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SUMARIO ● SUMMARY ● RESUMO

Editorial

In this second issue of the fourth volume of MLS Health & Nutrition Research, we reaffirm our commitment to directly confronting the challenges posed by public health and clinical nutrition from an evidence-based perspective and real-world applicability. The selection of articles reflects a diverse but complementary agenda that connects rigorous research with the need for practical and culturally adapted solutions.

This edition begins with a detailed analysis of the Impact of the Vegetarian Diet, the Low-Carbohydrate Diet, and the Mediterranean Diet on the Management of Generalized Anxiety Disorder. We emphasize that, although the evidence on the vegetarian diet is still limited and contradictory, the mediterranean diet is positioned as a robust and safe option, with high-quality evidence supporting its use in combination with pharmacological treatments to improve symptoms and population adherence. The low-carbohydrate diet, although with better quality studies in some cases, presents challenges in adherence and possible deficits of key nutrients that deserve careful clinical consideration.

Nutraceuticals are observed in the second contribution, focused on nutritional strategies for mitigating chemotherapy side effects in women with breast cancer. This article synthesizes recent evidence on the use of specific diets and supplements such as probiotics and melatonin, reaffirming the importance of a complementary nutritional approach to improve quality of life and reduce symptoms common to these treatments.

Overweight and obesity continue to be universal challenges, and the third article contrasts the impact of the ketogenic diet, the low-calorie Mediterranean diet, and mindful eating. Analyses indicate that hypocaloric dietary interventions, both ketogenic and Mediterranean, have a significant and rapid effect on weight reduction and metabolic improvements, whereas mindful eating appears to exert a more limited influence on eating behavior without significant metabolic changes.

In the area of integrative health, the fourth investigation evaluates the nutrition-sleep relationship by comparing the Mediterranean and ketogenic diets in healthy adults. The results support further scientific support for the Mediterranean diet as a non-pharmacological strategy to improve sleep quality and duration, while the evidence on the ketogenic diet is still insufficient to formulate recommendations.

The link between food and mental health is explored in the fifth article, which analyzes the correlation between levels of depressive symptoms and consumption of ultra-processed foods in university students. This study underscores the relevance of considering eating patterns in social and educational settings to address emerging mental disorders.

Finally, surgical safety and hospital management are the focus of the sixth paper, which examines adherence to the safe surgery checklist and its relationship to surgical complications. Although the statistical correlation found is low, the study highlights the checklist as a valuable tool for improving patient safety and optimizing hospital resources.

With this body of work, MLS Health & Nutrition Research continues its mission to be a platform that unites open science, academic rigor, and social applicability, inviting researchers, practitioners, and students to join this movement towards impactful and globally relevant nutrition.

Dr. Iñaki Elío Pascual
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The impact of the Vegetarian Diet, the Low-Carbohydrate Diet, and the Mediterranean Diet on the management of Generalized Anxiety Disorder

El impacto de la dieta vegetariana, la dieta baja en carbohidratos y la dieta mediterránea en el manejo del trastorno de ansiedad generalizada

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ABSTRACT

The Vegetarian Diet (VD), as a dietary intervention for Generalized Anxiety Disorder (GAD), is supported by studies of low methodological quality and presents a similar number of publications both in favor of and against its potential beneficial effect on the disorder. In contrast, the Low-Carbohydrate Diet (LCD) is supported by studies of higher quality; however, many of them involve small, homogeneous samples. Additionally, the LCD tends to show poor long-term adherence, potential adverse effects over time, and deficiencies in key nutrients such as fiber and magnesium, which are relevant to the gut–brain axis. Finally, there are high-quality studies that position the Mediterranean Diet (MD) as a promising dietary pattern for reducing GAD symptoms. These studies are well-designed in terms of sample size and follow-up; however, they often include homogeneous populations, limiting the generalizability of the findings to the broader population affected by this mental health condition. The MD emerges as a suitable nutritional approach for managing GAD alongside pharmacological treatment, supported by solid evidence of its positive effects on the disorder, high adherence in the general population, its content of fiber, omega-3 fatty acids, and magnesium, and the absence of known health risks.

Palabras clave:
Dieta Vegetariana. Dieta Baja en Carbohidratos. Dieta Mediterránea. Trastorno de Ansiedad Generalizada (TAG). Intervención dietética.

RESUMEN

La DV como intervención dietética en el TAG cuenta con una baja calidad de los estudios existentes y un similar número de estudios a favor de su efecto beneficioso en la enfermedad y en contra del mismo. Por otro lado, la DBC plantea estudios de mayor calidad, pese a ello, gran parte de ellos son con una muestra baja y homogénea. Asimismo, una DBC presenta efectos adversos a largo plazo, una baja adherencia a la dieta y déficits de nutrientes clave como la fibra o el magnesio en el eje microbiota-intestino-cerebro. Por último, existen estudios de alta calidad que posicionan a la DM como patrón dietético a seguir para la reducción de síntomas del TAG, estos estudios están correctamente planteados a nivel de número de muestra y seguimiento, sin embargo, la población resulta ser homogénea y no representa a la población general que padece esta afección mental. La DM se presenta como abordaje nutricional para el

TAG combinado con el tratamiento farmacológico debido a la existencia de estudios de calidad que verifican su efecto positivo en la enfermedad, su alta adherencia poblacional, el contenido de fibra, omega 3 y magnesio y, por último, la ausencia de riesgos conocidos.

Introduction

Today, there are numerous diets capable of reversing or minimizing symptoms of cardiovascular, endocrine, digestive, etc. diseases. More recently, scientific interest has grown exponentially in the impact of diet on mental health, suggesting that certain dietary patterns may modulate neurobiological processes related to disorders such as anxiety (1).

Generalized Anxiety Disorder (GAD) is a mental condition consisting of excessive worry about future events, which involves neurotransmitters and hormones capable of deregulating mood, sleep, concentration, etc. (2). This disorder, including signs/symptoms, has a prevalence of 10.4% in the world population, a figure that is increasing, as is the excessive consumption of drugs that treat it (3,4).

While it is true that many patients consider pharmacology as a beneficial therapy, a significant number of people establish this option as not accessible, tolerable and/or effective, so a practical therapeutic approach such as nutritional intervention is necessary (3).

The bidirectional communication between the gut and the brain through the Autonomic Nervous System (ANS) and Enteric Nervous System (ENS), which includes neurotransmitters such as GABA or serotonin, and the hypothalamic-pituitary-adrenal (HPA) axis, which regulates the adaptive response to stress by means of hormones such as cortisol, demonstrates the ability of the microbiota and thus the diet to influence the neurological communications involved in mental illnesses such as GAD (5).

It is known that a healthy diet and lifestyle pattern, including a varied and balanced diet and physical exercise, can have positive effects on mental health, reducing the risk of mental disorders such as GAD (6). This is because healthy habits directly influence the cognitive and emotional functions of those who practice them. Despite the obvious benefits of eating a varied and balanced diet, there is no specific approach to diet as an adjuvant in the treatment of GAD, i.e., one that helps to reduce the severity of its symptoms or even to completely remission (7).

In addition to the relationship between diet and mental health conditions, there is a bidirectional association between GAD and obesity and overweight. On the one hand, people who are overweight or obese are at increased risk of anxiety due to factors such as social stigmatization, body dissatisfaction and metabolic dysregulation such as chronic inflammation. On the other hand, anxiety may contribute to the development and maintenance of obesity, since it is associated with emotional eating. Likewise, in individuals with obesity there is also an imbalance in the neurotransmitters cortisol and serotonin (8).

Regarding the effects of diet on GAD, the microbiota-gut-brain axis plays a key role in emotional regulation and in the production of neurotransmitters related to this mental condition (7). Because of these connections between diet and mental health, it has been proposed that a dietary intervention, such as the Vegetarian Diet (VD), the Low Carbohydrate Diet (LCD) and the Mediterranean Diet (MD), could be an effective strategy that treats or decreases GAD symptomatology. These three diets are characterized by promoting the consumption of foods that promote brain health, in addition to decreasing inflammation and regulating the metabolic response, which could have a positive effect on the patient with GAD (9).

In addition to diet, it is important to consider certain nutrients that have a positive effect on mental health and to take them into account when choosing the most

appropriate option for the treatment of anxiety. Nutrients such as omega-3, fiber and magnesium have some evidence for their positive impact on GAD (10).

The omega-3 (PUFA) is a polyunsaturated fat obtained from foods such as oily fish, nuts, seeds, vegetable oils, etc.. Omega-3 is essential, that is, it cannot be synthesized by the body and must be acquired through the diet. At the brain level, this essential fatty acid promotes cognition, neuronal preservation and protects against neurodegeneration. In addition, several clinical trials relate low levels of omega-3 with the suffering of anxiety and, on the other hand, the use of these fatty acids as a treatment in the reduction of the symptoms of GAD (11-15).

Following the bidirectional communication between the gut and the brain, one nutrient capable of improving the composition of the microbiota is fiber. This nutrient is found in fruits, vegetables, whole grains, seeds, etc., so an adequate intake of these foods would meet the recommendations. However, the fiber intake of the population is far below the recommended intake of 25-35 g per day. Fiber has been studied through clinical trials as a possible improvement of the clinical picture of anxiety, stating that its integration in the diet exerts beneficial effects on mental health (16-18).

Magnesium (Mg) is the fourth most abundant cation in the human body. The recommended daily intake of this mineral is 375 mg per day from fruits, vegetables, legumes, nuts and whole grains. Its possible positive effects on GAD are due to the fact that Mg acts as a modulator of the central nervous system, being an agonist of the GABAA receptor and inhibitor of the NMDA receptor (N-methyl-D-aspartate), in addition, hypomagnesemia in adults has been related to the suffering of anxiety (19). Different clinical trials have related sufficient Mg intake to lower scores in GAD symptomatology (19-21).

Beyond the physiological effects of the diets, it is important to evaluate the level of adherence of each of the dietary interventions proposed in order to verify that it is a useful and effective strategy for people suffering from GAD (22).

In this context, it is essential to analyze in depth the role of different dietary interventions in the symptomatology of GAD. Among the most studied diets are the Vegetarian Diet (VD), the Low Carbohydrate Diet (LCD) and the Mediterranean Diet (MD), each with specific nutritional profiles that may differentially influence anxiety (1).

Method

This literature review consists of an analysis of several documents with the aim of comparing and evaluating the Vegetarian Diet, the Low Carbohydrate Diet and the Mediterranean Diet as a dietary intervention in Generalized Anxiety Disorder.

For the literature review, we included cross-sectional, observational studies and clinical trials examining the relationship of different diets to the treatment of GAD.

The search for articles and other publications began on February 5, 2025 and ended on April 18, 2025. In addition, a systematic search of two pages was carried out; PubMed and ScienceDirect, in which the following filters and key words in English were applied:

- Maximum 5 years old.
- Research articles.
- Sample size: no minimum due to the low proportion of studies related to the subject.
- Type of sample: in humans.
- Key words for the search of studies: (“anxiety”) AND ((“mediterranean diet”) OR

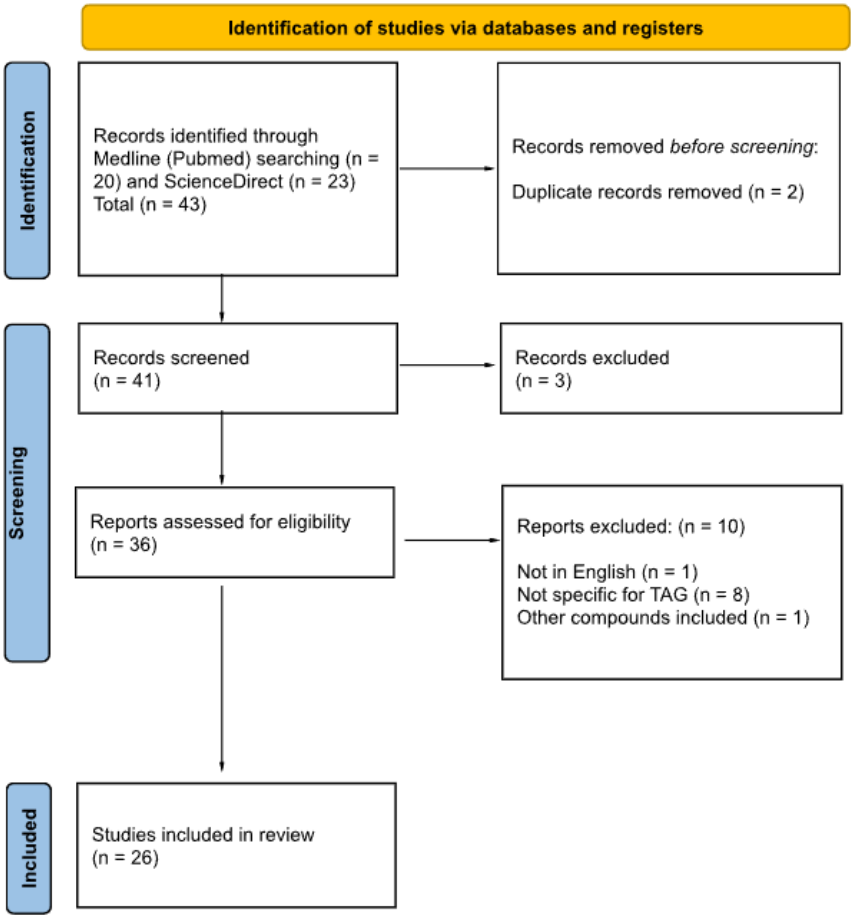
("low-carb diet") OR ("vegetarian diet") OR ("plant-based diet") OR ("omega 3") OR ("fiber") OR ("magnesium"))

- Keywords for general search terms:
  - ("Anxiety") AND (("prevalence") OR ("mechanism") OR ("treatment"))
  - ("gut-microbiota-brain axis")
  - ("gut-microbiota-brain axis") AND ("anxiety")
  - ("diet") AND ("anxiety")

In the end, 53 articles were found for the realization of the present Final Degree Project. Of these, 26 studies were selected and analyzed in depth to draw conclusions about the efficacy of different diets as possible nutritional interventions in the treatment of GAD.

Results

Figure 1. Outline of the bibliographic search. Selected and analyzed studies on different diets and their efficacy as a nutritional approach in GAD.



Discussion and Conclusions

A dietary intervention in GAD is presented as a practical and effective approach when it comes to reducing symptomatology, improving quality of life or even remission of GAD. Three diets have been compared, the Vegetarian Diet, the Low Carbohydrate Diet and, finally, the Mediterranean Diet.

If we begin by analyzing the plant-based dietary pattern, there are 8 studies that investigate this type of nutritional approach as a treatment for GAD as well as the possible improvement of the symptomatology of the mental condition presented in Table 1. (23-30).

Likewise, the three authors Zamani et al (23)wang et al (24) and Senturk et al (25) which establish DV as having a possible beneficial effect on GAD symptomatology. These studies are cross-sectional, so that the follow-up of the diet is not precise and, therefore, an adequate vegetarian dietary pattern cannot be assured. All three authors agree on the importance of the quality of the diet in terms of nutritional treatment as a treatment for GAD.

Two other studies by Conner et al (26) and Haghighatdoost et al (27) relate diet quality to lower scores on anxiety questionnaires and, conversely, also relate poorer quality of DV to higher prevalence of anxiety. So, like the above, the impact of DV depends more on the quality than on the diet itself.

On the other hand, three observational studies by Kohl et al (28), Saintila et al (29) and Bègue and Shankland (30) found worse results in GAD symptomatology, in addition to a higher prevalence of the disease, in individuals who followed a VD with respect to those who consumed an omnivorous diet. Research established a possible negative effect of VD on the incidence of anxiety in the populations studied. Although all three studies found a higher percentage of people with the disease in those individuals who had a plant-based dietary pattern, causal relationships cannot be established because they are observational studies with low follow-up of diet. It should be noted that the research by Saintila et al (29) despite finding an association of VD with greater episodes of anxiety and depression, found a lower BMI and emotional eating in people who follow a plant-based eating pattern. If we add the samples of the three studies that negatively relate VD to GAD, we obtain a representation of 21,562 people.

Despite the differences between the studies mentioned above, the planning of the VD carried out in each study must be taken into account, since a poorly designed VD may imply nutritional deficiencies such as deficiency of vitamin B12, iron or essential fatty acids (omega 3 and omega 6). Lack of these nutrients can negatively affect mood and, thereby, worsen GAD symptomatology (31). A properly structured VD also provides the ideal amount of omega-3 fatty acids, magnesium and, above all, fiber.

The beneficial effect of VD in the management of GAD cannot be proven due to the methodological limitations of the available studies. Most of the investigations analyzed present observational designs, cross-sectional or with unrepresentative samples, which makes it difficult to establish solid causal relationships between the follow-up of a VD and the improvement of anxiety symptoms. In addition, many of the investigations do not compare with an omnivorous diet, do not specify the degree of adherence to the diet, and do not specify the follow-up of the diet.

Therefore, it is not possible to affirm the use of a vegetarian dietary pattern for the improvement of GAD symptomatology. Thus, the impact of VD on GAD seems to depend more on the quality and planning of the diet than on the type of pattern itself.

Author	Reference	Year	Population	Sample	Duration of follow-up	Results
Zamani et al.	(23)	2020	Adult women	435	-	A healthy vegetarian diet was inversely associated with psychological disorders.
Wang et al.	(24)	2024	Older adults (>70)	11.971	20 years	A healthy vegetarian diet was positively associated with the prevention and management of anxiety in this population.
Senturk et al.	(25)	2023	Adults	1355	-	The meat-free diet group had lower anxiety scores, less emotional eating and less uncontrolled eating than the omnivorous diet group.
Conner et al.	(26)	2025	Young adults	78	10 weeks	They found no differences between individuals who consumed red meat and those who consumed meat of vegetable origin. Improved diet quality improves mental health.
Haghighatdoost et al.	(27)	2023	Adults	2033	1 year and 4 months	An unhealthy dietary index of a vegetarian diet resulted in higher levels of anxiety.
Kohl et al.	(28)	2023	Adults (35-70 years old)	14216	2 years	Vegetarian diet was associated with more depressive episodes and worse mental health.
Saintila et al.	(29)	2024	Adults	768	2 months	Vegetarian and vegan diets were associated with higher levels of anxiety and depression.
Bègue and Shankland	(30)	2022	Adolescents 18 and 19 years of age (mostly females)	6578	11 months	Individuals who performed a VD had higher anxiety scores than non-vegetarians.

Table 1. Studies on the use of a VD in GAD (from 23 to 30).

Secondly, there are 8 studies analyzing a CBD as a possible dietary intervention in GAD included in Table 2. (32-39)of which a greater proportion show a positive influence of CBD on the remission of GAD symptomatology.

There are 6 research studies that establish CBD as a possible treatment for GAD (32-37). The clinical trials of Danan et al. (32) Tidman (33), Calabrese et al. (34) and Bernia P. (35) have a very small, unrepresentative sample and, moreover, without a control group. The study by Danan et al. (32) is presented as a correctly planned research since it focuses on people with mental disorders such as anxiety and depression, it proposes the maximum daily dose of CH and the established period, however, there is no control group, the patients knew what they were undergoing, adherence to the diet was achieved after 4 weeks and, in addition, the state of ketosis was not monitored. Similarly, Tidman (33) carried out his study in a person with Parkinson's disease, so his results cannot be extrapolated. Like Danan et al. (32)calabrese et al. (34) conducted their research in patients with mental disorders; however, only 3 participants were included, so there was no room for a control group. Along the same lines, Bernia P. (35) finds positive results regarding CBD as a nutritional intervention for anxiety, in spite of this, the diet proposed contains more than the 40 g HC daily since it is an isocaloric DM to which he adds coconut oil and, in addition, they are patients with multiple sclerosis without a control group.

