Nutrition in Cancer Patients Undergoing Different Nutritional Strategies

Subjects: Others

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Malnutrition in cancer patients is one of the most influential factors in the evolution and mortality of such patients. To reduce the incidence of malnutrition, it is necessary to establish a correct nutritional intervention. For this purpose, precise tools and indicators must be developed to determine the patient's condition.

bioimpedance cancer therapy radiotherapy phase angle nutrition

1. Introduction

Cancer is a disease characterized by the development of abnormal cells, which can appear in any area of the organism, dividing, growing, or spreading with no mechanics of control [1]. Currently, neoplastic disease remains one of the main causes of morbidity and mortality worldwide, with an estimated incidence of 18.1 million new cases by the year 2020, making it one of the diseases with the greatest impact on healthcare [2]. Therefore, its monitoring is crucial since its clinical impact is of great relevance [3].

It has been observed that, at the time of diagnosis, there is a high percentage of patients who present involuntary weight loss, which causes the patient to begin the treatment of the disease with an impaired nutritional status [4]. Poor nutritional status is closely related to an increase in the toxicity and complications of treatment, longer hospital admissions, failure or interruption of treatments, infections, readmissions, and reduced quality of life, and is responsible for 10–20% of mortality in oncologic patients [5]. Currently, the multidisciplinary approach is considered the best option to deal with sarcopenia and cachexia caused by cancer, recommending nutritional intervention as an essential component of the therapy, being the efficient screening and also an indispensable complement [6].

Consequently, several consensus documents have been published to ensure early and proper nutritional monitoring and intervention in hospitals [7].

On the other hand, different studies emphasize the importance of finding markers or diagnostic protocols capable of differentiating between the different degrees of malnutrition in patients in a specific and reliable way [8]. In recent years, the role of bioimpedance and phase angle assessment has been analyzed because it allows to evaluate the nutritional status of the patient in a simple, fast, non-invasive, and convenient way, being able to obtain prognostic values. The phase angle is derived from bioelectrical impedance analysis (BIA), which measures the opposition (impedance) to the flow of an electrical current through body tissues. The phase angle is the arctangent of the reactance and resistance values obtained during the BIA [9]. A higher PA typically indicates better cellular health and integrity, while a lower PA suggests compromised cellular function or malnutrition [10]. Research has demonstrated that PA correlates well with changes in body composition and is a reliable indicator of nutritional status [11]. In this way, it is useful in prevention and diagnosis, complementing the other markers and improving the specificity and diagnostic sensitivity of the tools currently used to avoid late diagnoses and states of malnutrition that may complicate the treatment and recovery process [12]. In fact, some investigations utilized the PA as a marker to observe the role of different treatments in cancer patients with the aim of analyzing the unfavorable modifications at the body level that a certain treatment, such as radiotherapy, chemotherapy, or surgery, may cause, thereby implementing an early nutritional intervention that helps the patients to prevent potential malnutrition [13][14][15][16][17].

In several systematic reviews performed on patients with various types of cancer, it has been observed that a low-phase angle is associated with an impaired nutritional and functional status, which may increase the morbidity and mortality of the subject suffering from the disease [18][19]. It also seems to be a good marker of nutritional status, providing additional data and contributing to more rigorous nutritional evaluations in patients with neoplasms [20]. In fact, a recent meta-analysis, which included 14 studies and 2625 participants, concluded that the phase angle could become a major prognostic factor for survival in cancer patients [18].

On the other hand, dynamometry is a widely used method to assess muscle strength and functional capacity in patients with cancer [21]. The measurement of muscle strength using dynamometry has been proposed as a potential marker of malnutrition in these patients [22]. Several studies have been conducted to investigate the association between muscle strength and malnutrition in cancer patients.

