanizbeaskoa, M. S., Grandes, G., García-Álvarez, A., Coca, A., Mendizábal, N., del Hoyo, O., … Cacicedo, J. (2023). Protocol for the SEHNeCa randomised clinical trial assesing Supervised Exercise for Head and Neck Cancer patients. BMC Cancer, 23. https://api.semanticscholar.org/CorpusID:257698035

Virto, N., Etayo-Urtasun, P., Isla, J. R. S., Arietanizbeaskoa, M. S., Gallastegui, N. M., Grandes, G., Gutiérrez, B. R., Coca, A., & Río, X. (2023). Efectos de una intervención de 12 semanas de ejercicio en los niveles de hemoglobina glicada (HbA1c) en pacientes con cáncer (Effects of a 12-week exercise intervention on glycated hemoglobin (HbA1c) levels in cancer patients). Retos. https://api.semanticscholar.org/CorpusID:256772496

Anexo 3. Título Experto Universitario en Oncología

UNIVERSIDAD EUROPEA MIGUEL DE CERVANTES

El Rector de la Universidad Europea Miguel de Cervantes

considerando que, conforme a la legislación y normativa universitaria vigentes,

Don Borja Gutiérrez Santamaría

nacido el día 21 de julio de 1996 en Vitoria-Gasteiz, Araba Álava (España), de nacionalidad española,

ha superado los estudios correspondientes del programa de Título Propio de **Experto Universitario en Oncología**, conforme a lo dispuesto en la legislación vigente, a las Normas de Organización y Funcionamiento de la Universidad Europea Miguel de Cervantes, en colaboración con **Formación Alcalá y Grupo Editor RCA S.L.**,

con una asignación de 30 ECTS (750 horas), expide el presente título de

Experto Universitario en Oncología

por haber acreditado convenientemente los requisitos exigidos por el Reglamento de Títulos Propios de la UEMC y por el resto de normativa vigente aplicable.

Dado en Valladolid, a 29 de julio de 2022

El interesado,
BORJA GUTIÉRREZ SANTAMARÍA

El Rector,
DAVID GARCÍA LÓPEZ

El Secretario General
P.O. Rector Magnífico,
JUAN CASADO CANALES

Anexo 4. Certificado beca FPI UD

Deusto
Universidad de Deusto
Deustuko Unibertsitatea
University of Deusto

Dña. ROSA MARIA SANTIBAÑEZ GRUBER, con D.N.I: 30576420J, en calidad de Vicerrectora de Investigación y Transferencia de la Universidad de la Iglesia de Deusto

CERTIFICA:

Que D. BORJA GUTIÉRREZ SANTAMARÍA con D.N.I: 72848181M es investigador predoctoral en esta Universidad de Deusto, entidad sin ánimo de lucro, reconocida por el Estado español en virtud del Decreto de 07/09/1963 2367/63 (BOE Nº 222 16/09/1963).

Entidad Financiadora: Gobierno Vasco, en el marco de colaboración del Contrato-Programa de Investigación de Excelencia 2019-2022 entre la Administración General de la Comunidad Autónoma del País Vasco (Departamento de Educación) y la Universidad de Deusto suscrito el 24 de julio de 2019, dónde se recoge como línea de actuación de dicho Contrato - Programa la *"Formación, atracción y retención de talento investigador / Ayudas a la formación de investigadores (predoctorales (FPI)"*.

Fecha inicio de la ayuda: 15 de septiembre de 2020

Fecha prevista de finalización: 14 de septiembre de 2023

Y para que así conste firmo el siguiente certificado en Bilbao, a 9 de enero de 2023.

Firmado digitalmente por SANTIBAÑEZ GRUBER ROSA MARIA - 30576420J
Nombre de reconocimiento (DN): c=ES, serialNumber=IDCES-30576420J, givenName=ROSA MARIA, sn=SANTIBAÑEZ GRUBER, cn=SANTIBAÑEZ GRUBER ROSA MARIA - 30576420J
Fecha: 2023.01.09 13:23:48 +01'00'

Rosa María Santibáñez Gruber
Vicerrectora de Investigación y Transferencia

Anexo 5. Documento comité de ética

CEIm-E
Euskadiko Medikamentuen gaineko Ikerkuntza Batzorde Etikoa
Comité de Ética de la Investigación con medicamentos de Euskadi