Likewise, the other 2 studies that find beneficial effects of CBD on anxiety are observational, so the causes of the results obtained are not established, in addition to not having a sample of people with GAD or symptomatology of the disease to recognize the positive effects of CBD on it. Daneshzad et al. (36) found this relationship in his research on 265 women with type II diabetes mellitus, stating that clinical trials are needed to confirm his findings due to the non-heterogeneity of the sample and the type of study. Similarly, Daneshzad et al. (36)garner et al. (37) in their cohort study shows a positive association of CBD on mental health in healthy adults, so CBD is not analyzed as a treatment or adjuvant, but as a prevention of mental illness.

On the other hand, two other observational studies by Sangsefidi et al (38) and Tabesh et al (39) do not establish a correlation between CBD and GAD. It should not be overlooked that the sample size of both is very large (>10,000 in total), however, the way the results are collected through a semi-quantitative online Consumption Frequency Questionnaire does not support high dietary follow-up. In turn, the study by Sangsefidi et al (38) study does not establish its duration and that of Tabesh et al (39) lasts 2 years, a rather long period to maintain this dietary pattern that has shown quite a few adverse effects in the long term. As they are observational studies, they do not establish the causal relationships of their results.

In order to prove that a CBD is an effective strategy, it is essential to know the negative effects it has on health if implemented over the long term. A CBD maintained over time increases LDL and total cholesterol, which increases the risk of cardiovascular disease, and also increases the risk of metabolic acidosis, which decreases bone density, increases tiredness and fatigue, and worsens mood. In addition to that, CBD is a dietary intervention low in fiber and vitamins due to the low consumption of fruit and, in many cases, vegetables, which would eliminate all the benefits at intestinal, cerebral, renal, cardiovascular, etc. levels. (16,18,40).

Despite the fact that CBD studies are better designed than the previous ones, its use as a treatment for GAD cannot be confirmed due to the fact that most of these studies present small samples, non-randomized designs without a control group, and with a non-representative sample. In addition to all this, there are the possible adverse effects of long-

term CBD (40) such as lipid alterations, fiber and micronutrient deficiency, or adherence problems.

Author	Reference	Year	Population	Sample	Duration of follow-up	Results
Danan et al.	(32)	2022	Hospitalized adults with severe and persistent mental illnesses	31	6-248 days	A ketogenic diet is associated with considerable improvements in mental health symptoms.
Tidman	(33)	2022	Woman with Parkinson's disease	1	24 weeks	A ketogenic diet decreases anxiety symptoms in Parkinson's disease.
Calabrese et al.	(34)	2024	Adults aged 32 to 36 years with depression and/or anxiety	3	12-16 weeks	Complete remission of the disease was obtained 7-12 weeks after starting ketosis.
P. Bernia	(35)	2019	Patients with multiple sclerosis	27	4 months	A CBD in these patients improves anxiety levels.
Daneshzad et al.	(36)	2020	Women with type II diabetes mellitus	265	-	Patients who consume fewer carbohydrates have better sleep quality and lower incidence of mental disorders.
Garner et al.	(37)	2024	Healthy adults	260	7-8 months	A ketogenic diet was positively associated for mental health.
Sangsefidi et al.	(38)	2021	Healthy adults	7165	-	A CBD was not associated with mental disorders such as anxiety and depression. It was associated with a lower probability of depression in women.
Tabesh et al.	(39)	2023	Adults	5405	2 years	The insulinemic potential of the diet was not associated with anxiety.

Table 2. Studies on the use of a CBD in GAD (from 41 to 50).

Third and finally, there are 10 studies investigating DM as a possible treatment or adjuvant for GAD represented in Table 3.3. (41-50). DM is presented with greater scientific support in general terms, despite this, the evidence on its use as a nutritional intervention in GAD is not clear.

According to 8 studies, MD could be an effective strategy as a treatment or adjuvant for GAD (41-45). The research of Flor-Alemany et al (41), Alshahwan et al (42), Mikkawi et al (43), Godos et al (44) and Jasmin et al (45) are cross-sectional studies that do not establish the specific causes of the results. Likewise, the publications of Flor-Alemany et al (41), Alshahwan et al (42) and Mikkawi et al (43) are to a specific population such as pregnant women in the former and students in the latter two. Still, they establish DM as a dietary intervention that reduces anxiety symptoms in pregnant women and college students. Research such as that of Godos et al (44) and Jasmin et al (45) in addition to relating DM with an improvement in GAD, relate people who follow a Mediterranean dietary pattern with a better lifestyle.

On the other hand, the studies of Casas et al (46) martínez-Rodríguez et al (47) and Foscolou et al (48) are clinical trials that establish DM as a nutritional intervention for GAD. The study by Casas et al (46) is limited to pregnant women and therefore cannot be extrapolated to a larger population. It should be noted that this is a study with a large sample and, in addition, it has a control group with which to compare the results. The other trial by Martínez-Rodríguez et al (47) uses a rather low and, like the previous one, non-representative sample, since it is carried out on women with fibromyalgia. Likewise, this study includes 60 mg of tryptophan and magnesium derived from the consumption of nuts at breakfast and dinner in addition to following the Mediterranean dietary pattern, so the beneficial effect of nuts on GAD is contemplated. Despite the number and type of sample, the study has a correct follow-up of the diet and control group. Similar to the previous ones, the research of Foscolou et al (48) was conducted in adolescent women with PCOS, so it does not represent the general population with GAD. However, anxiety is a common symptom in PCOS and, moreover, establishes the importance of a correct support system to increase adherence to DM.

In contrast, two clinical trials do not recognize the relationship between DM and improvement of GAD. Esgunoglu et al (49) states in their clinical trial that their research conducted established a short period of time (5 days) that does not reflect the possible benefits of DM on anxiety. In turn, Radkhah et al (50) does analyze this dietary pattern for a longer period of time (12 weeks) but he himself states that they did not have sufficient follow-up of the diet and establishes MD as a possible dietary intervention to achieve mental well-being, since after adjusting for factors that could have influenced the outcome, the group that followed the Mediterranean dietary pattern obtained better results. It is worth noting that in the study by Radkhah et al (50) there was a control group that had a normal healthy diet, so the possible beneficial results in DM anxiety that the author found after the changes are favorable toward this intervention since the study itself was correctly approached.

A well-planned MD provides omega-3 fatty acids, fiber, magnesium, antioxidants and polyphenols, compounds that are essential for the correct functioning of the nervous system and, likewise, beneficial when considering a dietary intervention as a treatment and/or adjuvant for GAD (16,18,21,51). In addition to all this, there are no adverse effects in people who follow the diet, both in GAD and in general, and well-designed clinical trials that support its use, so that MD could be a nutritional intervention to follow in people suffering from GAD.

Table 3. Studies on the use of a DM in GAD (from 41 to 50).

Author	Reference	Year	Population	Sample	Duration of follow-up	Results
Flor-Alemany et al.	(41)	2022	Pregnant women	152	23 weeks	They associated greater adherence to MD with less anxiety during pregnancy.
Alshahwan et al.	(42)	2023	University students	1.134	-	Adherence to MD was associated with lower severity of anxiety/depression.
EI Mikkawi et al.	(43)	2024	University students	200	-	Greater adherence to MD was associated with lower levels of anxiety and/or depression.
Godos et al.	(44)	2023	Healthy adults	2044	-	Better mental and cognitive health in adults with greater adherence to MD.
Jasmin et al.	(45)	2023	Adults	100	-	Greater adherence to DM was associated with lower anxiety scores.
Casas et al.	(46)	2023	Pregnant women at high risk of suffering from anxiety and stress	1221	17-20 weeks	Identifies MD as an effective strategy to decrease anxiety and stress during pregnancy.
Martínez-Rodríguez et al.	(47)	2020	Women with fibromyalgia	22	16 weeks	A MD enriched with tryptophan and magnesium improves anxiety symptoms in women with fibromyalgia.
Fosculou et al	(48)	2024	Adolescent women with PCOS	40	3 months	A clinical decision support system improves adherence to MD. This increased adherence improves disease and anxiety levels.
Esgunoglu et al.	(49)	2024	Adults diagnosed with anxiety and/or mild depression	25	5 days	No association was found between MD and improvement of anxiety and/or depression symptomatology.
Radkh	(50)	2023	Adults with	60	12 weeks	No association was found

ah et al.			stress, anxiety and/or depression			between MD and improvement of anxiety and/or depression symptomatology. After some readjustments, he did identify the positive effects of MD.

In line with the above and considering the nutritional interventions that could contribute to the improvement of GAD, three micronutrients have been studied as possible components to take into account in the management of anxiety: omega-3, fiber and magnesium.

According to Al Sinani et al (12)the suffering of mental illnesses such as depression and/or anxiety is related to low omega-3 intake in pregnant women, so they recommend foods rich in this healthy fat such as oily fish or seafood or its supplementation to reduce the suffering of anxiety during pregnancy. Others, such as Wang et al (15) relate the optimal intake of omega-3 fatty acids with a decrease in GAD symptomatology. This essential fatty acid, in addition to its anti-inflammatory power, its protective effect at the cardiovascular level and its improvement in cognitive capacity, is a nutrient to be taken into account when recommending a dietary intervention to treat GAD. All three diets, VD, DBC and MD, well planned, reach adequate daily omega-3 levels.

A micronutrient capable of improving the composition of the microbiota, which is very influential in mental health due to the connections it has with the brain, is fiber (18). Authors such as Dalile et al (16) and Chen et al (18) recognize in their randomized triple-blind and double-blind clinical trials, respectively, the positive impact of this micronutrient on the intestinal bacterial population and, thus, on anxiety-related behaviors. Both VD and MD are fiber-rich interventions due to their high content of fruits, vegetables, whole grains, legumes and seeds. However, dietary interventions such as CBD restrict the amount of carbohydrates and, consequently, fiber, thus falling short of the recommended daily fiber intake.

Magnesium, on the other hand, acts as a modulator of the central nervous system, being an agonist of the GABAA receptor and an inhibitor of the NMDA receptor (21). Several studies have investigated its relationship with anxiety and whether its supplementation and/or optimal intake could improve GAD. Oddoux et al (19) and Noé et al (21) found in their randomized double-blind clinical trials an improvement of GAD symptomatology through magnesium supplementation with vitamin B6. Saba et al (20) analyzed in a randomized clinical trial magnesium supplementation in post-surgical patients, those who supplemented with the mineral reduced their anxiety. Although the studies presented are of high quality, we cannot affirm its supplementation as a treatment for GAD because the former are accompanied by vitamin B_6 and are not sufficient to establish magnesium as a treatment for the disease. Even so, it is advisable to achieve optimal magnesium intake through the diet because of its possible beneficial effects and the probable relationship of hypomagnesemia with the disease (19). Through properly planned VD and MD, magnesium requirements can be met thanks to its content in green leafy vegetables, legumes, nuts, seeds and whole grains. However, the CBD usually significantly limits some of these food groups because of their low HC content.

A relevant aspect in the interpretation of the results is the level of adherence to the respective dietary interventions. The lack of follow-up, especially in observational

studies, makes it very difficult to establish causal relationships in the results. Also, prolonged adherence to a dietary pattern such as CBD or VD is complicated due to its restrictive nature, whereas DM tends to have more long-term sustainability because it does not exclude any foods and the population recognizes its health benefits (52,53) (52,53).

Despite current limitations, MD is presented as the most practical and effective adjuvant option, thanks to its ample scientific evidence, the inexistence of studies that contraindicate it in GAD, its degree of adherence and its benefits in general health, including mental wellbeing. In addition, it contains the nutrients studied, namely fiber, omega-3 and magnesium, which exert a possible positive effect on overall mental health. Although there are not yet enough specific studies available on the effect of these nutrients on GAD, their benefits on general health and their impact on the mechanisms of the gut-brain axis are known.

In contrast, VD and CBD cannot currently be considered as nutritional treatment or adjuvant strategies. The VD lacks quality scientific literature, also showing a similar proportion of studies in favor and against its use as a dietary intervention in GAD. On the other hand, although there are clinical trials that recognize the positive effects of this dietary pattern, CBD has limitations in terms of adherence, numerous adverse effects if maintained over the long term, and difficulties in achieving the optimal requirements of nutrients of great importance in GAD, such as fiber and magnesium.

Likewise, it will be essential to investigate and determine the role of fiber, omega-3 and magnesium in GAD since the current evidence is still limited. These nutrients are involved in key physiological mechanisms such as the regulation of inflammation, neurotransmitter balance and gut microbiota health, all of which are implicated in mental health. However, the exact amount needed to exert a therapeutic effect is not yet established. Therefore, it is important to establish whether an adequate intake of these nutrients through diet is sufficient to achieve benefits in GAD and mental health in general or whether specific supplementation would be necessary.

In conclusion, MD could represent the most appropriate nutritional strategy as an adjuvant in the management of GAD due to the existence of research supporting it, its benefits in terms of general health and mental well-being, the high degree of adherence and the absence of known risks. Even so, future controlled clinical trials, with larger samples, rigorous nutritional follow-up and direct comparisons between the three diets, are required to establish more solid conclusions and determine whether a nutritional intervention could displace or reduce pharmacological treatment.

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Nutritional strategies for the mitigation of chemotherapy side effects in women with breast cancer

Estrategias nutricionales para la mitigación de efectos secundarios de la quimioterapia en mujeres con cáncer de mama

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ABSTRACT

The objective of this study was to evaluate the impact of nutritional interventions on reducing chemotherapy-induced side effects in women with breast cancer (BC). To this end, a literature review was conducted in scientific databases, compiling 13 articles published between 2020 and 2025 that addressed the use of diets and supplements in patients with BC undergoing chemotherapy. Official sources and websites specializing in oncology nutrition were also consulted to supplement the information. Mediterranean, ketogenic, plant-based, and intermittent fasting-mimicking diets showed mild to moderate benefits. These improvements were primarily observed in quality of life and in the reduction of common symptoms, such as fatigue, nausea, and gastrointestinal disorders. Furthermore, supplements such as probiotics, synbiotics, and melatonin showed positive effects on some specific symptoms, promoting the overall well-being of patients. Although the results obtained are promising, the studies agree that more scientific evidence is still needed to establish solid clinical recommendations. In this context, nutritional intervention could be considered a useful complementary strategy to mitigate the adverse effects of chemotherapy in women with breast cancer.

Palabras clave:
cáncer de mama; quimioterapia; intervención nutricional; efectos secundarios

RESUMEN

El objetivo de este trabajo fue evaluar el impacto de intervenciones nutricionales en la reducción de efectos secundarios provocados por la quimioterapia en mujeres con cáncer de mama (CM). Para ello, se realizó una revisión bibliográfica en bases de datos científicas, recopilando 13 artículos publicados entre 2020 y 2025 que abordaron el uso de dietas y suplementos en pacientes con CM bajo tratamiento quimioterápico. También se consultaron fuentes oficiales y sitios especializados en nutrición oncológica para complementar la información. Las dietas

mediterránea, cetogénica, basada en plantas y aquellas que simulan el ayuno intermitente mostraron beneficios leves a moderados. Estas mejoras se observaron principalmente en la calidad de vida y en la reducción de síntomas comunes, como la fatiga, las náuseas y los trastornos gastrointestinales. Por otro lado, suplementos como los probióticos, los simbióticos y la melatonina evidenciaron efectos positivos sobre algunos síntomas específicos, favoreciendo el bienestar general de las pacientes. Aunque los resultados obtenidos son prometedores, los estudios coinciden en que aún es necesaria una mayor cantidad de evidencia científica para establecer recomendaciones clínicas sólidas. En este contexto, la intervención nutricional podría considerarse una estrategia complementaria útil para mitigar los efectos adversos de la quimioterapia en mujeres con cáncer de mama.

Introduction

Cancer is one of the most significant public health problems and one of the leading causes of mortality on a global scale. Within this panorama, breast cancer (BC) is the malignant neoplasm with the highest incidence in the female population (1). Not only does it have the highest prevalence among women, but it is also the second most frequent cause of cancer death in this demographic group, second only to lung cancer in terms of lethality (2-5) (2-5). The figures reported by the World Health Organization (WHO) are alarming and underscore the magnitude of the problem: approximately 2.3 million new cases were diagnosed worldwide in 2020 and, by 2022, 670,000 deaths resulting from this disease were recorded. It is noteworthy that its incidence shows a continuous upward trend, a phenomenon particularly accentuated in developing countries, which is attributed to a complex interaction of factors such as the progressive aging of the population, the increasing exposure to certain environmental factors and the widespread adoption of lifestyles considered unhealthy (6).

From a histopathologic perspective, MC commonly originates in the epithelial cells lining the mammary ducts or lobules. In its early stages, the disease may be asymptomatic, making early detection difficult. However, as it progresses to more advanced stages, it usually manifests a number of obvious clinical signs, such as the appearance of palpable masses in the breast or axilla, visible skin alterations such as dimpling or redness, or the presence of abnormal secretions through the nipple (6,7). The diagnostic process is a fundamental pillar for the correct approach to the pathology and is based on a multimodal approach that includes a thorough physical examination by a professional, the use of high-resolution imaging techniques such as mammography, ultrasound or magnetic resonance imaging, and is confirmed definitively by histological analysis of a tissue sample (biopsy) (7-9).

Regarding its etiology, MC is widely recognized as a disease of multifactorial nature (10). Its development is the result of an intricate interaction between a genetic predisposition, in which mutations in high penetrance genes such as BRCA1 and BRCA2 stand out (11) and a series of hormonal, environmental factors and those directly related to the individual's lifestyle (12) For a better understanding and clinical management, these risk factors are usually classified into two large groups: on the one hand, the modifiable ones, which include habits that can be intervened upon such as diet, tobacco and alcohol consumption, or the management of body weight to avoid obesity (3,5,12)on the other hand, the non-modifiable ones, which are inherent to the individual, such as advanced age, female sex, and family history of the disease (2,13).

The therapeutic approach to MCC is intrinsically multidisciplinary and highly personalized, since the strategy to be followed is defined according to the molecular subtype of the tumor, its degree of progression at the time of diagnosis and other individual biological features (14-16). The therapeutic arsenal available is broad and includes procedures such as surgery, radiotherapy, chemotherapy, hormonal therapies and targeted therapies, which specifically target certain vulnerabilities of cancer cells (11,17,18) (11,17,18) Within this spectrum, surgery is established as the fundamental first line of treatment for newly diagnosed patients, who may opt for a total mastectomy or for breast-conserving surgery that preserves part of the breast (18). In addition, and often as an adjuvant therapy to surgery, chemotherapy, a systemic treatment consisting of the administration of powerful drugs, either orally or intravenously, can be used to destroy cancer cells, preventing their ability to grow and divide (3). Despite its proven efficacy in improving survival rates, chemotherapy is not without a considerable burden

of toxicity, being associated with a wide range of adverse effects that significantly impair patients' quality of life (QoL), including debilitating fatigue, nausea, vomiting, oral mucositis, neutropenia (decrease in white blood cells), profound metabolic changes, and various psychological disorders such as anxiety or depression (19-25).

Faced with this complex scenario, nutritional intervention emerges as a complementary strategy of great interest and potential. In recent years, different dietary strategies have been rigorously studied for their ability to mitigate chemotherapy-derived side effects in women diagnosed with MC (26-28). Among the most prominent is the Mediterranean diet (MD), a dietary pattern characterized by a high consumption of fruits, vegetables, legumes, whole grains, extra virgin olive oil and fish (29,30). Potent anti-inflammatory and antioxidant properties are attributed to this dietary model, which could contribute to reducing the severity of fatigue and improving the overall perception of QoL during treatment (31-33). In fact, recent studies in this field suggest that its follow-up may provide mild to moderate benefits, including a marked reduction in serum lipids and an improvement in several metabolic parameters (34) (34).