A study conducted by Barata et al. found that handgrip strength, as measured by dynamometry, was significantly correlated with nutritional status in patients with advanced lung cancer [23]. Similarly, another study by Kilgour et al. showed that handgrip strength was a significant predictor of survival in patients with advanced pancreatic cancer . In addition, a recent systematic review and meta-analysis carried out by López-Bueno et al. evaluated the relationship between muscle strength and mortality in cancer patients. The review included 48 studies and concluded that muscle strength measured by dynamometry was a reliable marker of mortality in patients with cancer [24]. In summary, the functional capacity measured by dynamometry is an important marker of malnutrition in people with cancer.

2. Study Characteristics

The main characteristics of the nine included studies are summarized in **Table 1**. The articles were published between 2006 and 2023. A total of 606 participants (43.9% of women) with a mean age of 58.6 ± 11.2 years were included in the present meta-analysis. The stage of the disease was reported in all studies. Regarding BMI, the mean value was 24.0 ± 3.6 Kg/m^2. In terms of geographical regions, five different countries were identified: Italy [25][26]; Thailand [27]; Germany [28]; Brazil [29][30][31]; Switzerland [32]. All the studies were conducted with participants from only one country. In five studies [25][26][28][29][30], a bioimpedance measurement was performed before and after the nutritional intervention, obtaining the phase angle. In six of them [25][26][27][28][31][32], functionality was analyzed via a handgrip strength test. On the other hand, the evolution of body weight was measured in seven articles [25][26][28][29][30][31][32], while BMI was only analyzed in five of them [27][28][29][30][31].

Table 1. Descriptive data of the study participants (N = 606).

Reference	Year	Study Groups	Total (*n*)	Women (%)	Age (Mean)	BMI (kg/m^2)	Cancer	Current Treatment	BIA Methods/Instrument	Nutritional Intervention	Hydraulic Hand Dynamometer
Cereda et al. [26]	2018	CS (*n* = 81) CS + ONS (*n* = 78)	159	28.3	65.1	24.2	Head and neck	Conventional (1.8-to-2 Gy/fraction) 3D conformal RT	NutriLAB, Akern/RJL	ONS (energy-dense, high-protein, omega-3-enriched oral formula)	DynEx
Cereda et al. [25]	2019	CS (*n* = 84) CS + WP (*n* = 82)	166	39.8	65.4	22.2	Lung, stomach, esophagus, pancreas, colon, blood, breast, head, and neck	Standard chemotherapy regimens	NutriLAB, Akern/RJL	Two sachets/day of cow milk WP (20 g of proteins)	DynEx
Norman et al. [28]	2006	Cr (*n* = 16) C (*n* = 15)	31	35.5	63.4	24.9	Colorectal cancer	Chemotherapy	BIA 2000 M	Creatine supplementation	Digimax electronic dynamometer
Cruz et al. [29]	2017	EPA (*n* = 29) C (*n* = 24)	53	20.8	55.5	21.6	Oral cavity	Without treatment	Biodynamics Model 450	EPA-enriched supplement from fish oil (2 g)	NR
Faccio et al. [30]	2020	C (*n* = 42) ONS (*n* = 43)	85	60	58.8	25	Colorectal, breast, lung, upper digestive tract, ovarian and other cancers	Chemo/radiotherapy	Biodynamics, 310	ONS (hyper-protein supplement, enriched with L-leucine, vitamins, and minerals	NR
Thambamroong et al. [27]	2022	C (*n* = 10) Cur (*n* = 10)	20	NR	59	NR	Head and neck cancer	Chemo/radiotherapy	InBody	Curcumin (4000 mg)	NR

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Reference	Year	Study Groups	Total (*n*)	Women (%)	Age (Mean)	BMI (kg/m^2)	Cancer	Current Treatment	BIA Methods/Instrument	Nutritional Intervention	Hydraulic Hand Dynamometer
Uster et al. [32]	2013	UC (*n* = 28) NT (*n* = 30)	58	20.7	65	22.8	Breast, lung, head and neck, pancreatic, colorectal, gastrointestinal, renal, prostate, and endometrium cancer. Sarcoma, lymphoma, myeloma, mesothelioma, neuroendocrine tumor, and unknown	NR	NR	Oral nutritional supplements and individual nutritional plan	Jamar
De Souza et al. [31]	2021	C (*n* = 15) NT (*n* = 19)	34	100	44.8	27.3	Breast cancer	Chemotherapy	NR	Hyper-protein personalized diet	Jamar