EUSKO JAURLARITZA
GOBIERNO VASCO
OSASUN SAILA
DEPARTAMENTO DE SALUD

INFORME DEL COMITÉ DE ÉTICA DE LA INVESTIGACIÓN CON MEDICAMENTOS DE EUSKADI (CEIm-E)

Arantza Hernández Gil
Secretaria del CEIm de Euskadi (CEIm-E)

CERTIFICA

Que este Comité, de acuerdo a la ley 14/2007 de Investigación Biomédica, Principios éticos de la declaración de Helsinki, y resto de principios éticos aplicables, ha evaluado el proyecto de investigación, titulado **BIZI ORAIN: "Ejercicio físico para todas las personas con cáncer".**

Código interno: PI2019016

Versión del Protocolo: 2018

Versión de la HIP: GENERAL / Version 1.1-3, 12 de marzo de 2019

Y que este Comité reunido el día 27/02/2019 (recogido en Acta 03/2019) ha decidido emitir informe favorable a que dicho proyecto sea realizado por el siguiente personal investigador:

- Nere Mendizabal Gallastegui *Unidad de Investigación Atención Primaria de Bizkaia*

Lo que firmo en Vitoria, a 15 de marzo de 2019

Arantza Hernández Gil
Secretaria del CEIm de Euskadi (CEIm-E)

EUSKO JAURLARITZA GOBIERNO VASCO
OSASUN SAILA
DEPARTAMENTO DE SALUD
2019 MAR. 15
Euskadiko Medikamentuen gaineko Ikerkuntza Batzorde Etikoa (CEIm-E)
Comité de Ética de la Investigación con medicamentos de Euskadi (CEIm-E)

Nota: Una vez comenzado el estudio, se recuerda la obligación de enviar un **informe de seguimiento anual** y el **informe final** que incluya los resultados del estudio (si el estudio dura menos de un año, con el informe final será suficiente). Más información en la página web del CEIm-E:
http://www.euskadi.eus/comite-etico-investigacion-clinica/

APÉNDICES

Apéndices

Comunicación Oral relacionada con la Tesis Doctoral

European College of Sports Medicine 2021- Cologne

EUROPEAN COLLEGE OF SPORT SCIENCE
Aachener Strasse 1053-1055
50858 Cologne
GERMANY

Cologne, 21.10.2021

Confirmation of Presentation

To whom it may concern,

We hereby confirm that **Borja Gutiérrez** from Deusto University has presented the below conventional poster at the 25^{th} congress of the ECSS (28^{th} – 30^{th} October 2020)

Title of the abstract:
Effects of a supervised physical exercise program on body composition, cardiorespiratory capacity and strength, as part of treatment for cancer patients

Authors:
GUTIÉRREZ-SANTAMARÍA, B., ARIETALEANIZBEASKOA, M.S., MENDIZABAL, N., GRANDES, G., COCA, A.

Yours sincerely,

Thomas Delaveaux
Executive Director

European College of Sport Science
Thomas Delaveaux, Executive Director, Aachener Strasse 1053-1055, 50858 Cologne, Germany
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Presentación en congreso TAPAS 2021

TAPAS 2021

International Conference on Technology in Physical Activity and Sport

Confirmation of Presentation

This is to certify that

Mendez Zorrilla, Amaia; Arietaleanizbeaskoa Sarabia, Soledad; Badiola Bengoa, Aritz; Badiola Martínez, Julen; Coca, Aitor; Grandes Odriozola , Gonzalo; Gutiérrez Santamaría, Borja; Mendizabal Gallastegui , Nere; Río De Frutos, Xabier ;

presented the following Oral Communication at the

II International Conference on Technology in Physical Activity and Sport

between 22th to 25th November

with the title

E- HEALTH PLATFORM TO STUDY THE BENEFITS OF PHYSICAL ACTIVITY IN CANCER PATIENTS

Borja Sañudo Corrales
Jerónimo García-Fernández
Congress Presidents

Jesús del Pozo Cruz
Secretary of the Physical Education and Sport Departament

AGIISD · GISDOR · Iberian Sportech · Vicerrectorado de Investigación · Consejo Superior de Deportes · Departamento de Educación Física y Deporte · Biofanex

Código Seguro De Verificación	zPo3LJFBYjhV40b0QoGcqQ==	Fecha	15/11/2021
Firmado Por	JERONIMO GARCIA FERNANDEZ		
	FRANCISCO DE BORJA SAÑUDO CORRALES		
	JESUS DEL POZO CRUZ		
Url De Verificación	https://pfirma.us.es/verifirma/code/zPo3LJFBYjhV40b0QoGcqQ==	Página	2/4