In parallel, another promising line of research focuses on diets that simulate the metabolic effects of fasting, especially the *Fasting Mimicking Diet* (FMD). This dietary protocol induces physiological responses similar to those of prolonged fasting without generating drastic weight loss or significant malnutrition (20,35,36). Accumulated scientific evidence suggests that its application may be effective in reducing gastrointestinal and hematologic toxicity associated with chemotherapy, as well as in improving certain immunological markers and, consequently, increasing overall tolerance to cancer treatment (37). Other variants within this approach, such as *Short Term Fasting* (STF) and *Time Restricted Eating* (TRE), have also demonstrated beneficial results in similar contexts (23,38,39) (23,38,39).

The ketogenic diet, defined by its high content of healthy fats and severe carbohydrate restriction, represents another strategy of interest. Its main mechanism of action is the induction of a metabolic state known as ketosis, which limits the availability of glucose as a major energy source for tumor cells, which often depend on it for proliferation (37). It has been observed in several studies that the implementation of this diet can improve QoL, decrease the sensation of fatigue and optimize the inflammatory and metabolic profile in some oncology patients (40) (40). In parallel, a predominantly *plant-based* nutritional approach, which is characterized by being high in plant-based proteins and rich in phytochemicals and bioactive compounds, has demonstrated in clinical studies its ability to significantly reduce fatigue and improve body composition, aspects of great relevance during the strenuous process of oncological treatment (41).

Finally, the field of nutritional supplementation has also been studied as a support in this context. It has been observed that the administration of synbiotics, which combine prebiotics and probiotics, can have a beneficial effect on the health of the gut microbiota, helping to reduce common digestive symptoms such as nausea and loss of appetite (42). Melatonin, a hormone known for its role in the regulation of the sleep-wake cycle, could modulate the perception of neuropathic pain altered by chemotherapy, although it has not shown significant effects on insomnia in these patients (43) (43). Likewise, administration of other specific probiotics, such as *Bacteroides fragilis* 839, has also shown positive results in protecting against myelosuppression and other treatment-induced digestive toxicities (44).

By way of conclusion, while it is true that the scientific evidence in this area is still in a phase of development and consolidation, the above findings as a whole strongly suggest that nutritional treatment has considerable potential to mitigate the side effects of chemotherapy and thus substantially improve the QoL of patients with MC. This reality underscores the imperative need to continue to drive research and the development of clinical nutritional guidelines that are personalized and based on the strongest available evidence.

Method

The purpose of this literature review is to carry out a detailed and critical analysis of a variety of academic papers, scientific research and specialized articles. The main purpose of this analysis is, based on currently available scientific evidence, to understand and demonstrate the relevance of having an adequate and personalized nutritional plan for patients diagnosed with MC undergoing chemotherapy treatment. This review also seeks to identify and establish the most effective and appropriate nutritional strategies that can contribute significantly to improving QoL in these patients. It also aims to evaluate how these interventions can help reduce or mitigate the side effects caused by chemotherapy, which often have a considerable impact on the general health and physical and emotional well-being of cancer patients.

The process of searching and compiling the scientific articles included in this review began on February 3, 2025 and concluded on April 13, 2025. During this period, an exhaustive, meticulous and systematic exploration of a large number of scientific publications from various recognized academic databases was carried out. To ensure the quality and relevance of the selected information, a series of filters were applied:

- Publication date between 2020 and 2025. However, some studies published prior to that date have been used due to their great relevance.
- Research articles and essays whose sample is human.
- Studies taken from indexed journals with an impact factor ≥ 1.5.

The search methods used in the databases were as follows:

1. **Pubmed:** The following filters were established: 5 years old and “free full text”. These were the keywords used:
   - ➢ **“Breast cancer treatment”:** a total of 5,979 articles were obtained from this search of which 10 were used for this review.
   - ➢ **“Breast cancer chemotherapy side effects”:** a total of 1,806 articles were obtained from this search of which 4 were used for this review.
   - ➢ **“Diet chemotherapy cancer side effects”:** a total of 143 articles were obtained from this search of which 2 were used for this review.
   - ➢ **"Mediterranean diet breast cancer":** a total of 57 articles were obtained from this search, of which 5 were used for this review.
   - ➢ **"Fasting chemotherapy breast cancer":** a total of 28 articles were

obtained from this search, of which 8 were used for this review.

- ➢ **"Keto chemotherapy breast cancer":** a total of 5 articles were obtained from this search of which 2 were used for this review.
- ➢ **"Supplementation breast cancer chemotherapy":** a total of 47 articles were obtained from this search of which 3 were used for this review.

2. **Frontiers:** These were the keywords used in this database to find the articles:
   - ➢ **"Diet chemotherapy cancer side effects":** a total of 36,450 articles were obtained from this search, of which 1 was used for this review.
   - ➢ **"Fasting chemotherapy breast cancer":** a total of 16,104 articles were obtained from this search of which 1 was used for this review.

3. **Google Scholar:** Thanks to this search engine, it was possible to access the full text of numerous articles, which was very useful for the development of the work.
4. **Internet:** In Google, official websites such as WHO, Heart, etc. were accessed in order to explain in detail updated concepts and statistics.

Finally, 44 articles were found for the present work. Of these, 13 studies were selected and analyzed in depth to establish more detailed conclusions on the effect of different nutritional strategies on the adverse effects of chemotherapy for MC.

Results

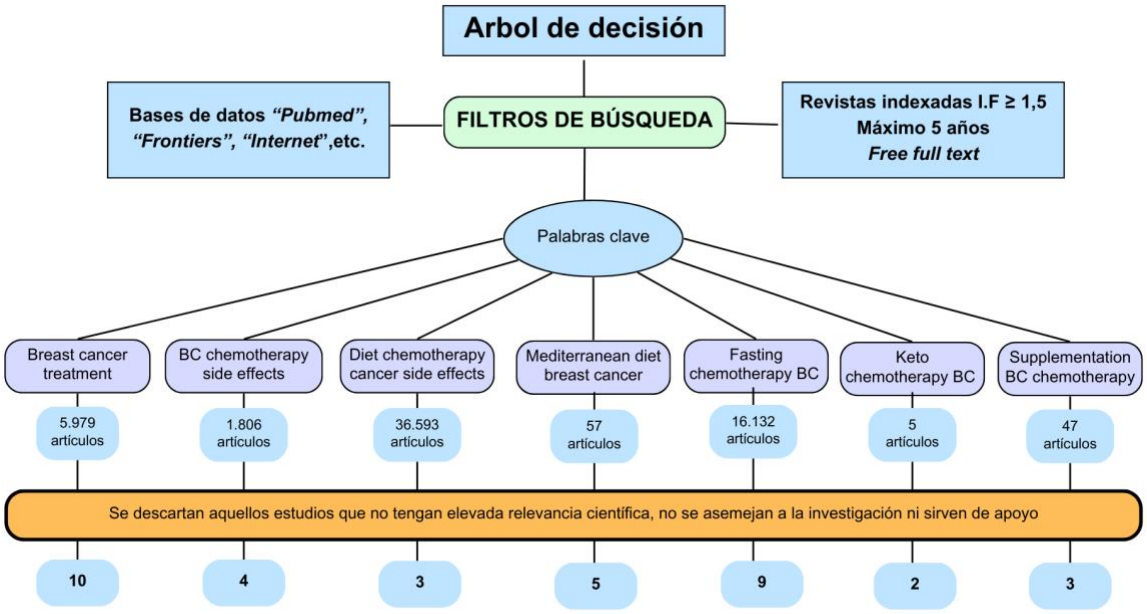

Figure 1. Outline of the bibliographic search. Studies selected and analyzed for this work .

Discussion and Conclusions

Nutritional intervention during chemotherapy treatment is proposed as an effective complementary strategy to improve QoL in women with MC, as well as to reduce the intensity and frequency of side effects derived from pharmacological treatment. Emerging scientific evidence suggests that proper nutrition can have a positive impact on the clinical course and overall well-being of oncology patients.

First, it is relevant to analyze certain dietary patterns that could offer specific benefits against chemotherapy-induced adverse effects. Among them, the Mediterranean Diet (MD), recognized for its healthy properties and balanced nutritional profile, stands out. This diet is based on a high consumption of vegetables, fruits, legumes, olive oil and fish, and has been associated with multiple protective effects against chronic diseases.

Several studies analyzed, summarized in Table 1, suggest that adherence to a DM can generate mild to moderate positive effects in patients with MS receiving chemotherapy (32,33) (32,33). The findings coincide in highlighting the antioxidant and anti-inflammatory character of this diet, attributable to its richness in bioactive compounds present in plant foods and healthy fats. These components seem to contribute to mitigate symptoms such as fatigue, one of the most common side effects of the treatment.

According to Kleckner et al. (32) this dietary pattern favors an adequate intake of macro and micronutrients, which improves energy production and helps to counteract processes related to metabolic dysfunction, oxidative stress and chemotherapy-induced inflammation.

In short, although further scientific support is still needed, the reviewed studies indicate that a well-planned DM, rich in antioxidant and anti-inflammatory foods, can be a useful tool as part of the adjuvant nutritional approach in patients with MC under chemotherapeutic treatment.

Table 1 Studies on the Mediterranean diet in women with CM.

Author	Year	Type of study	Population and sample	Duration	Results
Kleckner et al. (32)	2022	Randomized clinical trial	33 women aged 35-65 years with stage I-III CM scheduled for chemotherapy or with at least 6 weeks of treatment remaining	8 weeks	Patients demonstrated high adherence to DM benefiting from a mild-moderate effect on fatigue reduction between the 4th and 8th week.
Zuniga et al. (33)	2019	Randomized clinical trial	153 overweight or obese women with early stage I-III CM undergoing treatment	6 months	Patients with greater adherence to the anti-inflammatory dietary pattern experienced improvements in endothelial function and reductions in serum cholesterol and triglycerides as well as less mental and physical fatigue.

Second, several studies have been reviewed focusing on the effect of fasting-like diets on the side effects caused by chemotherapy in breast cancer (BC) patients. The most relevant results of this review are summarized in Table 2. This type of dietary intervention has attracted the interest of the scientific community for its potential to improve tolerance to treatment and reduce the toxicity associated with antineoplastic drugs.

As mentioned above, fasting or caloric restriction seems to activate certain physiological mechanisms that not only increase the sensitivity of tumor cells to treatments, but also protect healthy cells, reducing the adverse effects generated by chemotherapy. This protective effect has been explored in different clinical studies, especially through the *Fasting-Mimicking Diet* (FMD) model, a diet that mimics the effects of fasting by severe calorie and protein restriction during a controlled period.

Of the six studies analyzed, four of them (35,36,36,36,38) were (35,36,36,38) highlight the efficacy of FMD as an adjuvant nutritional intervention. This diet, applied during the three days prior to and the day of chemotherapy administration, showed important clinical benefits such as a decrease in gastrointestinal and hematological toxicities, as well as an improvement in metabolic parameters.

In terms of specific results, the studies by Lugtenberg et al. (20) and de Groot et al. (36) reported significant reductions in side effects such as fatigue, nausea, vomiting and insomnia. In parallel, research by Vernieri et al. (35) and Bahrami et al. (38) also observed hematological improvements, with higher levels of erythrocytes and neutrophils in the group following FMD versus the control group.

On the other hand, Bauersfeld et al. proposed an approach closer to traditional fasting, called *Short-Term Fasting* (STF), which involves a food deprivation of approximately 60 hours distributed before and after treatment. This strategy showed improvements in quality of life, a reduction in mental fatigue and a lower intensity of symptoms such as nausea or abdominal pain.

Finally, the study by Christensen et al. (23) explored a different modality: *Time-Restricted Eating* (TRE), with an intake window of 8 to 10 hours per day. The results showed not only improvements in quality of life, but also a significant reduction in visceral fat and an overall improvement in metabolic profile.

It should be noted that all the studies reviewed, regardless of the specific restriction approach, reported positive effects. Patients showed good adherence to these patterns, which reinforces their clinical feasibility. Taken together, the findings suggest that fasting-like diets may represent a promising nutritional intervention for breast cancer patients undergoing chemotherapy, improving both their tolerance to treatment and their quality of life (20,23,35,36,38,39).

Table 2 Studies on fasting-like diets in women with CM.

Author	Year	Type of study	Population and sample	Duration	RESULTS

Lugtenberg et al. (20)	2020	Randomized clinical trial	129 women with HER-2 negative CM stages II-III	4 years	Reduction of side effects (fatigue, nausea/vomiting and insomnia). Patients also perceived improvements in QoL and presented moderate weight loss.
Vernieri et al. (35)	2022	Clinical trial	101 women with MC receiving chemotherapy anti-tumor treatment	1 month	Patients experienced a greater response to treatment and a reduction in tumor size on the Miller and Payne scale, in addition to a significant improvement in QoL. The control group presents greater damage to T lymphocytes due to the toxicity of chemotherapy causing more aggressive effects.
De Groot et al. (36)	2020	Randomized clinical trial	131 women with stage II-III MC	2 years	Mild effect in reducing symptoms secondary to chemotherapy such as fatigue and nausea but do not demonstrate such different results between the two groups in perceived toxicity.

Bahrami et al. (38)	2024	Randomized controlled trial	44 women with HER-2 receptor-negative CM	2 years	Patients suffered less frequent vomiting. In addition, they also had higher erythrocyte and neutrophil counts, while their IGF-1 and hs-CRP levels were decreased. In contrast, the control group suffered a regular number of vomiting episodes and presented neutropenia.
Bauersfeld et al. (39)	2018	Randomized crossover trial	34 women officially diagnosed with MC or ovarian cancer scheduled for chemotherapy treatment	18 months	Short-term fasting is safe and appears to significantly improve the QoL of patients as well as improve symptoms such as fatigue.
Christensen et al. (23)	2020	Randomized clinical trial	130 women scheduled to receive chemotherapy who have been diagnosed with early stage I-III of MBC	2 years	Patients show a reduction in visceral fat accumulation and improvements in metabolic markers as well as a slight attenuation of common chemotherapy-derived symptoms.

Third, the results of recent studies examining the impact of two specific dietary approaches on the side effects of chemotherapy in patients with MC have been reviewed: the ketogenic diet and a high-protein plant-based diet. The key findings of these investigations are summarized in Table 3.

First, the ketogenic diet, characterized by high fat and low carbohydrate intake, has been

studied for its ability to induce a change in energy metabolism. This alteration may be beneficial in the oncological context, by hindering the growth of tumor cells that depend mainly on glucose as an energy source. In this regard, the study by Khodabakhshi et al. (40) suggests that this diet, used as an adjuvant during chemotherapeutic treatment, can contribute to an overall improvement in the clinical condition of patients. In their research, a significant decrease in both body mass index (BMI) and total body weight was observed in the group following the ketogenic diet. In addition, patients reported better QoL and a lower incidence of mild side effects, such as nausea and vomiting, compared to the control group. However, the authors clarify that the intervention showed no impact on more severe or persistent treatment-associated symptoms.

On the other hand, the study by Sathiaraj et al. (41) focused on a plant-based diet, rich in fruits and vegetables, combined with a high protein content. This diet stands out for its antioxidant and anti-inflammatory profile, which makes it potentially useful for mitigating chemotherapy-induced stress. In this case, the results showed a marked reduction in fatigue, which the authors attribute to the protective action of the antioxidant compounds. A significant decrease in BMI and body fat was also evidenced in the patients.

Overall, although the observed effects on QoL were modest, both nutritional approaches showed positive results and can be considered safe and potentially effective strategies as an adjunct to chemotherapeutic treatment in patients with MC.

Table 3 Studies on ketogenic diet and high-protein plant-based diet in women with CM.

Author	Year	Type of study	Population and sample	Duration	RESULTS
Khodabakhshi et al. (40)	**2019**	Randomized clinical trial	60 women with advanced localized metastatic CM scheduled for chemotherapy	3 months	In the intervention group, there was a reduction in blood glucose levels, as well as a reduction in weight and consequent BMI. In addition, they also reported better QoL and less frequent nausea and vomiting.
Sathiaraj et al. (41)	**2023**	Randomized controlled trial	103 women newly diagnosed with MC and scheduled for adjuvant chemotherapy	2 months	Patients who followed the prescribed diet demonstrated a significant

					reduction in mental and physical fatigue, as well as a decrease in BMI and body fat.

Finally, several studies evaluating the effect of nutritional supplementation in mitigating the side effects caused by chemotherapy in patients with MC have been compiled. The most important results of this line of research are summarized in Table 4. Once the different dietary patterns have been analyzed, it is relevant to address the potential role that certain supplements can play as part of complementary nutritional support during cancer treatment.

First, the study by Khazaei et al. (42) focuses on the administration of synbiotics, a combination of prebiotics and probiotics, for a period of eight weeks. The results obtained show a significant improvement in intestinal symptomatology, specifically in the regulation of intestinal transit and the reduction of diarrhea episodes associated with intestinal dysbiosis caused by chemotherapy drugs. Likewise, patients who received this supplement also reported a lower incidence of nausea and vomiting, as well as a notable decrease in the perception of fatigue, one of the most common and limiting symptoms during treatment.

Continuing with the intestinal axis, the study by Zeng et al. (44) specifically investigated the effects of the probiotic *Bacteroides fragilis* 839. This microorganism showed a positive effect in reducing myelosuppression, one of the most frequent hematological complications in patients under chemotherapy. Although the results on the improvement of gastrointestinal toxicities were less conclusive, benefits similar to those described with the use of symbiotics were observed. (42).

On the other hand, the study by Palmer et al. (43) addressed the effects of oral melatonin as an adjunct to cancer treatment. The administration of 20 mg daily during the chemotherapy cycle showed promising results in the regulation of the Descending Pain Inhibitory System (DPMS), helping to restore the function of this system affected by the drugs. In addition, improvements in dermal pain tolerance (DTT) and thermal pain threshold (TPU) were observed. However, despite the known relationship of melatonin with sleep quality, no significant improvements in insomnia were observed in this study.

Taken together, these findings support the use of certain supplements as support in the management of specific chemotherapy-derived symptoms, highlighting their potential usefulness as part of a comprehensive nutritional intervention in patients with CM.

Table 4 Studies on supplementation in women with CM

Author	Year	Type of study	Population and sample	Duration	Results
Khazaei et al. (42)	2023	Randomized double-blind clinical trial	67 women diagnosed with MC admitted as inpatients for chemotherapy	8 weeks	Patients experienced a significant reduction in fatigue and less frequent intestinal problems (diarrhea and constipation). Slight improvements were also recorded in the reduction of nausea and vomiting, in addition to minimizing the risk of developing anorexia.
Zeng et al. (44)	2024	Randomized trial	40 women in early stage of MC	2 months	A reduction in myelosuppression has been recorded, in addition to a lower decrease in white blood cells and neutrophils. Patients also experienced fewer events of nausea and diarrhea.
Palmer et al. (43)	2019	Randomized double-blind clinical trial	36 women aged 18-75 years scheduled for their first cycle of adjuvant CM chemotherapy	2 weeks	The study indicated improvements in DPMS functionality as well as pain thresholds. No conclusive results on sleep improvement were obtained.

After detailed analysis of the available scientific literature, it can be affirmed that an appropriate nutritional intervention has the potential to significantly improve tolerance to chemotherapy in patients with MC. Although the compiled findings are promising, further research is still needed to establish concrete clinical recommendations, as well as to determine precisely what would be the most effective and safe dietary approach in this context.