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3. Nutritional Intervention

All the studies included in this meta-analysis carried out a nutritional intervention or supplementation in the experimental group. The two studies conducted by Cereda et al. provide nutritional advice in both control and experimental groups [25][26]. In one of these two studies, the patients in the experimental group, called oral nutritional supplement (ONS), received two drinks a day with a high-energy and high-protein formula enriched in omega-3 [26]. In the second study, the experimental group received two sachets daily of a whey protein (WP) formula [25]. Norman et al. also used in their clinical trial a type of nutritional intervention targeted to the experimental group based on a supplement, in this case, creatine [28]. In the clinical trial conducted by Cruz et al., an amount of 2 g of fish oil with eicosapentaenoic acid (EPA) was given to the experimental group as a possible nutritional aid in addition to a diet rich in energy and protein, which was consumed by both groups [29]. Faccio et al. [30], Uster et al. [32], and de Souza et al. [31] provided the intervention group with a high-protein and personalized diet with nutritional supplements. Finally, Thambamroong et al. used curcumin supplementation in cancer patients, comparing the results with the control [27].

4. Risk of Study Bias

The RoB 2.0 tool developed by Cochrane was used for the risk of bias. The data from the eight studies are represented in **Figure 1** and **Figure 2** [25][26][27][28][29][30][31][32]. Three studies reported a medium overall risk of bias due to the D5 item 'selection of the reported result' [28][30][32]. In general, the included studies reported a low risk in overall risk of bias [25][26][27][31].

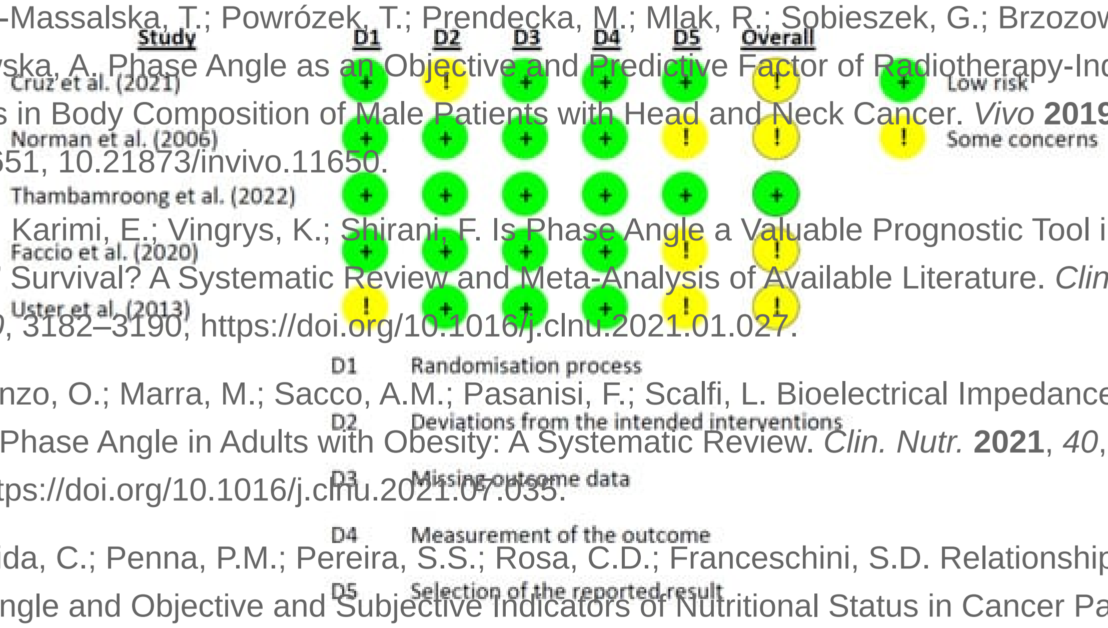

Figure 1. Graph of RoB 2.0 for each study according to the five domains defined by Cochrane for per protocol studies [27][28][29][30][32].