Hoja de registro

CIC:

FORMULARIO DE REGISTRO DE LA FORMA FÍSICA:

INBODY		Peso: Altura:	
Masa musculo-esquelética(kg)			
Masa magra (kg)		CARDIOTOXICIDAD	
Masa libre de grasa (kg)		radicales libres (test d-rom)	
Contenido mineral óseo(kg)		antioxidantes (test pat)	
Grasa (kg)		PRUEBA DE 400 m	
PGC (%)		Tiempo (min:seg)	
Agua intracelular(L)		RPE	
Agua extracelular(L)			
AEC/ACT			
Grasa visceral (cm^2)		TEST SILLA (5rep.)	
TMB(kcal)		Levantamientos completados	
Ángulo de fase(º)		Tiempo (seg,dds)	

DINAMOMETRIA	Brazo derecho	Brazo izquierdo	Fuerza máxima (kg)
kg			
kg			
kg			

PRUEBA DE FUERZA	
PRENSA DE PIERNA 5RM KG (1RM)	
PRESS PECHO 5RM KG (1RM)	

ERGOMETRÍA				ANOTACIONES
FC REPOSO (ppm)				
FC pico (ppm)				
W pico.(W)				
FC POST 1´(ppm)				
VO_2 PICO(mL/kg/min)				
VO_2 Max. INDIRECTO(mL/kg/min)				
VT1 (W, FC, MET)				
VT2 (W, FC, MET)				

PALIER	W	FC (ppm)	RPE	PALIER	W	FC (ppm)	RPE
0	0			10	110		
1	20			11	120		
2	30			12	130		
3	40			13	140		
4	50			14	150		
5	60			15	160		
6	70			16	170		
7	80			17	180		
8	90			18	190		
9	100			19	200		

PAS/PAD	
PRE	POST

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CIC:

CUESTIONARIO "SF-36" SOBRE EL ESTADO DE SALUD

(Instrucción: El presente cuestionario deberá ser cumplimentado por el paciente, salvo en los casos en los cuales esté impedido o no capacitado para poder leerlo)

INSTRUCCIONES: Las preguntas que siguen se refieren a lo que usted piensa sobre su salud. Sus respuestas permitirán saber cómo se encuentra usted y hasta qué punto es capaz de hacer sus actividades habituales.
Conteste cada pregunta tal como se indica. Si no está seguro/a de cómo responder a una pregunta, por favor conteste lo que le parezca más cierto.

1. En general, usted diría que su salud es: (marque un solo número)

Excelente 1
Muy buena 2
Buena 3
Regular....................4
Mala....................5

2. ¿Cómo diría usted que es su salud actual, comparada con la de hace un año? (marque un solo número)

Mucho mejor ahora que hace un año 1
Algo mejor ahora que hace un año 2
Más o menos igual que hace un año....................3
Algo peor ahora que hace un año 4
Mucho peor ahora que hace un año 5

3. Las siguientes preguntas se refieren a actividades o cosas que usted podría hacer en un día normal. Su salud actual, ¿le limita para hacer esas actividades o cosas? Si es así, ¿cuánto? (marque un solo número por cada pregunta)

ACTIVIDADES	Sí, me limita mucho	Sí, me limita un poco	No, no me limita nada
a. **Esfuerzos intensos**, tales como correr, levantar objetos pesados, o participar en deportes agotadores	1	2	3
b. **Esfuerzos moderados**, como mover una mesa, pasar la aspiradora, jugar a los bolos o caminar más de 1 hora	1	2	3
c. Coger o llevar la bolsa de la compra	1	2	3
d. Subir **varios** pisos por la escalera	1	2	3
e. Subir **un solo** piso por la escalera	1	2	3
f. Agacharse o arrodillarse	1	2	3
g. Caminar **un kilómetro o más**	1	2	3
h. Caminar **varias manzanas** (varios centenares de metros)	1	2	3
i. Caminar **una sola manzana** (unos 100 metros)	1	2	3
j. Bañarse o vestirse por sí mismo	1	2	3

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4. Durante las 4 últimas semanas, ¿ha tenido alguno de los siguientes problemas en su trabajo o en sus actividades cotidianas, a causa de su salud física? (marque un solo número por cada pregunta)