Even so, the studies reviewed allow us to draw preliminary conclusions that could serve as a basis for the development of future general guidelines. First, it has been shown

that following a healthy dietary pattern, such as the Mediterranean diet, may offer slight but clinically relevant benefits. This type of diet, characterized by its flexibility, richness in antioxidant compounds and easy adherence, has been shown to be effective in reducing symptoms such as fatigue, as well as representing a sustainable option for patients in the long term.

On the other hand, both the ketogenic diet and a high-protein plant-based diet have also shown positive effects, especially in improving QoL, reducing fatigue and decreasing body mass index and body fat. However, the evidence on these diets is still limited, and their effects need to be corroborated by research of greater scope and methodological rigor.

The dietary pattern that seems to have the strongest scientific basis is undoubtedly that of fasting-like diets. Among these, FMD stands out as one of the most promising options, combining safety, good tolerance and effectiveness in reducing the most common adverse effects of chemotherapy. The results obtained in the studies analyzed position FMD as a potentially effective tool for clinical implementation.

Finally, it is worth mentioning the complementary role of certain supplements such as symbiotics, the probiotic *Bacteroides fragilis* 839 and melatonin. Although the evidence on its use is still scarce, the reported beneficial effects point to its possible usefulness as an additional support to a broader nutritional intervention, especially in the management of specific symptoms such as gastrointestinal disturbances, fatigue or pain threshold dysfunction.

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Obesity and overweight: Ketogenic Diet, Mediterranean Diet or Mindful Eating?

Sobrepeso y obesidad: ¿Dieta congénica, dieta Mediterránea o mindful eating?

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ABSTRACT

Obesity continues to rise and, despite advances in medicine, there is no universally valid nutritional approach for all individuals. The objectives of this study are to compare the effects of the Mediterranean Diet, the Ketogenic Diet, and Mindful Eating in the treatment of overweight and obesity in adults.
Method: A literature review was conducted using scientific evidence generated over the past five years. 23 clinical trial articles published in PubMed (Medline) were selected, analysed, and compared.
Results and Discussion: The studies demonstrate benefits regarding weight, cardiovascular risk, and type 2 diabetes in favor of hypocaloric diets, whether Mediterranean or ketogenic. The benefits of Mindful Eating are related to improvements in eating behavior, without effects on the parameters evaluated in this study. It is concluded that both the hypocaloric Mediterranean Diet and low- and very-low-energy ketogenic diets are useful strategies for treating overweight and obesity in adults. Both dietary patterns lead to weight loss through fat mass reduction and decreased waist circumference, with these changes occurring more rapidly with ketogenic diets. Furthermore, when there is a weight loss of at least 5%, both diets lead to improvements in lipid and glycaemic profiles. Studies show that hypocaloric ketogenic diets do not increase cardiovascular risk; however, very low-calorie ketogenic diets should not be followed for more than two months and should always be supervised by a medical professional..

Palabras clave:
Obesidad, sobrepeso, Mindful Eating, Dieta Cetogénica, Dieta Mediterránea.

RESUMEN

La obesidad continúa en aumento y a pesar de los avances en la medicina, no hay un abordaje nutricional válido para todas las personas. Los objetivos de este trabajo son comparar los efectos de la Dieta Mediterránea, la Dieta Cetogénica y el Mindful Eating en el tratamiento del sobrepeso y la obesidad en adultos. Método: Se realizó una revisión bibliográfica de la evidencia científica generada en los últimos cinco años.

	Se seleccionaron, analizaron y compararon 23 artículos de ensayos clínicos publicados en Pubmed (Medline). Resultados y discusión: Los estudios demuestran beneficios en cuanto al, peso, riesgo cardiovascular y de diabetes tipo 2, a favor de las dietas hipocalóricas ya sea mediterráneas o cetogénicas. Los beneficios del Mindful Eating se relacionan exclusivamente con mejoras en el comportamiento alimentario, sin efectos en los parámetros evaluados. Se concluye que tanto la Dieta Mediterránea hipocalórica como las dietas cetogénicas bajas y muy bajas en energía son estrategias útiles para el tratamiento del sobrepeso y la obesidad en adultos. Ambos patrones alimentarios producen descenso de peso a partir de la masa grasa y disminución de la circunferencia de cintura, siendo estos cambios más veloces con las dietas cetogénicas. Además, cuando se produce un descenso de al menos el 5% del peso, ambas dietas generan mejoras en el perfil lipídico y glucémico. Los estudios demuestran que las dietas cetogénicas hipocalóricas no aumentan el riesgo cardiovascular, sin embargo las que son muy bajas en calorías no deberían realizarse por más de dos meses y sin supervisión médica.

Introduction

Obesity is currently a major health problem throughout the world. According to WHO (1) in 2022, one in eight people were obese, and since 1990, obesity has doubled among adults and quadrupled among adolescents. Children are also a high-risk group for obesity, with increasing prevalence.

Every year, 42 million deaths are caused by non-communicable diseases (NCDs). Two-thirds of these deaths are caused by just four conditions: cancers, coronary heart disease, stroke and diabetes. All of these conditions are closely associated with excess weight (2,3).

Obesity is a chronic, multifactorial disease that originates throughout life due to two mutually reinforcing processes. On the one hand, early effects that occur even before birth, due to parental obesity or during pregnancy; and on the other hand, unhealthy habits such as poor diet and lack of physical activity, influenced by environments that favor the development of obesity. These processes lead to an imbalance between the energy metabolized and the energy used by the body, which favors an accumulation of fat in the body, with consequences for health. This imbalance is caused by multiple factors, such as lack of physical or economic access to fresh food, obesogenic environments, lack of time for cooking, and psychosocial factors (1,3,4). This is why both environmental and behavioral aspects must be addressed when dealing with such a complex chronic pathology (5).

Several therapeutic strategies have been investigated in recent years. Among them are pharmacological ones, such as GLP-1 analogues, and nutritional ones, such as the low glycemic index diet, the ketogenic diet or the Mediterranean diet. However, there is currently no validated and definitive treatment that is effective for all patients and obesity must be approached on an individual and multidisciplinary basis (5).

In this paper, the available scientific evidence will be analyzed to establish a comparison between the effects of the Ketogenic Diet (KD), Mindful Eating (ME) and the Mediterranean Diet (MD) in the treatment of obesity and overweight in adults. On the one hand, changes in weight and waist circumference will be evaluated, and, on the other hand, the reduction in the risk of cardiovascular disease and diabetes will be analyzed by means of plasma lipoprotein and glycemia values. Finally, the possibility and potential benefits of the long-term incorporation of each of the tools will be assessed, with the objective of maintaining or achieving a good nutritional and health status.

Method

This Final Degree Project consists of a bibliographic review of the updated scientific evidence. For its elaboration, articles corresponding to clinical studies have been examined in order to compare the effects of Mindful Eating, the Ketogenic Diet and the Mediterranean Diet in the treatment of obesity and overweight. Only articles with results related to changes in body weight, waist circumference, lipid profile and/or glycemic profile of the participants were included.

For this literature review, a systematic search was carried out in Pubmed (MEDLINE) to compile the relevant studies. In addition, Google Scholar was used to search for information related to each topic, such as clinical practice guidelines, publications of important health organizations and articles more than five years old that were relevant to

the theoretical framework. The search began on February 10, 2025 and ended on April 29, 2025.

The inclusion criteria for the scientific articles were: that they were published between 2019 and 2025, that they were experimental clinical trials, and that they included the results of interest already mentioned. In addition, the study population was observed to be between 18 and 70 years of age, with a BMI between 25 and 45 kg/m2 and without prevalent pathologies (fatty liver or diabetes, for example). The exclusion criteria were: that less than 20 subjects participated, that the subjects had been diagnosed with pathologies and that the studies had a duration of less than 6 weeks. In addition, articles not indexed, not found on the web and those published in journals corresponding to quartiles 3 or 4 of the Scimago Journal and Country Rank were discarded. On the other hand, articles that were not comparable were excluded because they did not present the main characteristics of the intervention in question.

The searches performed in Pubmed, applying the filters of last 5 years and clinical trials, were:

- "Mindful Eating and obesity": 18 articles were obtained from this search, of which 7 were used, as they met the inclusion criteria and did not have the characteristics to be excluded.
- "Mindful Eating and overweight": this search yielded 15 articles of which none were used. The vast majority were included in the previous search.
- "Mediterranean diet and obesity": 179 articles were obtained from this search, of which 7 were used because they met the inclusion criteria and were exempt from the exclusion criteria.
- "Mediterranean diet and overweight": 132 results were obtained, of which 1 study was used. Most of them also corresponded to the previous search.
- "Ketogenic Diet and obesity": this search yielded 48 articles of which 8 were used in this work.
- "Ketogenic diet and overweight": 40 results were obtained and none of the articles were used. Most of them were included in the previous search.
- Google Scholar: This search engine was used to access the full text of some of the selected articles, as well as to search for official web pages, guides and relevant articles used for the theoretical framework and not included in the discussion.

Finally, a total of 23 articles were obtained for the completion of this final degree project.

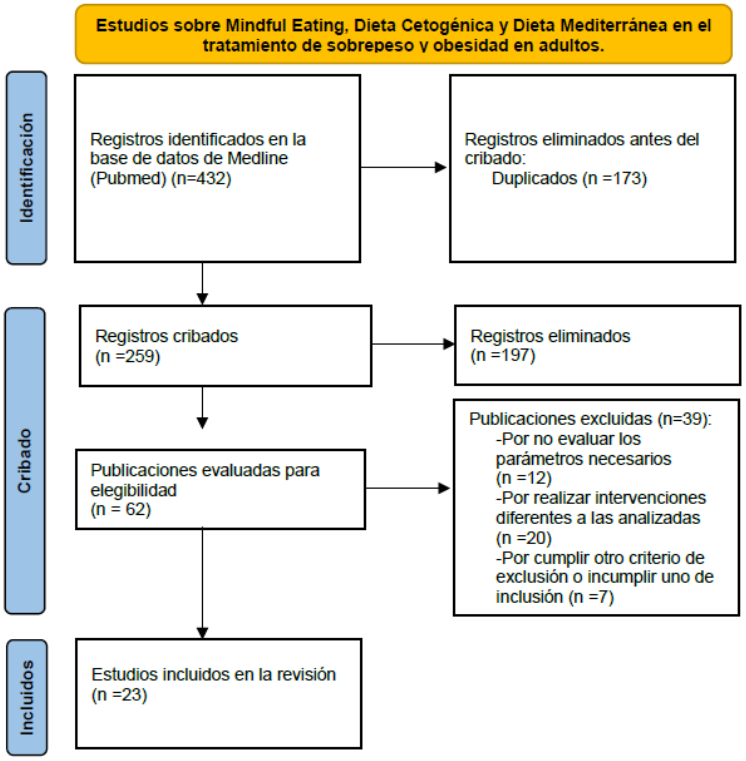

Figure 1. Item selection flowchart.

Discussion and conclusions

The studies on Mindful Eating in the treatment of overweight and obesity are summarized in Table 1.

The vast majority of the articles (6–10) do not show positive results for the parameters studied in this literature review, i.e., EM did not produce changes at the physical or biochemical level in the participants. It should be noted that the Mindful Eating or MB-EAT tool produced improvements in different psychological and eating behavioral aspects. In the study by Salvo et al. (8) the EM intervention achieved a slight decrease in weight (not significant) but with an increase in fat mass and a decrease in lean mass. This effect may be explained by an observed reduction in physical activity levels for the group that received the EM intervention. However, 60% of the program participants reported not performing the mindful eating practices for 7 days or more, which may have affected the results of the study. The study by Moreira et al. (7) also had multiple limitations, caused by the COVID-19 pandemic. This caused many volunteers to drop out of the study and only 45 subjects completed the study. In addition, anthropometric measurements were performed by each individual and EM practices were conducted virtually, which may produce biases. On the other hand, in the trial by Morillo-Sartó et al. (6) the number of participants was low and the subjects knew whether they had been assigned to the experimental or control group, which could affect their expectations and create a bias.

However, Zergani et al. (11) Zergani and Henninger et al. (12) found, in women, improvements in favor of Mindful Eating for body weight. The first showed significant

differences in the two interventions that included ME, compared to the control group, in relation to weight loss (BMI), level of physical activity and self-efficacy. However, the number of subjects who completed the study was small and may not be generalizable to the general population. The limitations reported in the article are very brief, which may indicate a lack of analysis. In addition, changes in weight were greater in the group whose intervention consisted of ME along with implementation intention therapy. In the second study, conducted by Henninger et al. (12)in 8 weeks, the practice of ME generated improvements in fat percentage, waist circumference and weight. They also observed improvements in eating behavior and quality of life. However, the changes were not significant and were only found after complete analysis of the cases, so they should be interpreted carefully as an estimate of efficacy when adherence to treatment is high. On the other hand, the small number of subjects who completed the study and the high dropout rate, unevenly distributed among the groups, are limitations that may have caused a bias and detract from the validity of the result. In addition, adherence to EM treatment was low, indicating that women's acceptance of the intervention was limited. This low adherence may also have minimized the effects of the intervention. Further studies are needed to confirm the effects of EM on weight in the female population.

In summary, the evidence indicates that ME interventions applied in overweight or obese adults do not result in significant benefits in weight and central adiposity. Nor do they appear to generate improvements in health as reflected in the blood lipoprotein profile or glycemic profile. It appears that the points in favor of EM are related solely to eating behavior in both female and male populations. However, the quality of the studies is generally low and the results should be interpreted carefully.

Table 1 Studies on Mindful Eating in the treatment of overweight and obesity.

REFERENCE	TYPE OF STUDY	SUBJECTS	DURATION OF OPERATION	OBJECTIVES	RESULTS
Moreira et al. 2024 (7)	Randomized clinical trial.	45 overweight and obese subjects over 18 years of age.	4 months	To evaluate the effect of EM compared to conventional nutritional treatment on eating behavior, physical activity and weight.	Restrictive eating behavior decreased significantly in the ME group and increased in treatment as usual. Weight decreased only in the usual treatment group.
Morillo Sartó et al. 2023 (6)	Randomized clinical trial with control group.	76 overweight or obese subjects, aged 45 to 75 years.	7 weeks	To evaluate the effect of the ME + conventional treatment program on eating behavior, weight, waist circumference and biochemical parameters, compared to conventional treatment without ME.	A significant reduction in short- and long-term "emotional eating" was seen in the ME group. There was no decrease in weight or waist circumference in any of the groups in the short term, but there were significant differences between the groups in the long term.
Pepe et al. 2023 (9)	Randomized clinical trial.	70 women with obesity. From 18 to 50 years old.	6 months	To compare the effects of ME+hypocaloric diet with those of ME and diet individually, on weight and eating behavior.	There were no differences in the decrease in weight and waist circumference between the groups. The ME group was favored in terms of improvements in eating behavior (uncontrolled eating and emotional eating). The groups that included ME decreased in anxiety and depression.
Salvo et al. 2022 (8)	Randomized clinical trial.	133 low-income, overweight or obese women. From 18 to 60 years old.	10 weeks	To compare the effects of ME + conventional treatment, Mindfulness + conventional treatment and the control group (conventional treatment) on eating behavior, biochemical, anthropometric parameters and body composition.	The ME group had greater improvements in eating behavior (binge eating) followed by the Mindfulness group. Weight decreased in all three groups, favoring the ME group, but not significantly. However, in the ME group, fat mass increased and fat-free mass decreased. There were no significant changes in biochemical parameters.

Zergani et al. 2024 (11)	Randomized, controlled clinical trial.	56 women over 20 years of age, overweight or obese.	3 months	To compare the effects of ME, ME + implementation intention therapy and control group on weight, self-efficacy and physical activity level.	Both experimental groups had significant improvements in physical activity level, weight and self-efficacy. Weight and physical discomfort decreased to a greater extent in the ME + implementation intention group than in the ME group.
Radin et al. 2023 (10)	Randomized, controlled clinical trial.	144 overweight or obese subjects over 18 years of age.	8 weeks	To compare the effects of 4 interventions: Mindfulness meditations, ME+healthy eating, meditations+ME+healthy eating and control group (no intervention), on stress, cravings, and adiposity.	Perceived stress decreased in the ME+meditation group and not in the ME group. No treatment had any effect on weight or BMI.
Henninger et al. 2023 (12)	Randomized, controlled clinical trial.	39 overweight and obese women, aged 18 to 65 years.	8 weeks	To compare the effects of ME and one type of Yoga *("YogaDance"),* jointly and individually, on body fat, weight, waist circumference, quality of life and eating behavior.	In the ME and ME+*"YogaDance"* groups, fat percentage and waist circumference decreased, while quality of life and eating behavior improved, compared to the control group. However, the differences were not significant.

ME: Mindful Eating.

Regarding the use of the Mediterranean Diet (MD) to treat obesity and overweight, Table 2 summarizes the studies analyzed in this work.

Regarding DM without caloric restriction, Meslier et al. (13) and Uffelman et al. (14) observed a significant decrease in total and HDL cholesterol, as a function of adherence to the diet, without changes in glycemia. In Meslier's study, LDL cholesterol was also reduced. HDL lowering is not desirable at the cardiovascular level, but both interventions lasted only 8 weeks, possibly insufficient for profound changes.

Jospe et al. (15)with isocaloric DM, found reductions in weight, body fat and waist circumference at 6 and 12 months, associated with high adherence (2.2% and 3% decrease in body weight, respectively). Of note was the significant decrease in HbA1c, linked to a higher fiber intake, although there were no changes in plasma lipids. This could be explained by the lack of exhaustive control over intake, the higher consumption of processed meats and the absence of randomization, which introduces biases but also provides realism. The high completion rate (171 people) reinforces the validity of the findings.

Picklo et al. (16)evaluated an isocaloric DM with and without eggs. The diet without eggs improved total cholesterol, LDL and triglycerides; the one that included eggs showed no benefit. This crossover study (4 weeks per phase) showed great individual variability with respect to dietary cholesterol, a relevant aspect when evaluating results. However, the small sample size limits the validity of the study.

Barnard et al. (17)compared, in a crossover clinical trial, normocaloric DM with a low-fat vegan diet, with no findings in favor of DM. However, the records showed an unplanned caloric deficit of 500 kcal during the vegan diet, probably because of its greater restrictiveness. This could have generated a compensatory increase in intake during the DM period, diminishing its effect. In addition, the weight gain observed during the washout period suggests subsequent offsets. It is possible that biases have been introduced, intentional or not, favoring the vegan diet.

Regarding DM with caloric restriction, Rosi et al. (18) found that both the diet with high pasta intake (AP) and the diet excluding pasta (BP) reduced blood glucose, insulin and HOMA index in 6 months. The AP diet reduced total cholesterol and increased HDL, while the BP reduced triglycerides. Although there were statistical differences, both improved the lipid profile in a similar way. Weight loss was significant in both groups (7% BP and 10% AP), coming from body fat without muscle loss. Allocation by preference, and not randomization, could generate biases but also greater adherence, suggesting that including preferred foods in hypocaloric diets could improve outcomes.

Dellis et al. (19)compared two hypocaloric DM, one excluding carbohydrates at breakfast. Both reduced weight, body fat and waist circumference, with better results in the carbohydrate-free diet in the morning (9% vs. 6% in 2 months), possibly due to greater satiety of protein and fatty foods. The loss was greater in men. Glycemia, insulin and HOMA index decreased in both, as did triglycerides and HDL. LDL only decreased in the diet that included carbohydrates in the morning, perhaps due to the higher consumption of saturated fats in the other group.

The study by Luo et al. (20)the study, with a large number of participants, showed that DM significantly improved glycemic control, total cholesterol and LDL, with weight decreases of 6.5% at 3 months and 7.2% at 6 months. As with many diets, the initial decline was greater and then plateaued, suggesting possible sustained loss and long-term benefits.