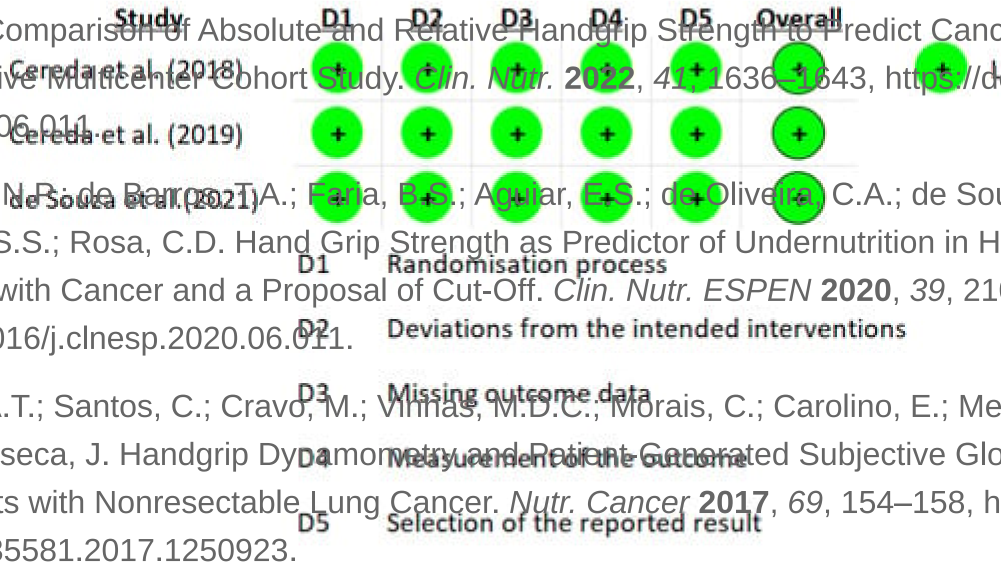

Figure 2. Graph of RoB 2.0 for each study according to the five domains defined by Cochrane for intention to treat studies [25][26][31].

5. Findings from Meta-Analysis

Four meta-analyses were conducted to test the effects of different types of nutritional strategies on the variables phase angle, handgrip strength, BMI, and weight. A random-effects model was used for the phase angle variable, and a fixed-effects model for the rest of the variables.

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Figure 3 shows the positive and significant correlation between phase angle and nutritional strategy (SMD: 0.43; 95% CI: 0.10 to 0.77; p = 0.01) (I^2 = 65.62%; p = 0.02).