	SÍ	NO
a. ¿Tuvo que **reducir el tiempo** dedicado al trabajo o a sus actividades cotidianas?	1	2
b. ¿**Hizo menos** de lo que hubiera querido hacer?	1	2
c. ¿Tuvo que **dejar de hacer algunas tareas** en su trabajo o en sus actividades cotidianas?	1	2
d. ¿Tuvo **dificultad** para hacer su trabajo o sus actividades cotidianas (por ejemplo, le costó más de lo normal)?	1	2

5. Durante las 4 últimas semanas, ¿ha tenido alguno de los siguientes problemas en su trabajo o en sus actividades cotidianas, a causa de algún problema emocional (como estar triste, deprimido, o nervioso)? (marque un solo número por cada pregunta)

	SÍ	NO
a. ¿Tuvo que **reducir el tiempo** dedicado al trabajo o a sus actividades cotidianas, **por algún problema emocional**?	1	2
b. ¿**Hizo menos** de lo que hubiera querido hacer, **por algún problema emocional**?	1	2
c. ¿No hizo su trabajo o sus actividades cotidianas tan **cuidadosamente** como de costumbre, **por algún problema emocional**?	1	2

6. Durante las 4 últimas semanas, ¿hasta qué punto su salud física o los problemas emocionales han dificultado sus actividades sociales habituales con la familia, los amigos, los vecinos u otras personas? (marque un solo número)

Nada..........1
Un poco..........2
Regular..........3
Bastante..........4
Mucho..........5

7. ¿Tuvo dolor en alguna parte del cuerpo durante las 4 últimas semanas? (marque un solo número)

No, ninguno..........1
Sí, muy poco..........2
Sí, un poco..........3
Sí, moderado..........4
Sí, mucho..........5
Sí, muchísimo..........6

8. Durante las 4 últimas semanas, ¿hasta qué punto el dolor le ha dificultado su trabajo habitual (incluido el trabajo fuera de casa y las tareas domésticas)? (marque un solo número)

Nada..........1
Un poco..........2
Regular..........3
Bastante..........4
Mucho..........5

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9. Las preguntas que siguen se refieren a cómo se ha sentido y cómo le han ido las cosas durante las 4 últimas semanas. En cada pregunta responda lo que se parezca más a cómo se ha sentido usted. Durante las últimas 4 semanas ¿cuánto tiempo... (marque un solo número por cada pregunta)

	Siempre	Casi siempre	Muchas veces	Algunas veces	Sólo alguna vez	Nunca
a. se sintió lleno de vitalidad?	1	2	3	4	5	6
b. estuvo muy nervioso?	1	2	3	4	5	6
c. se sintió tan bajo de moral que nada podía animarle?	1	2	3	4	5	6
d. se sintió calmado y tranquilo?	1	2	3	4	5	6
e. tuvo mucha energía?	1	2	3	4	5	6
f. se sintió desanimado y triste?	1	2	3	4	5	6
g. se sintió agotado?	1	2	3	4	5	6
h. se sintió feliz?	1	2	3	4	5	6
i. se sintió cansado?	1	2	3	4	5	6

10. Durante las 4 últimas semanas, ¿con qué frecuencia la salud física o los problemas emocionales le han dificultado sus actividades sociales (como visitar a los amigos o familiares)? (marque un solo número)

Siempre 1
Casi siempre 2
Algunas veces 3
Sólo alguna vez 4
Nunca 5

11. Por favor, diga si le parece CIERTA o FALSA cada una de las siguientes frases:
(marque un solo número por cada pregunta)

	Totalmente cierta	Bastante cierta	No lo sé	Bastante falsa	Totalmente falsa
a. Creo que me pongo enfermo más fácilmente que otras personas	1	2	3	4	5
b. Estoy tan sano como cualquiera	1	2	3	4	5
c. Creo que mi salud va a empeorar	1	2	3	4	5
d. Mi salud es excelente	1	2	3	4	5

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CIC:

Cuestionario AUDIT (OMS): si en las 3 primeras pregunta <5 en varones o <4 en mujeres parar.