In summary, DM without caloric restriction can generate a slight weight loss in overweight adults, although this effect could be more related to participation in the study

than to the diet itself. Improvements in glycemic control and lipid profile are inconclusive, and the loss of at least 5% of body weight appears to be a key factor in optimizing these parameters.

In contrast, the evidence indicates that energy-restricted DM achieves sustained reductions in weight and body fat, even after one year, with significant improvements in blood glucose, total cholesterol, LDL and triglycerides. These effects appear to be linked to high fiber intake, low caloric density foods and lower consumption of red or processed meats. It would be useful to investigate why HDL cholesterol decreases in various studies. Finally, for overweight people, DM could be established as a habitual eating pattern and not only as a diet for specific purposes.

Table 2 Studies on the Mediterranean Diet in the treatment of overweight and obesity.

REFERENCE	TYPE OF STUDY	SUBJECTS	DURATION OF OPERATION	OBJECTIVES	RESULTS
Jospe et al. 2020 (15)	Non-randomized clinical trial.	171 Subjects overweight grade 2 or obese. Over 18 years old.	12 months.	To compare the effects of the Paleo diet, DM and intermittent fasting, with or without HIIT (high-intensity intermittent exercise) on adherence, intake, and anthropometric and cardiometabolic parameters.	DM produced more significant improvements in glycemic control. All groups lost weight at 6 months, but at 12 months only with intermittent fasting and DM. Those who adhered more to DM showed a greater decrease in weight. Fat mass and waist circumference decreased similarly in all 3 diets.
Meslier et al. 2020 (13)	Randomized controlled clinical trial.	82 overweight or obese subjects	8 weeks	To compare the effects of a Mediterranean Diet (normocaloric) with a control group (usual Western diet) on cardiometabolic health, markers of inflammation and microbiota.	DM produced a significant decrease in LDL cholesterol compared to the control group, which was directly proportional to dietary adherence.
Picklo et al. 2022 (16)	Randomized crossover clinical trial.	33 overweight or obese subjects aged 20 to 75 years.	4 weeks per procedure, with a 4-week washout period between each procedure.	To compare the effect of a DM without whole egg, a DM with 1 egg/1000 kcal/day and an average American diet on lipid profile. All three diets were isocaloric.	Total and LDL cholesterol were significantly reduced in the egg-free DM and in the American diet. Triglycerides also decreased with DM. Consumption of 1 egg per 1000 kcal. It did not increase cardiovascular risk.

Uffelman et al. 2024 (14)	Randomized clinical trial.	60 subjects aged 30 to 69 years with overweight or obesity.	2 months	To compare the effects of DM with DM with high mushroom intake on cardiometabolic health. The diets were normocaloric.	The implementation of both Mediterranean diets produced a non-significant decrease in total and HDL cholesterol. DM with mushrooms slightly decreased blood glucose levels.
Rosi et al. 2020 (18)	Non-randomized clinical trial.	49 subjects with obesity, 18 years of age and older	6 months	To compare the effects of two hypocaloric DM, one high in pasta (minimum 5 servings per week) and the other low in pasta (up to 3 servings per week), on weight, anthropometric parameters, body composition, quality of life and intake of the subjects. As well as in the lipid and glycemic profile.	Both diets significantly decreased body weight, waist circumference and body fat. They also improved insulin sensitivity and lipid profile.
Dellis et al. 2019 (19)	Randomized clinical trial.	70 obese or overweight subjects aged 18 to 65 years.	2 months	To compare the effect of a hypocaloric DM with a hypocaloric DM deprived of carbohydrates during the morning on weight, waist circumference, body fat, insulin sensitivity and lipid profile.	Only in the unrestricted group was LDL cholesterol reduced. In both groups, HDL cholesterol, triglycerides, waist circumference and insulin sensitivity decreased and there was a decrease in weight greater than or equal to 5%. In the group that avoided carbohydrates in the morning, weight loss was faster.
Luo et al. 2022 (20)	Randomized clinical trial.	202 overweight and obese subjects in Asia (BMI greater	6 months	To compare the effects of three hypocaloric diets: a DM, a typical traditional Chinese plant-based diet, and a diet high	In all three groups, weight decreased by 7% of body weight at 6 months and the lipid profile improved significantly The DM

		than or equal to 24)		in animal products, on weight and insulin sensitivity.	group had the best glycemic control.

DM: Mediterranean Diet

Regarding the effects of ketogenic diets (KD) for treating obesity and overweight, Table 3 describes the included studies.

Trials of very low calorie ketogenic diets (VLCKD) have shown a rapid decrease in weight and waist circumference (21–25) show a rapid decrease in weight and waist circumference. Di Rosa et al. (21)with 268 participants, found that the VLCKD achieved a 5% reduction in body weight in one month, compared to the three months required with the Mediterranean Diet (MD). Although the increase in fat-free mass was lower, no fat loss was observed, despite the rapid weight reduction. The use of supplements (vitamins, minerals, bicarbonate and omega 3) could have favored the results.

Sanchez et al. (25) also compared VLCKD and DM, observing a significant decrease in weight and body fat at 6 months, without affecting muscle mass. Although only 20 subjects completed the study, adherence was high. In the studies of Cunha et al. (22) and Caprio et al. (23)in addition, the VLCKD achieved greater reductions in weight (9.8% and 8.9%, respectively) and waist circumference than a conventional hypocaloric diet, in addition to reducing fasting blood glucose. However, both trials included few participants, which limits the validity of the results, although adherence was high.

In the trial by Basciani et al. (24)in addition, the VLCKD with vegetable or whey proteins produced a greater loss of weight and abdominal fat than that based on animal proteins. Although the differences were small, all three interventions significantly reduced waist circumference. As for glycemia, only the diet with animal and whey protein achieved a significant decrease. However, the HOMA index and insulin improved in all three groups, as did plasma lipids (total cholesterol, LDL and triglycerides). Adverse effects were mild and there were no dropouts, although the intervention lasted only 45 days and the number of participants who finished was 48.

Regarding low-calorie ketogenic diets (LCKD), Michalczyk et al. (26) observed a 15% reduction in body weight in 3 months with a 20% caloric deficit. Waist, blood glucose, triglycerides and HDL also improved. The diet included 70% fat, so the effect on LDL cholesterol was not evaluated. The study focused on women, which is relevant given the paucity of evidence in this group. Adherence was good, possibly due to less restriction compared to VLCKDs, and participants received calcium, vitamin D and multivitamin supplementation.

Lim et al. (27)in a 6-month study, they found weight reductions of 6.9% at 3 months, lower than in the previous study, despite a similar caloric deficit. This could be explained by a lower adherence to macronutrient distribution. Over time, weight loss slowed and some recovery was observed at one year. HbA1c and triglycerides decreased significantly, while total cholesterol decreased slightly. Supplementation was also used, although its impact is unknown. Notably, the CD group had a dropout rate twice as high as the control group, with no clear explanation in the study.

Wu et al. (28) evaluated a hypocaloric DC in phases, designed according to the Chinese food culture. This produced improvements in weight, fat mass, visceral fat and waist circumference, with an 8% weight loss in 3 months, slightly higher than that achieved with a drug (GLP-1 agonist). HbA1c, HOMA and triglycerides were also reduced, and HDL increased without raising LDL. Adverse effects were minor and adherence was high. No randomization was performed, since the participants chose their intervention, which may have generated bias, although it provides a perspective closer to real life.

In summary, VLCKD allows a rapid weight loss (more than 6% in two months) and a decrease in waist circumference, due to its low energy intake (600-800 kcal/day). They also generate early improvements in glycemic metabolism and could benefit the lipid

profile, although the evidence is still limited. The loss of fat mass without affecting muscle mass reinforces its usefulness in people with severe obesity who require rapid reductions. However, most studies have a maximum duration of 2 months, so prolonged application is not recommended. Supplementation and medical supervision are essential due to the low caloric intake.

LCKDs also promote relevant weight reductions (more than 5% in 3 months), improving waist circumference, glycemia, triglycerides and HDL. They do not increase total or LDL cholesterol if unsaturated fats are prioritized. As with VLCKDs, their effectiveness is greatest in the first 3 months, and it is not recommended to extend them beyond 6 months due to the paucity of long-term evidence. The reported good adherence could be related to the anorexigenic effect of ketone bodies. Although it is not known whether these diets cause a rebound effect, the observed preservation of muscle mass could contribute to avoid it.

Table 3 Studies on the ketogenic diet in the treatment of overweight and obesity.

REFERENCE	TYPE OF STUDY	SUBJECTS	DURATION OF OPERATION	OBJECTIVES	RESULTS
Cunha et al. 2020 (22)	Randomized clinical trial.	39 subjects with obesity, over 18 years of age.	2 months	To compare the effects of a VLCKD with a standard hypocaloric diet on visceral fat and liver fat.	In the VLCKD group, compared to the hypocaloric diet, a significant decrease in weight, waist circumference, visceral fat and liver fat was observed.
Di Rosa et al. 2022 (21)	Randomized clinical trial.	268 subjects aged 18 to 70 years, overweight or obese.	3 months	To compare the time it takes for VLCKD and hypocaloric DM to generate a 5% decrease in body weight and changes in body composition.	To decrease 5% of body weight, it took 1 month with VLCKD and 3 months with DM. However, in the DM group there was a greater decrease in fat mass and waist circumference and a greater increase in fat-free mass.
Lim et al. 2024 (27)	Randomized controlled clinical trial.	59 subjects aged 21 to 65 years, with obesity (BMI greater than 27.5 kg/m2 in Asia).	6 months	To compare the effects of a healthy hypocaloric CD with those of a usual hypocaloric diet on weight loss at 3, 6 and 12 months, together with changes in metabolic parameters.	A significant difference was seen in favor of DC in weight loss at 3 and 6 months. For HbA1 and triglycerides the difference was also significant at 12 months. Total and LDL cholesterol showed significant differences at 12 months only.
Michalczyk et al.2020 (26)	Randomized controlled clinical trial.	91 overweight or obese women aged 30 to 60 years.	3 months.	To compare the effects of a LCKD on blood glucose, insulin, HbA1c, waist circumference and lipid profile, compared to a control group (no intervention)	Significant improvements were seen in blood glucose, insulin, HbA1c, HDL cholesterol and triglyceride values compared to the control group. In addition, there was a significant difference in the decrease in weight and waist circumference.

Caprio et al. 2023 (23)	Randomized clinical trial.	39 overweight or obese subjects, aged 18 to 65 years, who suffered from frequent migraines.	2 months	To compare VLCKD with a balanced hypocaloric diet, in parameters respective to migraine, anthropometric parameters, plasma lymphocytes, inflammation, changes in aldosterone and renin.	A significantly greater decrease in weight, waist circumference and visceral fat was seen in the VLCKD group. four months later, they had not regained weight. Glycemia decreased significantly in this group.
Wu et al. 2022 (28)	Non-randomized clinical trial.	90 subjects with obesity (BMI higher than 28 kg/m2 in Asia)	12 weeks	To compare the effects of a CD intervention (in phases), with one of lifestyle changes + hypocaloric diet, with a pharmacological one (GLP-1 agonist) on anthropometric and metabolic parameters.	The effect of CD on weight loss was significant and somewhat superior to pharmacological treatment. CD significantly decreased fat mass, visceral fat, waist circumference, insulin sensitivity and blood pressure. It did not increase triglycerides or LDL cholesterol.
Basciani et al. 2020 (24)	Randomized clinical trial.	48 subjects with obesity, aged 50 to 70 years old.	45 days	To compare the effects of three types of VLCKD: with animal, vegetable or whey protein, on microbiota, body composition, lipid profile, insulin sensitivity.	Blood pressure, waist circumference, HOMA index, insulin, total and LDL cholesterol and triglycerides decreased significantly in all three groups. Weight and abdominal fat decreased significantly in the whey and vegetable protein group.
Sanchez et al. 2021 (25)	Randomized clinical trial.	20 obese or overweight subjects, aged 18 to 65 years.	6 months	To compare the effects of a VLCKD compared to a hypocaloric DM, on weight and fat mass reduction, endothelial function and vasa vasorum density.	VLCKD produced a reduction in markers of endothelial dysfunction and atheromatous disease. Results associated with a significant decrease in body weight and total body fat, compared to DM.

DC: Ketogenic Diet; VLCKD: Very low calorie ketogenic diet; LCKD: Low-calorie ketogenic diet; DM: Mediterranean Diet.

It is concluded that Mindful Eating does not produce changes in body weight or waist circumference, nor in plasma lipoprotein values or glycemic profile. Therefore, it also does not reduce the risk of cardiovascular disease or type 2 diabetes. On the other hand, the hypocaloric Mediterranean Diet produces weight loss and a decrease in waist circumference, as well as improvements in the lipid and glycemic profile. This could be realized in the long term by promoting cardiovascular health and reducing the risk of type 2 diabetes. On the other hand, low and very low calorie ketogenic diets produce a very significant weight loss in a short period of time (more than 5% in two months), as well as a reduction in waist circumference and plasma triglycerides. They also improve glycemic control and increase HDL cholesterol. These diets do not raise LDL cholesterol and do not produce a loss of lean mass. However, they should be performed in the short term, especially VLCKD (maximum 2 months for very low calorie and 6 months for low calorie) as there is no evidence of their application for longer periods.

Thus, both DC and energy-restricted DM are effective in preventing cardiovascular disease and type 2 diabetes in people who are obese or overweight. With both diets, a loss of at least 5% of body weight is required to observe improvements in plasma lipoprotein and glycemia values.

The limitations of this work are diverse. On the one hand, there are those related to the low quality of the available evidence on EM in the treatment of this disease; also the short duration of the studies of the three interventions and the lack of follow-up of the patients after the end of the interventions. In addition, most of the studies were concluded for very few subjects, limiting the possibility of extrapolating the results to the population. Nor was it possible to evaluate the different effects according to sex and degree of overweight/obesity, since these divisions are not made in the analyses of the studies. On the other hand, comparing a behavioral strategy with a dietary strategy can be complex and even unnecessary, since they are not mutually exclusive.

It would be interesting to conduct long-term studies (1 year or more) that analyze the effects of Mindful Eating in the treatment of obesity and overweight, carrying out periodic face-to-face interventions with a large number of participants. As well as performing long-term (years) follow-up of subjects participating in studies on ME, CD and DM in obesity and overweight, after the interventions have ended. It would also be useful to analyze, in cohort studies, the long-term impact of ketogenic diets on cardiovascular risk and type 2 diabetes, differentiating the effects in men and women. Finally, it would be important to analyze the effects of ketogenic and Mediterranean low-calorie diets on visceral fat (by bioimpedance) and markers of inflammation.

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References (14 points)

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Effect of the Mediterranean diet and the ketogenic diet on sleep quality and duration in healthy adults

Efecto de la dieta mediterránea y la dieta cetogénica en la calidad y duración del sueño en adultos sanos

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ABSTRACT

Objective: To investigate the relationship between the Mediterranean diet, ketogenic diet, and sleep quality in healthy adults. Materials and Methods: A literature review was conducted based on articles published within the last five years, selected from databases such as PubMed, Google Scholar and Scopus. A total of 15 studies were included, 12 of which focused on the Mediterranean diet and 3 on the ketogenic diet. Variables such as study design, sample size, tools used to assess sleep quality (PSQI, actigraphy), and main findings were evaluated. Results and Discussion: The Mediterranean diet was consistently associated with improvements in parameters such as sleep duration, latency, and efficiency. This relationship was primarily observed in healthy adults with high adherence to the dietary pattern and when validated subjective assessment tools were used. In contrast, evidence regarding the ketogenic diet was scarce and limited to specific contexts, such as studies in military populations, with no significant improvements observed. Conclusions: The Mediterranean diet presents stronger scientific support as a nonpharmacological dietary strategy to promote better sleep quality. The ketogenic diet, although not associated with negative.

Keywords:

Mediterranean diet. Ketogenic diet. Sleep quality. Healthy adults.

RESUMEN

Palabras clave:

Dieta mediterránea. Dieta cetogénica. Calidad del sueño. Adultos sanos.

Objetivo: Investigar sobre la relación entre la dieta mediterránea, dieta cetogénica y la calidad del sueño en adultos saludables. Material y métodos: Revisión bibliográfica a partir de artículos publicados en los últimos cinco años, seleccionados en bases de datos como PubMed, Google Scholar y Scopus. Se incluyeron un total de 15 estudios, de los cuales 12 analizaron la dieta mediterránea y 3 la cetogénica. Se valoraron variables como el tipo de diseño, el tamaño muestral, las herramientas empleadas para medir la calidad del sueño (PSQI, actigrafía) y los resultados obtenidos. Resultados y discusión: La dieta mediterránea se asoció de forma consistente con mejoras en parámetros como la duración, latencia y eficiencia del sueño. Esta relación se observó principalmente en adultos sanos, con alta adherencia al patrón dietético, y cuando se utilizaron herramientas validadas de evaluación subjetiva del sueño. En cambio, la evidencia sobre la dieta cetogénica fue escasa y limitada a contextos específicos, como estudios en población militar, sin mejoras significativas observadas. Conclusiones: La dieta mediterránea presenta un mayor respaldo científico como estrategia dietética no farmacológica para favorecer la calidad del sueño. La dieta cetogénica, aunque no mostró efectos negativos, aún requiere más estudios para valorar su aplicabilidad en este ámbito.

Introduction

Sleep is an essential biological process for human well-being, as it contributes to nervous system recovery, memory consolidation, metabolic regulation and emotional stability (1). However, in recent years there has been an increase in sleep disorders, such as insomnia and sleep apnea, which, in general, do not provide an optimal quality of life and health. Among the various factors that influence the quality and duration of sleep, diet is considered a key aspect that can be modified to promote better sleep (2). Currently, two dietary patterns have been the subject of several investigations due to their possible effects on health and sleep, namely the Mediterranean diet and the ketogenic diet. The Mediterranean diet is based on a high consumption of fruits, vegetables, legumes, whole grains, olive oil and fish, and has had a great impact for its role in reducing the risk of metabolic and cardiovascular diseases (3). Studies have suggested that following this type of diet may be related to better sleep quality. On the other hand, the ketogenic diet is characterized by a very low carbohydrate intake, a moderate amount of protein and a high fat intake. In this paper we propose to investigate in depth how these two dietary patterns may influence sleep quality, a crucial aspect of health that has traditionally been little explored. The relevance of this study lies in several fundamental aspects. First, the increasing prevalence of sleep disorders in the general population represents a public health problem that requires an innovative and multidisciplinary approach. Second, the possibility of modifying sleep quality through dietary interventions offers a nonpharmacological and potentially accessible strategy for improving overall well-being. In addition, the comparison between the Mediterranean diet and the ketogenic diet will allow a more precise understanding of how different nutritional compositions may impact sleep patterns.

General Objective:

To investigate the relationship between Mediterranean diet, ketogenic diet and sleep quality in healthy adults.

Specific objectives:

- Investigate the influence of the Mediterranean and ketogenic diet on aspects of sleep, such as fatigue or rest, through studies using validated sleep quality questionnaires, such as the *Pittsburgh Sleep Quality Index*, or sleep monitoring devices.
- To evaluate the differences and similarities between the effects of the Mediterranean diet and the ketogenic diet on sleep.
- To analyze whether adherence to the Mediterranean or ketogenic diet influences sleep latency and sleep efficiency in healthy adults.
- To examine the possible long-term effects of both diets on sleep quality and the presence of sleep disorders, such as insomnia or sleep apnea.