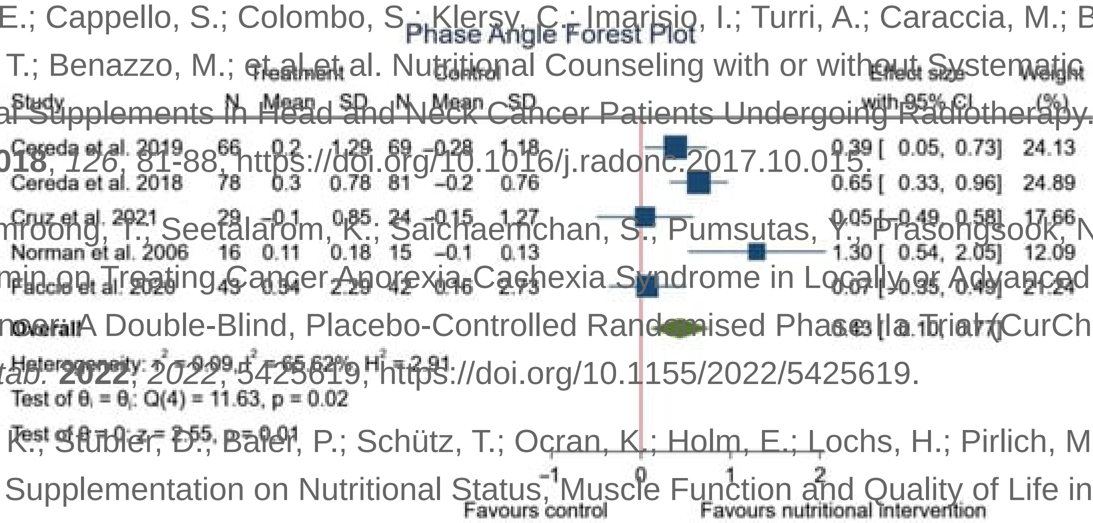

Figure 3. Forest plot detailing the mean difference and 95% confidence intervals (CI) for the effect of nutritional intervention on phase angle [25][26][28][29][30].

Regarding handgrip strength, the meta-analysis found significant differences between experimental group with nutritional strategy (WP; ONS; creatine; hyper-protein personalized diet or curcumin) and control group. **Figure 4** shows the analysis according to handgrip strength (SMD: 0.27, 95% CI: 0.08 to 0.47; p = 0.01) (I^2 = 30.70%; p = 0.21).

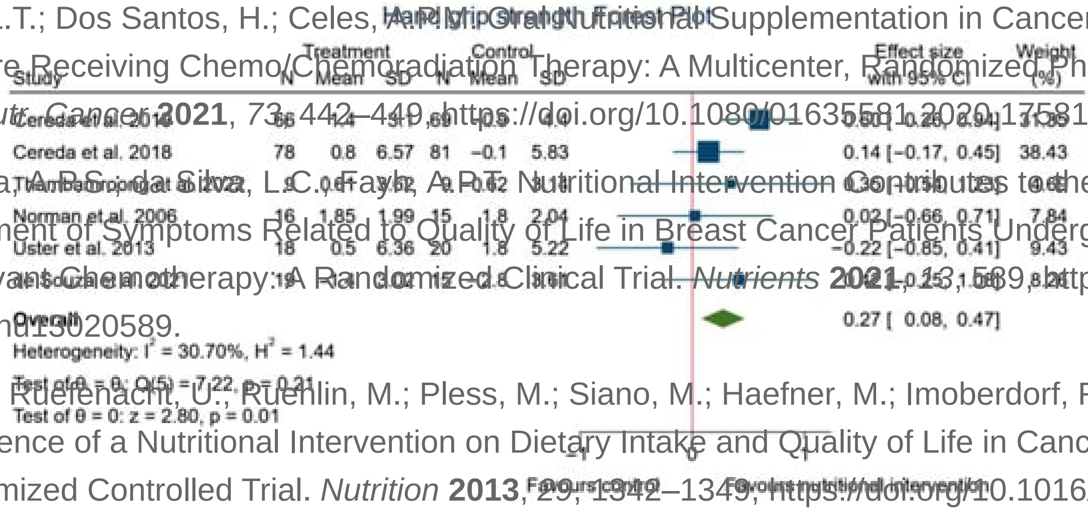

Figure 4. Forest plot summarizing the impact of nutritional intervention on handgrip using a fixed-effects model. Pooled summary data are presented as standardized mean differences and 95% confidence interval [25][26][27][28][31][32].

After performing the meta-analysis, significant differences were observed in the changes in weight (SMD: 0.25, 95% CI: 0.08 to 0.42; p < 0.00) (I^2 = 46.85%; p = 0.08) (**Figure 5**), but no significant differences were observed in

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BMI (SMD: 0.10, 95% CI: −0.16 to 0.36; p = 0.44) (I^2 = 41.30%; p = 0.15) (**Figure 6**) in the experimental group, although a trend to an increase in weight can be appreciated.