1. ¿Con qué frecuencia consume alguna bebida alcohólica?
   (0) Nunca
   (1) 1 o menos veces al mes
   (2) 2 o 4 veces al mes
   (3) 2 o 3 veces a la semana
   (4) 4 o más veces a la semana
2. ¿Cuántas consumiciones de bebidas alcohólicas suele realizar en un día de consumo normal?
   (0) 1 o 2
   (1) 3 o 4
   (2) 5 o 6
   (3) 7 a 9
   (4) 10 o más
3. ¿Con qué frecuencia toma 6 o más bebidas alcohólicas en una sola ocasión de consumo?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
4. ¿Con qué frecuencia en el curso del último año ha sido incapaz de parar de beber una vez había empezado?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
5. ¿Con qué frecuencia en el curso del último año no pudo hacer lo que se esperaba de usted porque había bebido?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
6. ¿Con qué frecuencia en el curso del último año ha necesitado beber en ayunas para recuperarse después de haber bebido mucho el día anterior?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
7. ¿Con qué frecuencia en el curso del último año ha tenido remordimientos o sentimientos de culpa después de haber bebido?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
8. ¿Con qué frecuencia en el curso del último año no ha podido recordar lo que sucedió la noche anterior porque había estado bebiendo?
   (0) Nunca
   (1) Menos de 1 vez al mes
   (2) Mensualmente
   (3) Semanalmente
   (4) A diario o casi a diario
9. ¿Usted o alguna otra persona han resultado heridos porque usted había bebido?
   (0) No
   (2) Sí, pero no en el curso del último año
   (4) Sí, en el último año
10. ¿Algún familiar, amigo, médico o profesional sanitario han mostrado preocupación por su consumo de bebidas alcohólicas o le han indicado que deje de beber?
   (0) No
   (2) Sí, pero no en el curso del último año
   (4) Sí, en el último año

Puntuación: Se suman los resultados de cada respuesta que están entre paréntesis delante de la misma.

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CIC:

EORTC QLQ-C30 (versión 3)

Estamos interesados en conocer algunas cosas sobre usted y su salud. Por favor, responda a todas las preguntas personalmente, rodeando con un círculo el número que mejor se aplique a su caso. No hay contestaciones "acertadas" o "desacertadas". La información que nos proporcione será estrictamente confidencial.

Por favor ponga sus iniciales:

Su fecha de nacimiento (día, mes, año):

Fecha de hoy (día, mes, año): 31

	En absoluto	Un poco	Bastante	Mucho
1. ¿Tiene alguna dificultad para hacer actividades que requieran un esfuerzo importante, como llevar una bolsa de compra pesada o una maleta?	1	2	3	4
2. ¿Tiene alguna dificultad para dar un paseo largo?	1	2	3	4
3. ¿Tiene alguna dificultad para dar un paseo corto fuera de casa?	1	2	3	4
4. ¿Tiene que permanecer en la cama o sentado/a en una silla durante el día?	1	2	3	4
5. ¿Necesita ayuda para comer, vestirse, asearse o ir al servicio?	1	2	3	4

Durante la semana pasada:	En absoluto	Un poco	Bastante	Mucho
6. ¿Ha tenido algún impedimento para hacer su trabajo u otras actividades cotidianas?	1	2	3	4
7. ¿Ha tenido algún impedimento para realizar sus aficiones u otras actividades de ocio?	1	2	3	4
8. ¿Tuvo sensación de "falta de aire" o dificultad para respirar?	1	2	3	4
9. ¿Ha tenido dolor?	1	2	3	4
10. ¿Necesitó parar para descansar?	1	2	3	4
11. ¿Ha tenido dificultades para dormir?	1	2	3	4
12. ¿Se ha sentido débil?	1	2	3	4
13. ¿Le ha faltado el apetito?	1	2	3	4
14. ¿Ha tenido náuseas?	1	2	3	4

Por favor, continúe en la página siguiente

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CIC:

Durante la semana pasada:	En absoluto	Un poco	Bastante	Mucho
15. ¿Ha vomitado?	1	2	3	4
16. ¿Ha estado estreñido/a?	1	2	3	4
17. ¿Ha tenido diarrea?	1	2	3	4
18. ¿Estuvo cansado/a?	1	2	3	4
19. ¿Interfirió algún dolor en sus actividades diarias?	1	2	3	4
20. ¿Ha tenido dificultad en concentrarse en cosas como leer el periódico o ver la televisión?	1	2	3	4
21. ¿Se sintió nervioso/a?	1	2	3	4
22. ¿Se sintió preocupado/a?	1	2	3	4
23. ¿Se sintió irritable?	1	2	3	4
24. ¿Se sintió deprimido/a?	1	2	3	4
25. ¿Ha tenido dificultades para recordar cosas?	1	2	3	4
26. ¿Ha interferido su estado físico o el tratamiento médico en su vida familiar?	1	2	3	4
27. ¿Ha interferido su estado físico o el tratamiento médico en sus actividades sociales?	1	2	3	4
28. ¿Le han causado problemas económicos su estado físico o el tratamiento médico?	1	2	3	4

Por favor en las siguientes preguntas, ponga un círculo en el número del 1 al 7 que mejor se aplique a usted

29. ¿Cómo valoraría su salud general durante la semana pasada?