1.2. The dream

Sleep is an essential biological function in human beings, occupying approximately one third of a person's life. It is a fundamental process for the maintenance of cognitive and physiological functions (4). During nighttime rest, the body regulates various homeostatic

processes, including thermoregulation, endocrine balance and strengthening of the immune system. It also plays a crucial role in memory consolidation and learning (5). Therefore, far from being a passive state, sleep represents an active and complex mechanism, indispensable for the correct functioning of the organism and therefore the preservation of physical and mental health, where its alteration can have significant consequences on general well-being (6).

Sleep is organized in cycles that are repeated several times during the night, each of which consists of several stages (7-10):

Non-REM (Non-rapid Eye Movement) sleep:

- Stage 1 (Transition to sleep): This is the lightest phase where it is very easy to wake up here, brain activity begins to decrease, muscles relax and breathing slows down. However, sleep is very light and the person can be easily awakened by any external stimulus. Jerky movements may also be experienced.
- Stage 2 (Light sleep): The body begins to relax, and brain activity slows down. Although it is a light sleep phase, the body is already in a more stable state of rest.
- Stage 3 (Deep Sleep): Also called "slow wave sleep" (SWS), this is the most restorative phase of the cycle. During this stage, the body performs essential functions such as cell regeneration, tissue repair and strengthening of the immune system. It is also key to memory consolidation and learning. At this point, waking the person up is more difficult, and doing so can lead to disorientation.

REM (Rapid Eye Movement) sleep: In this phase, the brain is very active, and most dreams occur. It is crucial for emotional regulation and long-term memory consolidation.

These cycles, which last approximately 90 minutes each, are repeated 4 to 6 times per night. The quality of sleep depends on the adequate proportion of these stages and on the continuity of uninterrupted sleep (11).

Sleep plays a fundamental role in our health and general well-being, being directly related to our quality of life (8,10,12). To evaluate its quality, various parameters are analyzed, such as the time it takes a person to fall asleep (latency), the total duration of rest, the frequency of nighttime awakenings and the percentage of time in bed where the human being actually sleeps. There are different methods to study sleep: the most accurate is polysomnography, a test where brain activity, breathing and movements are monitored by sensors. And also, the most widely used method because it is a more accessible option is the Pittsburgh Sleep Quality Questionnaire (PSQI), a tool that, by means of 24 questions, evaluates aspects such as latency, duration, disturbances or daytime sleepiness. Each response is scored from 0 to 3, adding up to 21 points, where a score above 5 indicates that the person has significant sleep problems. These tools allow us to identify sleep disorders that, if left untreated, can seriously affect our physical and mental health (13).

1.2.1. Impact of sleep on health

Circadian rhythm disorders significantly impact physical and mental well-being and are considered a major health issue (14). Appropriate rest is essential for several vital functions: it consolidates memory, preserves eye health, regulates body temperature, restores energy and improves brain metabolism (11,15). In Spain, the data are alarming: according to the Spanish Society of Neurology (8), between 25-35% of adults experience occasional insomnia, while 10-15% suffer from chronic insomnia. These alterations not only impair the quality of life and daily performance, but are also related to a deterioration of the general state of health.

People are vulnerable to the consequences of sleep disorders at various stages of life. At the individual level, these disorders can cause hormonal and biochemical imbalances, increase the risk of developing psychological or cognitive problems (11), and even increase mortality by increasing conditions such as hypertension, diabetes or obesity (8,18,19). On the other hand, on a social and economic scale, they decrease labor productivity and increase the probability of accidents. These effects highlight the importance of addressing sleep disorders not simply as isolated symptoms, but as critical public health risk factors. Therefore, their prevention and adequate treatment could substantially improve not only the quality of individual life, but also the efficiency of the healthcare system.

1.2.2. Sleep disturbances

Sleep disturbances are problems that compromise the ability to sleep adequately, either sufficiently or restoratively. These alterations can be transient or chronic and have a considerable effect on health and well-being. Some of the most common alterations include:

Insomnia: Insomnia is difficulty initiating or maintaining sleep, nocturnal awakenings during the night. According to Riemann et al. (10), chronic insomnia affects approximately 10-15% of the adult population and is associated with functional impairment during the day, such as fatigue, difficulty concentrating, and mood changes.

Sleep apnea: Sleep apnea is a disorder in which breathing is repeatedly interrupted during sleep. These pauses can last from a few seconds to minutes and can occur many times per hour. Khan and Aouad (8) emphasize that sleep apnea not only affects sleep quality, but can also cause daytime sleepiness and increase the risk of cardiovascular problems.

Circadian rhythm disorders: These disorders occur when the body's internal clock is not synchronized with the natural light-dark cycle. These disorders can make it difficult to fall asleep and cause daytime sleepiness.

Restless legs syndrome (RLS): RLS is characterized by a need to move the legs when falling asleep. This disorder is related to alterations in the levels of dopamine and iron in the brain.

Taken together, these alterations not only affect quality of life, but can also have long-term health consequences. For example, chronic sleep deprivation has been associated with an increased risk of metabolic problems, cognitive impairment, and mood disorders (8).

1.2.3. Factors influencing sleep quality

Sleep quality is influenced by a variety of factors, including biological, psychological, environmental and behavioral aspects. Biological factors include age, gender and

underlying medical conditions such as metabolic or endocrine disorders (2). Psychological factors such as stress, anxiety and depression are also major causes of insomnia and unrefreshing sleep. It has been shown that chronic stress can increase sleep latency and reduce sleep efficiency, leading to fragmented and non-refreshing sleep (2). In addition, lifestyle habits such as caffeine, alcohol and tobacco consumption, as well as lack of physical activity, can negatively affect sleep quality (20). The environmental setting, including exposure to artificial light at night and noise, can also interfere with circadian rhythms and the ability to fall asleep (21). Finally, diet is a modifiable factor that has recently gained attention for its potential to improve or worsen sleep quality. Several studies have shown that dietary patterns such as the Mediterranean diet and the ketogenic diet can influence sleep duration and quality through mechanisms such as neurotransmitter regulation and reduction of systemic inflammation (21,22).

1.3. Nutritional interventions

The quality of the diet depends on the variety, balance and nutritional adequacy of the foods consumed, ensuring that the body's energy and metabolic needs are met. A diversified and healthy diet not only satisfies nutritional needs, but also plays a key role in disease prevention. It has been shown that certain foods or dietary patterns may increase the risk of developing chronic noncommunicable diseases (such as diabetes, obesity, or cardiovascular disease) or, conversely, exert a protective effect (18). Given this evidence, it is crucial to assess diet quality in order to design personalized and effective nutritional intervention strategies. To measure it, internationally validated scales, called *diet quality indexes*, are used. Among the most recognized are:

Healthy Eating Index (HEI)

Dietary Quality Index (DQI)

Healthy Diet Indicator (HDI)

Mediterranean Diet Score (MDS)

These tools assign a score based on the consumption of key food groups, allowing the diet to be classified as adequate or inadequate. Its application in research and public health facilitates the identification of risky dietary patterns and the promotion of healthier habits, thus contributing to improve health outcomes at the population level (23).

1.3.1. Mediterranean Diet

The Mediterranean diet is a dietary pattern based on the traditional habits of Mediterranean countries characterized by a high intake of fruits, vegetables, whole grains, legumes, nuts and olive oil, as well as a moderate consumption of fish and dairy products, and a low consumption of red meat and ultra-processed products is recommended. This diet has been widely studied due to its multiple health benefits such as reducing the risk of cardiovascular diseases, metabolic syndrome, neurodegenerative diseases and cancer (3). Its great positive impact is attributed to antioxidants, dietary fiber, monounsaturated and polyunsaturated fatty acids, which have anti-inflammatory properties. In addition to its effects on physical health, the Mediterranean diet has also been associated with mental health benefits, such as the possibility of reduced risk of depression and anxiety (3). Since sleep quality and mental health are related, this suggests that the Mediterranean diet may also play a role in sleep regulation. (14)

1.3.2. Mediterranean Diet and Sleep

The relationship between the Mediterranean diet and sleep has been the subject of several investigations and most studies suggest that this dietary pattern may be associated with better sleep quality along with a lower frequency of disorders such as insomnia and sleeping difficulties. Mohammadi et al. (24) conducted a cross-sectional study with 535 Iranian adults to investigate the relationship between adherence to the Mediterranean diet, serum brain-derived neurotrophic factor (BDNF) levels, and sleep quality. The results showed that participants with greater adherence to this dietary pattern were less likely to have short sleep duration and poor sleep quality. These suggest that the Mediterranean diet could positively influence sleep not only through direct nutritional mechanisms, but also by modulating neurotrophic factors such as BDNF. Theorell-Haglöw et al. (21) conducted a cross-sectional study with 23,829 Swedish adults to analyze the relationship between sleep duration/quality and adherence to healthy dietary patterns. Using validated questionnaires, they evaluated two models: the modified Mediterranean diet (mMED) and the Nordic Food Index (HNFI). The results showed that participants with short sleep combined with poor quality were less likely to follow these healthy diets, while those with normal sleep and good quality maintained greater adherence. Similarly, Lopes et al. (25) conducted a cross-sectional study in Brazilian adults to evaluate the association between dietary habits and sleep quality in adults. They used food frequency questionnaires to assess dietary patterns and the Pittsburgh Sleep Quality Index to measure sleep quality. As a result, they found that greater adherence to healthy dietary patterns, characterized by high consumption of fruits, vegetables and whole grains, was associated with better sleep quality, also that higher consumption of processed foods and refined sugars was associated with sleep disturbances. Zuraikat et al. (3) analyzed the association between adherence to the Mediterranean diet and sleep quality in U.S. women with a cross-sectional study that assessed the association between adherence to the Mediterranean diet and sleep quality in U.S. women. This used the alternative Mediterranean diet index (aMED) to measure dietary adherence, which includes a high intake of fruits, vegetables, whole grains, legumes, fish and healthy fats, as well as a moderate intake of alcohol and so on, concluding that those with a higher adherence to this dietary pattern had better sleep quality, greater sleep efficiency and fewer interruptions according to the Pittsburgh Sleep Quality Index. Similarly, Godos et al. (20) conducted a cross-sectional study but in Italian adults where dietary intake was assessed using a validated food frequency questionnaire, and adherence to the Mediterranean diet was measured using a specific score reflecting the consumption of foods characteristic of this dietary pattern. And they found a lower prevalence of insomnia and nighttime awakenings since of the 1,936 participants, 67.9% reported good sleep quality and for each point increase in the Mediterranean diet adherence score individuals were 10% more likely to have adequate sleep quality, but this association was significant in normal weight or overweight individuals, and not in those participants who were obese. The study by Gupta et al. (22), carried out in Costa Rican adults, also suggested a good relationship between compliance with the Mediterranean diet, in which a food frequency questionnaire was used to evaluate dietary intake and calculate a Mediterranean diet score based on the consumption of foods typical of this dietary pattern, also obtained a result where the duration of sleep was greater, generating a hypothesis that the content of omega-3 fatty acids could improve sleep regulation. In another context, in the study by Jansen et al. (26) investigated the relationship between Mediterranean diet and sleep in 4,467 middle-aged Mexican women through a cross-

sectional study where they identified three main dietary patterns by means of principal component analysis: Fruits and vegetables: Characterized by a high consumption of fruits and vegetables. Western: Focused on the consumption of meats and processed foods. Modern Mexican: Includes high consumption of tortillas and soft drinks, with low consumption of fiber and dairy products.

As a result, they observed that those with a diet closer to the Mediterranean diet had fewer problems falling asleep and fewer nighttime awakenings suggesting a likelihood of a better quality of rest. Similarly, the results of the study by Zaidalkilani et al. (27) where they evaluated Arab women with insomnia problems and they were submitted to a questionnaire about adherence to the Mediterranean diet, and their nocturnal habits measured by the Athens Insomnia Scale questionnaire, indicate that a higher adherence to the Mediterranean diet is associated with a lower prevalence of insomnia among the Arab women studied. Specifically, participants with high adherence to this diet presented better sleep quality and a reduction in insomnia symptoms compared to those with low adherence. Hashimoto et al. (28) conducted a study to relate a diet with low energy but not in a balanced and nutritious diet in general, focusing on adequate intake of vitamins, minerals and tryptophan. This diet could be classified as a Mediterranean diet since the diet was evaluated with a questionnaire based on the amount of food ingested, which closely resembles the Mediterranean diet questionnaire. Sleep quality was measured by actygraph and their lifestyle had null changes, as a result they obtained that an adequate energy intake and a high quality diet, rich in vitamins, minerals and tryptophan, are associated with better sleep quality and suggest that maintaining a balanced and nutritious diet may contribute to prevent sleep problems in this population. Ramón-Arbués et al. (29) conducted a cross-sectional study with 868 Spanish university students to evaluate the association between eating habits and sleep quality. Using validated questionnaires, they found that a low consumption of foods characteristic of the Mediterranean diet together with a high consumption of sugary soft drinks and sweets was significantly associated with poorer sleep quality and increased risk of sleep disorders. However, it is important to mention that not all studies have found a direct relationship between the Mediterranean diet and sleep quality. For example, Oliveira and Marques-Vidal (30) analyzed data from a large middle-aged cohort where multiple dietary components were analyzed with detailed validated questionnaires and concluded that there was no association between adherence to this diet and the presence of insomnia suggesting that other factors such as genetics, lifestyle and environmental conditions however, suggest that some components such as sugary foods or red meat may be associated with poorer sleep quality. Likewise, Verkaar et al. (2) explored the relationship between different dietary patterns and sleep duration and quality in a cohort. Various dietary patterns were identified and assessed using food frequency questionnaires and objective and subjective sleep parameters were measured in the participants. Their results showed that people with a more Mediterranean diet-focused diet reported better subjective sleep quality, but no improvement in objective sleep quality scores could be observed.

1.3.3. Ketogenic Diet

The ketogenic diet is an eating pattern characterized by a very low carbohydrate intake, a moderate amount of protein and a high fat intake. Its main objective is to induce a state of ketosis, in which the body uses ketone bodies as the main source of energy instead of

glucose (21). Initially, the ketogenic diet was used as a treatment for refractory epilepsy in children, as it was observed that it could significantly reduce the frequency of epileptic seizures. In recent years, its use has expanded into other areas, including weight loss, management of type 2 diabetes, sports performance and prevention of neurodegenerative diseases.

1.3.4. Ketogenic Diet and Sleep

Some research has indicated possible benefits of the ketogenic diet in relation to sleep. Gangitano et al. (31) suggest that the ketogenic diet could affect circadian rhythms and sleep, because of its impacts on energy metabolism and neurotransmitter production. In particular, it has been proposed that ketosis could affect the regulation of adenosine, a key neuromodulator in the induction and maintenance of sleep. This diet, characterized by a very low consumption of carbohydrates and a high intake of fats, could have certain benefits on sleep quality and it has been suggested that the ketogenic diet could contribute to reduce sleep interruptions, in addition to favoring an increase in the slow-wave sleep phase, considered the deepest stage. Iacovides et al. (32) conducted a controlled study with 11 healthy young people to compare the effects of a low-carbohydrate ketogenic diet with a conventional high-carbohydrate diet. For three weeks, participants followed both diets at different periods. The results showed that the ketogenic diet did not generate significant changes in sleep quality compared to the traditional diet. Both the time taken to fall asleep and the total hours of rest remained similar in both cases. Although the ketogenic diet did induce a state of ketosis that did not negatively affect sleep, this study suggests that at least in young, healthy people, this type of diet does not impair rest when applied for short, controlled periods. In a different context, Henderson et al. (33) conducted a crossover clinical trial with 7 male military personnel with a mean age of 34 years to examine the effects of a 2-week ketogenic diet versus a high-carbohydrate diet during 36 hours of controlled sleep deprivation. The results showed that the ketogenic diet improved cognitive performance during prolonged wakefulness, with greater accuracy in tests of attention and working memory compared to the conventional diet. In addition, participants reported less subjective sleepiness and better mood under this dietary pattern. This pilot study suggests that the ketogenic diet may be a promising strategy for maintaining performance in military operations requiring prolonged periods of alertness. Similarly, Shaw et al. (16) conducted a randomized, controlled, crossover clinical trial of 36 military men with a mean age of 36 years to examine the effect of a 2-week ketogenic diet versus a conventional carbohydrate diet on cognitive performance, mood, sleep, and heart rate variability. Using standardized assessments, they found that the ketogenic diet did not produce significant changes in sleep parameters, but observed a reduction in heart rate variability, suggesting a possible increase in physiological stress during metabolic adaptation.

Method

The present work consists of a bibliographic review of scientific articles, with the aim of analyzing the existing connection between the Mediterranean diet and the ketogenic diet, as well as its influence on the quality and quantity of sleep. In order to carry out this TFG, an exhaustive search was made in different databases. The search began on February 20,

2025 and ended on April 29, 2025. The bases consulted were as follows: **PubMed, ScienceDirect, Google Scholar**

These sources provided access to both original studies and relevant scientific literature on the subject. Search strategy:
Key terms used included:

- "Mediterranean diet"
- "Ketogenic diet"
- "Sleep quality"
- "Sleep quantity"

In addition, to expand and refine the results, related terms such as:

- "Nutrition"
- "Circadian Rhythm"
- "Insomnia"
- "Apnea"

Inclusion criteria

Studies were selected that met the following characteristics:

- They address sleep quality or sleep disorders as a dependent variable.
- They explore nutrition or type of diet as an independent variable.
- Published between 2019 and 2025.
- Studies in adult humans (over 18 years of age)
- Healthy participants, without pathologies that affect sleep in a secondary way.
- Randomized clinical trial, cohort or cross-sectional study designs.

Exclusion criteria

The following types of studies were excluded:

- Studies conducted in hospitalized patients.
- Research focused on high-performance athletes, due to the specificity of their physiological requirements.

The terms that have been used in the PubMed database are:

- sleep AND ((diet*) OR (nutrition*)): 763 results were obtained, of which 17 were selected.
- (diet*) AND(circadian) OR (insomnia) OR (apnea)): 143 results were obtained, of which 3 were selected.
- circadian OR apnea OR sleep OR insomnia: 6344 results were obtained, of which 4 were selected. This search had a more general character and was mainly used to obtain definitions and a better understanding of the dream, serving as a theoretical basis to contextualize the subject

Results

The nutritional approach to the orientation towards the prevalence of problems in the conciliation or duration of sleep is presented as one of the fundamental tools for the improvement of sleep quality, without incurring in the possibility of supplements and/or nutritional complements. To begin the analysis of both diets mentioned above that may have benefits for sleep quality, the use of a Mediterranean diet should be highlighted. Twelve studies were included (2,3,20-22,24-28,30) that analyze this relationship more specifically and whose characteristics and results are detailed in Table 3.1. Most of these aforementioned studies suggest that greater adherence to this dietary pattern is associated with more favorable sleep parameters, such as longer sleep duration, shorter sleep latency and better sleep efficiency. However, for the correct interpretation of these results, it is necessary to compare the methodologies. Several studies, such as those of Zuraikat et al. (3) and Mohammadi et al. (24), have demonstrated a shorter sleep latency, longer sleep duration and greater sleep efficiency in those participants who showed greater adherence to this dietary pattern. In line with the results of these studies, Godos et al. (20) and Ramón-Arbués et al. (29) agree that those who do not adhere to this diet show an increased risk of sleep disturbances, such as frequent nighttime awakenings or perception of unrefreshing sleep.