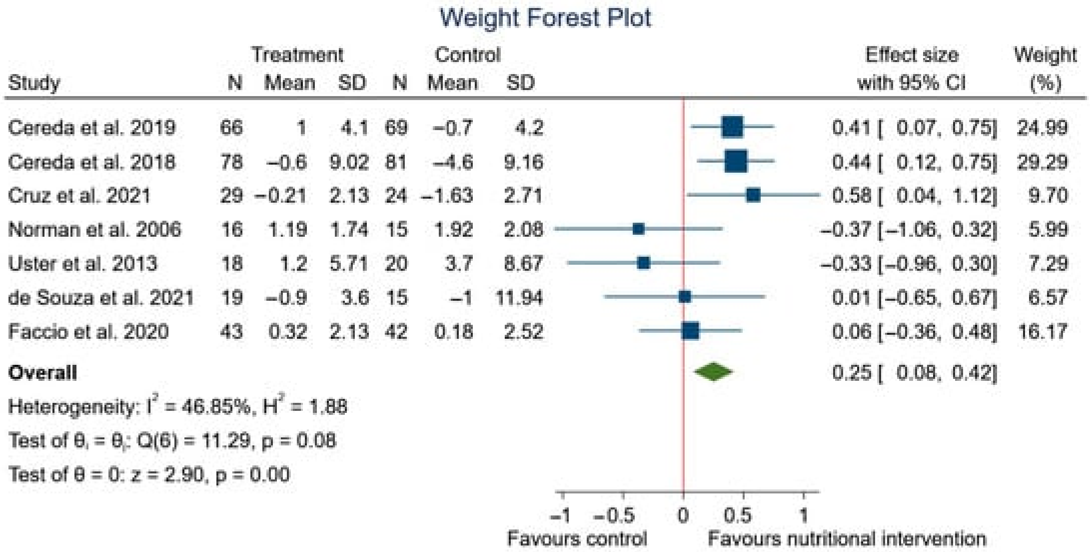

Figure 5. Forest plot summarizing the impact of nutritional intervention on weight using a fixed-effects model. Pooled summary data are presented as standardized mean differences and 95% confidence interval [25][26][28][29][30][31][32].

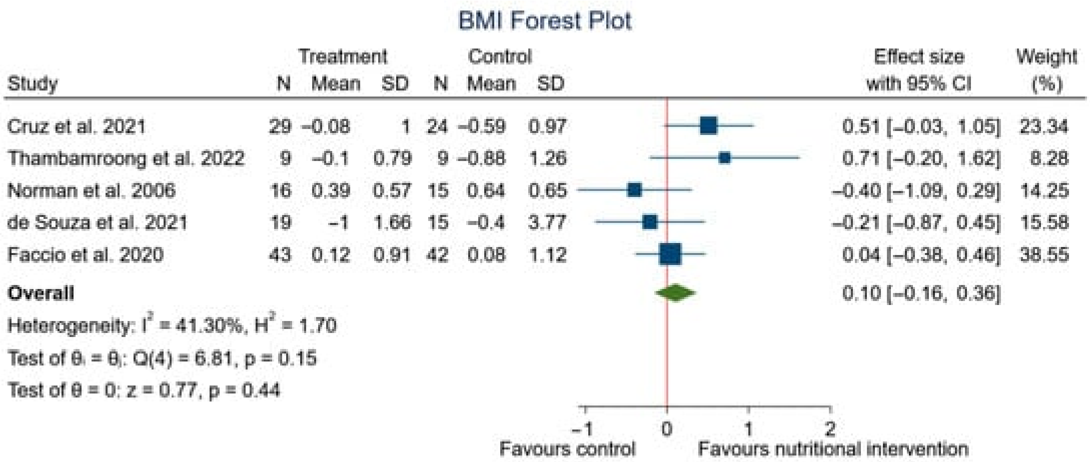

Figure 6. Forest plot summarizing the impact of nutritional intervention on weight using a fixed-effects model. Pooled summary data are presented as standardized mean differences and 95% confidence interval [27][28][29][30][31].

The Egger regression test showed no significant differences in phase angle, handgrip strength, and BMI (p > 0.1), indicating an absence of publication bias. Egger's test revealed a statistically significant result for the weight (p = 0.02). However, in the evaluation of phase angle, a visual assessment using the funnel plot suggests publication bias, although the result of Egger's test is not statistically significant.