1	2	3	4	5	6	7
Pésima						Excelente

30. ¿Cómo valoraría su calidad de vida en general durante la semana pasada?

1	2	3	4	5	6	7
Pésima						Excelente

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CIC:

Escala FACIT de fatiga (Versión 4)

A continuación encontrará una lista de afirmaciones que otras personas con su misma enfermedad consideran importantes. **Marque un solo número por línea para indicar la respuesta que corresponde a los <u>últimos 7 días</u>.**

		Nada	Un poco	Algo	Mucho	Muchí-simo
HI7	Me siento agotado(a)	0	1	2	3	4
HI 12	Siento debilidad en todo el cuerpo	0	1	2	3	4
An1	Me siento decaído(a)..	0	1	2	3	4
An2	Me siento cansado(a)	0	1	2	3	4
An3	Tengo dificultad para <u>comenzar</u> las cosas porque estoy cansado(a)	0	1	2	3	4
An4	Tengo dificultad para <u>terminar</u> las cosas porque estoy cansado(a)	0	1	2	3	4
An5	Tengo energía	0	1	2	3	4
An7	Soy capaz de hacer mis actividades habituales (trabajar, ir a la escuela, hacer las compras)	0	1	2	3	4
An8	Necesito dormir durante el día	0	1	2	3	4
An 12	Estoy demasiado cansado(a) para comer	0	1	2	3	4
An 14	Necesito ayuda para hacer mis actividades habituales	0	1	2	3	4
An 15	Estoy frustrado(a) porque estoy demasiado cansado(a) para hacer las cosas que quiero hacer	0	1	2	3	4
An 16	Tengo que limitar mis actividades sociales debido al cansancio	0	1	2	3	4

Spanish (Universal)

17 December 2010
Page 1 of 1

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CIC:

CUESTIONARIO DE SALUD DE GOLBERG GHQ-12

Lea cuidadosamente las siguientes preguntas.
Nos gustaría saber si usted ha tenido algunas molestias o trastornos y como ha estado su salud en las últimas semanas. Estamos preguntando en relación al último tiempo, no al pasado. Marque con una cruz en la casilla correspondiente a su respuesta.

Nº	CONDUCTAS	ALTERNATIVAS	RESPUESTAS
1	¿Ha podido concentrarse bien en lo que hace?	Mejor que lo habitual	
		Igual que lo habitual	
		Menos que lo habitual	
		Mucho menos que lo habitual	
2	¿Sus preocupaciones le han hecho perder mucho el sueño?	No, en absoluto	
		Igual que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
3	¿Ha sentido que está desempeñando un papel útil en la vida?	Más que lo habitual	
		Igual que lo habitual	
		Menos que lo habitual	
		Mucho menos que lo habitual	
4	¿Se ha sentido capaz de tomar decisiones?	Más capaz que lo habitual	
		Igual que lo habitual	
		Menos capaz que lo habitual	
		Mucho menos capaz que lo habitual	
5	¿Se ha sentido constantemente agobiado y en tensión?	No, en absoluto	
		Igual que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
6	¿Ha sentido que no puede superar sus dificultades?	No, en absoluto	
		Igual que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
7	¿Ha sido capaz de disfrutar de sus actividades normales de cada día?	Más que lo habitual	
		Igual que lo habitual	
		Menos que lo habitual	
		Mucho menos que lo habitual	

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Nº	CONDUCTAS	ALTERNATIVAS	RESPUESTAS
8	¿Ha sido capaz de hacer frente adecuadamente a sus problemas?	Más capaz que lo habitual	
		Igual que lo habitual	
		Menos capaz que lo habitual	
		Mucho menos capaz que lo habitual	
9	¿Se ha sentido poco feliz o deprimido?	No, en absoluto	
		No más que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
10	¿Ha perdido confianza en sí mismo/a?	No, en absoluto	
		No más que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
11	¿Ha pensado que usted es una persona que no vale para nada?	No, en absoluto	
		No más que lo habitual	
		Más que lo habitual	
		Mucho más que lo habitual	
12	¿Se siente razonablemente feliz considerando todas las circunstancias?	Más feliz que lo habitual	
		Igual que lo habitual	
		Menos feliz que lo habitual	
		Mucho menos feliz que lo habitual	

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