Table 1. *Studies relating the Mediterranean diet to the quality/quantity of sleep.*

Author, year	**Type of study**	**Population**	**Age range**	**Feature**	**Results**	**Dietary pattern**
Verkaar et al. 2024 (2).	Cohort study	Dutch men and women (N= 553), excluding those who <500 or 5000kcal/day>	Media: 51 years old	To examine the cross-sectional and longitudinal associations of various types of dietary patterns with self-reported sleep quality and with actigraphy-estimated sleep parameters.	No evidence was found that dietary patterns are associated with actigraphy-estimated and self-reported sleep.	Dutch dietary guidelines Mediterranean
Godos et al. 2019 (20).	Cross-sectional study	Italian men and women (N= 2044)	Over 18 years old	To evaluate the association between sleep quality and adherence to the Mediterranean dietary pattern.	High adherence to a Mediterranean dietary pattern is associated with better sleep quality.	Mediterranean
Gupta et al. 2022 (22).	Case-control study	Costa Rican men and women (N=2169) 70% men.		The objective was to examine whether sleep inconsistencies are due to lack of adherence to the Mediterranean diet.	Sleep duration was longer, generating a hypothesis that omega-3 fatty acid content could improve sleep regulation.	Mediterranean

Jansen et al. 2020 (26).	Longitudinal study	Mexican women (N=4469)	Media: 41 years old	To assess whether dietary patterns are associated with sleep quality in middle-aged Mexican women.	A dietary pattern based on fruits and vegetables was associated with higher sleep quality, whereas an unhealthy dietary pattern was associated with poorer sleep quality.	Mediterranean
Zaidalkilani et al. 2022 (27).	Cross-sectional study	Arab women (N=917)	Media: 36 years old	To determine whether adherence to the Mediterranean diet (MD) is related to reduced insomnia in Arabic-speaking adult women in Jordan.	Participants' adherence to DM was significantly associated with improved sleep and reduced insomnia symptoms, highlighting the need for further research.	Mediterranean
Hashimoto et al. 2020 (28).	Cross-sectional study	Japanese women (N=80)	18-27 years old	To assess habitual inadequate dietary intake with dietary behavior that are associated with low objective sleep quality in adolescents and young women.	No significant associations were observed between objective sleep quality.	Mediterranean

Oliveira et al. 2023 (30).	CoLaus|PsyCoLaus Study	Women and men (N=3751)	Media: 57 years old	To assess the association between sleep quality and a variety of dietary markers among middle-aged community-dwelling participants.	No consistent associations were found among a large panel of nutritional markers and quality of sleep.	Mediterranean
Zuraikat et al. 2020 (3).	Prospective cohort study	U.S. women (N=432)	20-76 years	To prospectively assess whether adherence to a modified Mediterranean diet for US populations.	increased adherence to an aMed dietary pattern and intake of its main components, as a possible lifestyle intervention to promote sleep quality in women.	Mediterranean
Mohammadi et al. 2023 (24).	Cross-sectional study	Iranian adults (N=535)	20-60 years	To investigate the relationship between serum MD and brain-derived neurotrophic factor (BDNF) levels and sleep quality and quantity in Iranian adults.	Adults with greater adherence to the Mediterranean diet had significantly lower odds of having short sleep duration and poor sleep quality.	Mediterranean

Theorell-Haglöw et al. 2020 (21)	Cross-sectional cohort study	Men and women (N= 23,829)	45-75 years	To investigate the relationships between sleep duration and adherence to healthy diets.	Short sleep duration combined with poor sleep quality is associated with poor adherence to healthy diet and meal patterns regular.	Mediterranean
Enrique Ramón-Arbués et al. 2022 (29).	Cross-sectional study	Students (N= 868)		To evaluate the association between diet and sleep quality among a group of Spanish university students.	There is a strong correlation between dietary habits and sleep quality, the low consumption of certain foods, as well as the excessive consumption of others that were associated with an increased risk of suffering from a sleep disorder of sleep.	Mediterranean

Lopes et al. 2019 (25)		Patients diagnosed with mild to severe OSA (N = 296).		To analyze the association between dietary inflammatory potential and sleep parameters in individuals with obstructive sleep apnea.	Diets with higher inflammatory potential could increase the risk of OSA symptoms, such as daytime sleepiness.	Mediterranean

Most of the studies reviewed, whether cross-sectional, cohort or longitudinal, show an association between the Mediterranean diet and better sleep quality. This relationship has been evidenced in parameters such as longer sleep duration, shorter latency to fall asleep and greater sleep efficiency. However, a comparison of the different studies shows that the results are not entirely homogeneous. A key aspect that influences the results is the instrument used to assess sleep quality. Research such as that of Mohammadi et al.(24), Zuraikat et al. (3) and Godos et al. (20) used the Pittsburgh Sleep Quality Index (PSQI), a validated subjective questionnaire. In all these cases, significant associations were observed between greater adherence to the Mediterranean diet and better sleep quality, expressed as longer duration, shorter latency and less frequent interruptions. However, studies such as Verkaar et al. (2) and Hashimoto et al. (28) used objective measures such as actigraphy did not report significant relationships. This difference suggests that the effects of the Mediterranean diet may be more related to the subjective perception of rest than to measurable physiological parameters such as those mentioned above. However, this does not invalidate the positive effects of diet, and raises a possible difference in the type of impact where diet may improve sleep quality from the point of view of overall well-being or perception of rest, although this is not always reflected in objective data collected by devices. Another determining factor is the profile of the people included in each study. For example, Godos et al. (20) observed that the beneficial effects of the Mediterranean diet were more clearly manifested in people with normal weight, in contrast to Oliveira et al. (30), which included participants with obesity and other health conditions, the relationship between diet and sleep was less evident. In addition, when comparing studies with similar results, relevant differences can be observed in the indicators evaluated. For example, both Zuraikat et al. (3) how Jansen et al. (26) agreed that greater adherence to healthy eating patterns and especially those similar to the Mediterranean was associated with fewer nighttime awakenings and greater sleep efficiency. However, only the first of these studies also evaluated the latency to fall asleep, a variable in which a significant improvement was observed. Otherwise, studies with negative results, such as those of Verkaar et al. (2) and Hashimoto et al. (28), used different methodologies and not only that, but also in the sample size and sociocultural context. These differences can affect both the way in which information is received and the Mediterranean pattern is applied, as well as the way in which sleep is experienced and perceived. Finally, research such as that of Ramón-Arbués et al. (29) and Zaidalkilani et al. (27) agree that low adherence to the Mediterranean diet is related to poorer sleep quality, despite having been conducted in very different contexts such as Spanish university students and Arab women with insomnia.

***Table 2**. Studies relating the ketogenic diet to the quality/quantity of sleep.*

Author , year	**Type of study**	**Population**	**Age range**	**Feature**	**Results**	**Dietary pattern**
Shaw et al. 2022 (16)	Randomized, controlled, crossover clinical trial (pilot)	36 military men	Media: 36 years old	This pilot study examined the effect of a 2-week ketogenic diet compared with a carbohydrate diet in military personnel on sleep and heart rate variability.	A 2-week induction to a ketogenic diet in male military personnel does not appear to affect sleep, but it may reduce heart rate variability, which indicating increased physiological stress.	Ketogenic
Iacovides et al. 2019 (32)	Randomized controlled clinical trial	11 participants	Media: 30 years	To determine the effects of a CD compared to a high-carbohydrate, low-fat isocaloric diet on cognitive function, sleep, and mood in healthy, normal-weight individuals.	Sleep quality and morning alertness did not differ between dietary interventions.	Ketogenic
Henderson et al. 2023 (33)	Randomized crossover trial	7 military men	Media: 34 years old	To examine the effect of a 2-week CD, compared with a CHO-based diet, on subjective sleepiness during 36 h of prolonged wakefulness in military personnel.	The 2-week CD, compared to the CHO-based diet, demonstrated beneficial effects sleepiness during 36 h of prolonged wakefulness in military personnel male.	Ketogenic

Compared to the Mediterranean diet, the ketogenic diet has received less attention for investigation regarding its relationship to sleep quality. In this review, only three studies were found that directly analyze this connection and clearly focus on the targets, and two of them were conducted in military populations (33,34), making it difficult to generalize the results to the adult population as a whole. Existing studies, such as those conducted by Shaw et al. (16), Iacovides et al.(32) and Henderson et al. (33) agree that the ketogenic diet does not appear to negatively impact sleep quality in the short term and under controlled conditions. In certain circumstances, positive effects have been observed (16,33), especially in situations of prolonged wakefulness or when alertness is required in cognitively demanding contexts, such as in military environments. In this sense, the ketogenic diet could benefit cognitive performance and attention under certain conditions. Although this does not necessarily imply an objective improvement in sleep quality. Compared with other isocaloric diets (32), mainly high in carbohydrates, no significant differences in sleep parameters such as latency, duration or efficiency have been found. This suggests that the ketogenic diet not only does not improve sleep, but also does not negatively affect it, at least in young, healthy adults. However, minor complications have also arisen. For example, the study by Shaw et al. (16) identified a decrease in heart rate variability during diet implementation which could indicate an increase in physiological stress during the ketosis adaptation phase. This aspect could influence sleep quality if it were to persist over time, although the studies reviewed have not reported significant alterations in sleep quality associated with this phenomenon. It should be emphasized that the current evidence on the ketogenic diet and its impact on sleep remains limited. Most studies have small samples, short intervention periods and have been conducted in specific contexts. With all of the above, more research needs to be conducted, especially with varied populations and in long-term application scenarios, as, two of the three studies were conducted in young, healthy men under controlled military conditions. This gives the possibility of an important bias, since it does not allow us to evaluate how this diet might behave in middle-aged adults, women, or people with already diagnosed sleep disorders. When comparing the Mediterranean diet and the ketogenic diet in relation to their impact on sleep, several significant differences can be noted in terms of the results and the quality of the available evidence. First, the Mediterranean diet is supported by a considerable number of studies that positively link it to sleep quality (3,20-22,24,26-29). The variety of methodological approaches, the diversity of the populations investigated and the consistency of the results strengthen this pattern as an effective tool to improve sleep. In contrast, the ketogenic diet has been scarcely addressed in this context. Only three studies have been identified in this review that specifically evaluate their relationship with sleep, and that meet the requirements. In addition, two of these studies were carried out in a military population (33,34), which seriously limits their applicability to other profiles. Furthermore, none of these studies used validated sleep quality scales such as the PSQI, making direct comparison with the Mediterranean diet studies difficult.

In the study by Iacovides et al. (32), conducted in healthy young adults, no significant differences were observed between the ketogenic diet and a high-carbohydrate diet in terms of sleep duration or sleep efficiency. Shaw et al. (34) also did not identify direct negative effects on sleep, although they detected a reduction in heart rate variability, possibly associated with increased physiological stress during metabolic adaptation,

and Henderson et al. (33) as a result obtained a lower subjective sleepiness during prolonged wakefulness under ketogenic diet, but without directly assessing sleep quality. These results are limited and do not allow consistent benefits to the ketogenic pattern. On the other hand, studies on the Mediterranean diet not only show subjective improvements in sleep, but are also reflected in different cultural settings and levels of health. Thus, for example, benefits have been observed in Spanish university students (29) Iranian women (24), American women (3) and Italian adults (20), this strengthens the validity, as all have consistent methods for measuring sleep quality. In addition, the feasibility and sustainability of each dietary pattern should be considered. The Mediterranean diet, being based on common, culturally accepted foods, has a high long-term adherence (3,20,22)

Discussion and conclusions

After the analysis carried out in this study, it can be concluded that the dietary patterns evaluated, in particular the Mediterranean diet, have a relevant potential as a tool to promote sleep quality in healthy adults. Regarding the Mediterranean diet, its association with improvements in parameters such as sleep latency, duration or efficiency has been supported by a consistent base of studies where these have been conducted in diverse populations and using varied methodologies, and on the contrary, the ketogenic diet, despite not having shown negative effects on rest in the studies reviewed, nor favorable effects, still does not have the necessary evidence to be recommended for this purpose. In conclusion, the Mediterranean diet stands out as a dietary pattern for the improvement of sleep quality, but it would be necessary to incorporate longitudinal studies, with representative population samples, to understand more clearly only the effects of diet on sleep.

Conflict of interest

There is no conflict of interest.

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Levels of depression symptoms and consumption of ultra-processed foods in university students

Niveles de síntomas de depresión y consumo de alimentos ultraprocesados en estudiantes de Ciencias de la Salud.

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Depression, ultra-processed foods, NOVA, university students

ABSTRACT

Depression is a common mental disorder characterized by a depressed mood or loss of interest and pleasure in daily activities over prolonged periods. This condition can influence basic decisions such as eating habits. Currently, the high availability of ultra-processed foods (UPF) and fast-paced lifestyles have encouraged their consumption due to their quick preparation and extended shelf life. The increase in the intake of these products has generated significant health repercussions by contributing to inadequate nutrition and a higher risk of obesity, hypertension, and vascular and metabolic diseases. The objective of the present study was to analyze the relationship between the levels of depressive symptoms and the consumption of UPF among university

students in the health sciences field. This was a descriptive, observational, cross-sectional, and correlational study. It was conducted with a population of 179 students from the Nutrition and Nursing academic programs, considering the following variables: sex, age, depressive symptoms —assessed using the DASS-21 scale—, depression level, and consumption of ultra-processed foods in kilocalories, based on the NOVA classification. Dietary intake was evaluated through a food and beverage diary. As a result, a positive relationship of moderate strength was observed between the score of depressive symptoms and UPF consumption (rho = 0.493, with a 99% confidence level), indicating a higher consumption of UPF as depressive symptom scores increased.

RESUMEN

Keywords:
Depresión, ultraprocesados, NOVA, universitarios.

La depresión es un trastorno mental común caracterizado por un estado de ánimo deprimido o por la pérdida del interés y el placer en las actividades cotidianas durante periodos prolongados. Este trastorno puede influir en decisiones básicas como la alimentación. En la actualidad, la alta disponibilidad de alimentos ultraprocesados (AUP) y los estilos de vida acelerados han favorecido su consumo, debido a su rápida preparación y prolongada vida de anaquel. El incremento en la ingesta de estos productos ha generado importantes repercusiones en la salud, al contribuir a una alimentación inadecuada y al aumento del riesgo de padecer obesidad, hipertensión y enfermedades vasculares y metabólicas. El objetivo del presente estudio es analizar la relación de los niveles de síntomas de depresión y del consumo de los AUP en estudiantes universitarios del área de ciencias de la salud. Es un estudio descriptivo, observacional, de tipo transversal y correlacional. Se llevó a cabo con una población de 179 estudiantes del programa educativo de nutrición y enfermería, teniendo como variables: sexo, edad, los síntomas de depresión - evaluados mediante la escala DASS-21-, nivel de depresión y el consumo de alimentos ultraprocesados en kcals, basándose en la clasificación NOVA. Se evaluó mediante Diario o registro de alimentos y bebidas. Como resultados, se observó una relación positiva con una fuerza moderada, de la relación entre el puntaje de síntomas depresivos y el consumo de AUP, ya que obtuvo rho= 0.493 con un nivel de confianza del 99%, aprecia un mayor consumo de AUP conforme aumenta la puntuación en los síntomas de depresión.

Introduction

A balanced and adequate diet that meets the macro and micro needs of students and youth is necessary to maintain good health and physical activity for a variety of daily activities. On the contrary, an unbalanced diet can lead to malnutrition, either by caloric shortage or excess, manifesting itself in the form of underweight or obesity (1). The latter can lead to weight loss and obesity. Adolescence and youth represent key stages for the acquisition of healthy habits, and it is during this period that eating patterns can be consolidated or, on the contrary, deteriorate due to multiple factors. Academic demands, fast-paced lifestyles, social pressure, and easy access to products of low nutritional value have led to an environment in which dietary decisions are driven more by convenience than by well-being (2). This reality has generated a growing concern in the scientific community, especially when observing the correlation between the type of food ingested and the impact it can have on mental health (3).

Accumulating evidence suggests that low-quality diets, particularly those rich in ultra-processed foods, are not only associated with adverse metabolic conditions (4) but also with impaired affective states (3). This link can be explained from a physiological perspective: a diet rich in simple sugars, trans fats and additives can trigger chronic low-grade inflammatory processes, alter the hypothalamic-pituitary-adrenal axis and affect the intestinal microbiota, all mechanisms associated with the onset of depressive symptoms (7). In view of this, consumption of ultra-processed foods represents a quarter in developing countries and more than half in high-income countries. According to the Pan American Health Organization (PAHO) health Organization (PAHO) (2)in 13 Latin American countries: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Mexico, Peru, Uruguay and Venezuela, between 2000 and 2013, sales of Ultraprocessed Foods (AUP) has grown rapidly by 26.7%. In Peru, per capita consumption of ultraprocessed foods grew by approximately 22% between 2009 and 2014**,** an increase that has been associated with increased body weight and higher prevalence of obesity and arterial hypertension in the population, especially in children and young people (4).

For some years now, the relationship of UPA consumption with risk factors such as obesity, hypertension, vascular and metabolic disease has been documented (5). At the societal level, it is also important to note that the food environment has evolved into an industry-dominated model, where advertising messages and misleading labeling significantly influence consumer choices, especially among younger consumers (2, 6). This phenomenon, known as "obesogenic environment", has been widely described as a structural factor that hinders access to and preference for healthier options, favoring the perpetuation of UPA consumption and its consequences (5, 6).

These foods are subjected to industrial processes in order to modify their natural conditions, allowing their preservation and improving their appearance, with the purpose of prolonging their shelf life and making available to the consumer a wide variety of products throughout the year, regardless of seasonality. The application of these processes varies their nature and alters their nutritional profile (4, 6).

The term "ultra-processed," according to Monteiro (6) is defined as; "Formulations of various ingredients that, in addition to salt, sugar, oils and fats, include food substances not used in culinary preparations, in particular, flavorings, colorings, sweeteners, emulsifiers and other additives used to imitate the sensory qualities of unprocessed or minimally

processed foods and their culinary preparations, or to mask undesirable qualities of the final product".

In addition, changes in lifestyle have modified the dietary pattern of society. The increase in the production of industrialized foods has also favored the growth of marketing and the greater availability of beverages and ultra-processed foods. This group of products contributes the highest amount of calories, saturated fats, sugars and preservatives to the diet, contributing to the development of metabolic diseases (7). Recent research also suggests a possible association between its consumption and the presence of depressive symptoms (3). In this sense, ultra-processed foods can not only affect the metabolism in a negative way, but also be related to mood states such as depression.

In general, emotions play an important role in the choice, quality and quantity of food eaten, which affects the increase or decrease in body weight. The relationship between emotions and eating behavior is bidirectional and depends on the context, the variability of emotions in terms of valence, arousal and intensity, as well as the physiological variability of the subject. There are also differences in food intake. This is related to the intensity of emotions; human beings ingest more food in the presence of positive or negative emotions than in the presence of neutral emotions, which explains why the greater the intensity of the emotions experienced, the greater the food inhibition. Control that is often found even in people who have dietary restrictions or strict diets (8).

According to the American Psychiatric psychiatric Association (9) defines depression as: "A mood disorder, where the main characteristic is an alteration of mood and, according to its temporality and symptomatic origin, has a particular classification; in this way, major depressive disorder, dysthymic disorder and bipolar disorders are distinguished as the main ones. The World Health Organization (WHO) (10)refers to depression as: "a common mental disorder. It involves a depressed mood or loss of pleasure or interest in activities for long periods of time." Therefore, depression does not always occur in the same way and is not always considered in the same context for all people, therefore, there are multiple types of classifying depression depending on the symptomatology according to the National Institute of Mental Health (NIMH) (11).

Against this background, there have been studies that have analyzed the relationship between consumption of UPAs and depression in different population groups, such as the one that examined the association between high consumption of ultra-processed foods (UPAs) and recurrence of depressive symptoms (DepS) in a British population group, in general relationship between diet and depression, with the result that high consumption of ultra-processed foods is associated with increased likelihood of recurrent depressive symptoms, and contribute to the overall association between diet quality and depressive symptoms(12). Scientific evidence has been accumulating that frequent and excessive consumption of UPA not only has implications for physical health, but is also associated with the development of mental disorders, particularly depression (7). Depression, previously considered a purely psychological disorder, has been progressively recognized as a multifactorial disease in which genetic, environmental, emotional and also dietary aspects converge. Some recent studies have identified dietary patterns based on ultra-processed products as an important risk factor in the onset or recurrence of depressive symptoms, especially in youth and young adults (12, 7).

Therefore, understanding the relationship between the consumption of ultra-processed foods and the mental health of university students in the Health Sciences area is

fundamental, not only because of its clinical implications, but also because of the impact it may have on their academic performance and quality of life. In addition, this group represents the future food educators and promoters, whose own well-being and nutritional habits will be decisive for the formation of healthy behaviors in the population they will guide in their professional practice. This population group represents a critical transition stage, in which factors of emotional vulnerability and food autonomy are combined, which makes students a key population for the implementation of prevention and health promotion strategies. The objective of this study was to determine the relationship between the level of depressive symptoms and the consumption of AUP foods in new students of the health sciences area of a university in southeastern Mexico.

Method

2.1. Type of study

It is a descriptive and correlational study, oriented towards the collection and analysis of numerical data to examine the proposed hypothesis, based on the interrelation between the level of depressive symptoms and the consumption of AUP. Using statistical analysis techniques, with the objective of determining the relationship between the level of depressive symptoms and the consumption of ultraprocessed foods in new university students.

This study was evaluated and approved by the Ethics Committee of the Universidad Internacional Iberoamericana, in its session of March 31, 2023.

2.2. Sampling

The study was conducted with a population of 179 first-year students of the nutrition education program (PEN) and the nursing education program (PEE) at the Faculty of Health Sciences of a public university in Ciudad del Carmen. Stratified probability sampling was used, taking the educational program as the stratum. The sample size was calculated using nQuery Advisor Version 4.0 software, based on a confidence level of 95% and a margin of error of 5%. A sample of 118 participants was determined, distributed among 80 nursing students and 38 nutrition students.

The inclusion criteria were: students enrolled in the first semester of the Educational Programs of Nutrition and Nursing, who wished to participate voluntarily in the study, without previously diagnosed chronic degenerative pathologies, and who were not taking medications that could affect blood pressure. Exclusion criteria: students who were not present during data collection, students who were in advanced semesters, students from other educational programs. And as elimination criteria; surveys with incomplete data, students who did not want to continue in the study, inconsistent or contradictory data in the answers provided.

2.3. Variables and their measurement

The variables that were analyzed were: sex, age, symptoms of depression and level of depression. For the latter, the abbreviated version called Depression, Anxiety and Stress Scales - 21 (DASS-21) was used, which fulfills the objective of evaluating the presence of negative affect of depression and achieving maximum discrimination between these conditions (13), applying it to each of the participants in the study, and using the cut-off

points indicated by the same scale for depression: 5-6 pts. mild depression, 7-10 pts. moderate depression, 11-13 pts. severe depression, 14 pts. or more extremely severe depression (14).

The consumption of ultra-processed foods was evaluated by means of a food and beverage diary or register, requesting the completion of the form provided to the participants, during three days, including a weekend day, using for the estimation of portions; photographic models with reference to objects of daily life (15). Calories from ultraprocessed foods were estimated using the Nutrein software, free of charge and freely available on the Internet, which manages the Mexican food equivalents system, and counts calories and nutrients consumed from the foods recorded (16).

This program was used to obtain the total kcal consumed on each of the recording days, as well as the kcal from the UPAs, which were identified from a list of regional UPAs based on the NOVA system (17) which defines the categories and criteria for classifying foods and beverages according to the degree of industrial processing of the food. The program was also used to calculate the sodium consumption in mg and sugars in g per day by the participants. These calculations were carried out by an expert in dietary calculations, the same person who was in charge of receiving the food records and verifying with the participants whether what was recorded in the food diary forms was correct.

2.4. Code of Ethics

The study adhered to the provisions of the regulations of the Regulations of the General Health Law on Health Research 1987, considering the latest reform (Ley General de Salud en Materia de Investigación para la Salud, 2014)(18). Also to the Mexican Official Standard NOM-012-SSA3-2012, which establishes the criteria for the implementation of research projects for health in humans, so that there was informed consent of the subjects who participated in the research, which included the aspects required to provide the necessary information, the data collection was carried out by health professionals, with knowledge and experience to care for the integrity of the human being (19).

2.5. Type of data analysis.

The Statistical Package for the Social Sciences (SPSS) version 23.0 for Windows was used for data analysis. Descriptive and correlational statistics were used. Descriptive analysis was performed using frequencies, proportions, measures of central tendency and variability. The Kolmogorov-Smirnov normality test was performed to determine the normality of the variables. Simple ordinal regression using Sperman's correlation statistical test was used to evaluate the association between the level of depression as an independent variable and the possible associated factor as a dependent variable, consumption of UPA in kcal, with a 95% confidence interval. As well as Student's t-test, to analyze the statistical difference in the means of UPA consumption and depression levels, between the nutrition and nursing educational programs.

Results

The study population was 179 students and the sample obtained from incoming students (n=118), being 80 Nursing students and 38 Nutrition students. Obtaining as a result 78 % (n=92) of females and 22 % (n=26) of males in the study, with an average age

of 20±4 years, both in the general sample and in the PEE that registered a SD±5 years, and in the PEN it was 19±2.5 years showing a lower SD, indicating that the age of the PEN students is more homogeneous than that of the PEE students.

Of the total kcal consumption in the global registry, the mean was 1618±551 kcal, in the nursing students it was 1641±565 kcal and in the nutrition students it was 1569±525 kcal, it is worth mentioning that no statistically significant difference was identified between the two educational programs p=0.510. By sex in men the mean was 1732±564 kcal, and in women it was 1586±547 kcal, the analysis shows that there is no statistically significant difference p=0.235 between sexes as shown in Table 1.

Table 1
Overall caloric intake by educational program and sex

Variable	Ẋ	DE	*p*
Overall consumption	1.618	551	-
Educational program			
Nursing	1.641	565	*p* = .510
Nutrition	1.569	525	
Sex			
Men	1.732	564	*p* = .235
Women	1.586	547	

Note. Values correspond to the mean (Ẋ) and standard deviation (SD) of the overall calorie intake. Statistical significance was determined by Student's *t* test for independent samples.

In the Table 2 it can be observed that the average consumption of total kcal from AUP in the overall consumption was 750±401, in nursing students it was 745±360 kcal and in nutrition students it was 761±480 kcal, it is worth mentioning that no statistically significant difference was identified between both educational programs p=0.839. By sex in men the mean was 783±419 kcal, and in women it was 741±397 kcal, the analysis shows that there is no statistically significant difference p=0.644 in kcal consumption from AUP between both sexes

Table 2
Overall consumption of calories from ultra-processed foods by educational program and sex

Variable	Ẋ	DE	*p*
Overall consumption	750	401	-
Educational program			
Nursing	745	360	*p* = .839
Nutrition	761	480	
Sex			
Men	783	419	*p* = .644
Women	741	397	

Note. Values correspond to the mean (Ẋ) and standard deviation (SD) of the consumption of calories derived from ultra-processed foods. Statistical significance was determined by Student's *t* test for independent samples.

Similarly, it is observed that, in terms of the classification of levels of depression, 71% (n=84) of the students in the general sample are classified at some level of depression, and 58% (n=69) are between moderate and extremely severe. In addition, the levels corresponding to severe and extremely severe, are higher in the Nutrition educational program 43 % (n=16), compared to Nursing 22 % (n=26) and the overall sample 35.5 % (n=42) as shown in Table 3 Table 3.

Table 3.

Results of frequencies of depression levels in participants.

	General Sample		**Nursing**		**Nutrition**	
Level of Depression	***f***	**%**	***f***	**%**	***f***	**%**
Normal (absence of depression)	34	28.90	21	26	13	34
Slight	15	12.70	10	13	5	13
Moderate	27	22.90	23	29	4	10
Severa	22	18.60	14	17	8	21.50
Extremely Severe	20	16.90	12	15	8	21.50

TOTAL	118	100	80	100	38	100

Source: Own elaboration. *f*: absolute frequency, *%*: percentage.

In the Figure 1 a positive relationship with moderate strength is observed, as a result of the relationship between levels of depressive symptoms and consumption of AUP, since it obtained rho= 0.493 with a confidence level of 99%, so that a higher consumption of AUP is visualized as a higher score is obtained in the symptoms of depression levels in some of the students.

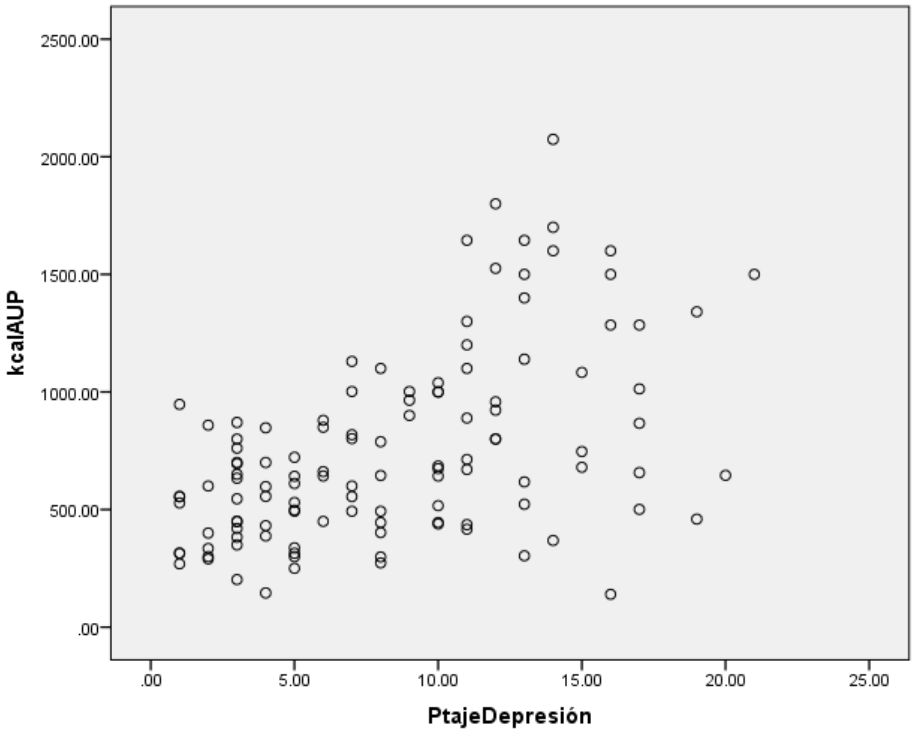

Figure 1. Correlation results of Kcal from AUP and depression levels.

Discussion and Conclusions

If we consider the daily calorie intake recommendations by the WHO (20) (20) which should be between 1,600 to 2,000 kilocalories per day for women and between 2,000 to 2,500 kilocalories for men, and compared with the caloric intake recorded in this study; in the women, 1586±547 kcal and in the men an average of 1732±564 kcal, it can be seen that the averages were close to what is considered optimal for an average person; however, it is imperative to emphasize that the recommended kcal consumption is individual, therefore, it is difficult to ensure that the consumption recorded was convenient for all the participants.

The results obtained in this investigation were consistent with those reported by Detopoulou and colleagues (21), who conducted a study on the consumption of ultra-processed foods (UPA) in students from different academic areas of the University of Peloponnese, in Greece, including the field of health sciences. In that study, the authors observed that 44.3 ± 11.9 % of the daily caloric intake came from UPA. In the present work, considering an average caloric intake of 1618 ± 551 kcal and an intake of 750 ± 401 kcal derived from UPA, it was estimated that approximately 46 % of the total energy consumed by the participants came from this type of food. These findings reflect a remarkable similarity between the two populations and suggest that high consumption of UPAs is a common problem among college students, regardless of geographical or contextual differences.

The results obtained for the levels of depression exceed those obtained by Ramón and Cabrera(22) in a study carried out with university nursing students, where the levels of depression reached the following percentages: 55.2 % obtained some degree of depression where 17.6 % (n=39) present a mild level, 16.7 % (n=37) a moderate level 7.2 % (n=16) a severe level and 13.6 % (n=30) an extremely severe level, while in this study the results of depression obtained were 71.1 % some degree of depression where 15 12.7 % (n=15) presented a mild level, 22.9 % (n=27) moderate level, 18.6 % (n=22) severe level and 16.9 % (n=20) extremely severe. This may be due to several factors, the first one being that the study conducted by Ramón and Cabrera (22) this differs from the sociocultural and economic expressions of university students in Mexico, and the sample used by these researchers is almost twice the size of the one used in this study.

The results of the present study evidenced a positive and moderate relationship between the consumption of ultra-processed foods (UPA) and the presence of depressive symptoms ($\rho = 0.493$; 99 % CI), suggesting that, as depressive symptomatology increases, so does the consumption of this type of products. When contrasting these results with those reported by José and collaborators (23), relevant coincidences are observed, carried out with students from a public university in Brazil, it was identified that 38.9 % of the participants presented a high consumption of AUP, with a mean of 4.5 points (95 % CI): 4.3-4.7). Although the authors found no significant differences between UPA consumption and the presence of depressive symptoms, they did report that a higher intake of fresh or minimally processed foods was associated with a lower likelihood of depressive symptoms. In contrast, the findings of the present study show a statistically significant association between UPA consumption and depressive symptomatology, which could be explained by cultural, contextual or methodological differences, such as the instruments used for the assessment of mental health, the time of the academic cycle in which the measurement was applied or the particular psychosocial conditions of the university environment.

The moderate strength of the observed correlation reinforces the hypothesis that a diet based on ultra-processed products could be related to an increased risk of emotional disturbances. Several studies have supported this trend, indicating that a diet high in PUFAs - characterized by their low nutritional value and high content of saturated fats, sugars and additives - can negatively affect mood regulation through metabolic and inflammatory mechanisms, alterations in the intestinal microbiota and reduced availability of neurotransmitters linked to psychological well-being (24, 25).

Similarly, the results of the present study coincide with the findings of Contreras-Rodríguez and collaborators (26), who analyzed fifty-two adults subjected to a dietary regimen, simultaneously evaluating their depressive symptoms, anatomical parameters by

magnetic resonance imaging and various biochemical indicators. These authors reported that higher consumption of ultra-processed foods (UPA) was associated with higher levels of depressive symptomatology in the total participants (r = 0.178; 95 % CI: 0.008-0.261) and, particularly, in those with obesity (r = 0.214; 95 % CI: -0.004-0.333).

In agreement, in the university population analyzed in this study, a positive and moderate relationship was observed between UPA consumption and the categories of depressive symptoms (ρ = 0.498; 99 % CI), indicating that the greater the severity of depressive symptoms, the greater the caloric intake derived from this type of food. In other words, students with severe or extremely severe levels of depression showed significantly higher consumption of UPA than those with mild symptomatology, reinforcing the evidence that diet may play an important role in the manifestation and maintenance of depressive states.

CONCLUSIONS

The results of the present study show a direct and moderate relationship between depressive symptoms and the consumption of AUP in university students in the area of Health Sciences. This finding is particularly relevant, given that these are future professionals in charge of promoting healthy habits and lifestyles. The inconsistency between the knowledge acquired during their academic training and their own dietary practices could represent a challenge for their professional performance and for the credibility of the health interventions they carry out in the future.

In this sense, the implementation of interdisciplinary strategies, particularly in the areas of nutrition and psychology, by higher education institutions, is essential to address this problem in a comprehensive manner. Such strategies could contribute not only to improving the mental and physical health of students, but also to strengthening their role as promoters of wellness within and outside the university environment.

Among the main limitations of the study is the small sample size, which could limit the generalizability of the results. Also, the cross-sectional design precludes establishing causal relationships, and the absence of additional variables, such as academic stress or sleep habits, restricts a broader understanding of the situation.

For future research, it is recommended to include clinical diagnoses of depression confirmed by psychologists, as well as to incorporate biochemical indicators to identify possible related metabolic risks. In addition, it would be pertinent to conduct longitudinal studies to establish causal relationships between UPA consumption and depressive symptomatology, and to explore the mediating role of factors such as academic stress, physical activity and sleep patterns.

Similarly, it is suggested to continue analyzing the relationship between depression and UPA consumption in conjunction with other physiological and psychosocial indicators, in order to strengthen the evidence on the comprehensive risks that this relationship entails. This study also opens the possibility of new lines of research aimed at understanding the social, cultural and environmental factors that influence the dietary decisions of young university students.

The academic environment plays a determining role in the adoption or abandonment of healthy habits. Therefore, universities should take an active role in promoting healthy eating environments, through the regulation of eating spaces, clear nutritional education and

the provision of accessible psychological counseling. These actions can have a positive impact on the mental and physical health of students.

Furthermore, the observed relationship between PUA consumption and negative emotional states, such as depression, suggests a potentially harmful feedback loop: high consumption of these products may contribute to the development of depressive symptoms, while depression may, in turn, increase PUA consumption as an emotional coping mechanism in the face of academic or personal stress. This model strengthens a risk dynamic that must be identified and addressed in a timely manner.

Finally, this phenomenon should not be interpreted in isolation, but as part of a broader context that involves the challenges of the educational system, socioeconomic conditions, family dynamics, the media and national food policies. Therefore, the consumption of ultra-processed foods and their effects on mental health should be addressed from an approach in which the system combines interventions at the individual level with collective initiatives aimed at comprehensive wellness.

In conclusion, the present study makes visible a growing problem in the university population, particularly in those who are being trained as future health agents. Addressing the relationship between UPA use and depressive symptomatology is an essential step in building healthier, more resilient and coherent university environments where students can fully develop their professional potential without compromising their emotional and physical well-being.

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Conflict of Interest

The authors involved in this research declare that there is no conflict of interest.

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Correlation between the rate of adherence to the safe surgery checklist by healthcare professionals and the appearance of surgical complications

Correlação entre o índice de adesão ao checklist da cirurgia segura pelos profissionais de saúde e a ocorrência de complicações cirúrgicas

Correlación entre la tasa de adherencia a la lista de verificación de cirugía segura por parte de los profesionales de la salud y la aparición de complicaciones quirúrgicas

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ABSTRACT

Introduction: The aim is to investigate whether there is a direct correlation between the rate at which healthcare professionals adhere to the Safe Surgery Checklist (SSC) and the occurrence of surgical complications. To examine the current rates of application of the CCS, as well as to analyze how the use of the CCS contributes to the hospital's administrative and financial management. A cross-sectional, documentary, retrospective study with a quantitative approach. Non-experimental design and descriptive statistical analysis, using information collected from sectors related to patient safety, 240 surgical records *(n=240)* and the contract signed between the research setting and the city hall. The correlation value between the use of CCS and the occurrence of surgical complications was 0.006, which is considered low as the *phi correlation* coefficient (Φ) varies between -1 and +1. The highest rate of use of the checklist was 88.2% of the operations carried out and the lowest, 58.8%. The surgical checklist makes a significant contribution to the management of the hospital in question, because the more it is used, the greater the amount of funds transferred via the Unified Health System. Although the correlation found between adherence to the CCS and the occurrence of surgical complications was low, it is possible to defend its use as a tool that provides greater safety

for surgical patients, since each item on the checklist represents the chance of avoiding a harmful episode for the patient undergoing an operation. There is a need to improve the rate of application of the CCS, which is still a challenge for hospital management.

RESUMO

Palavras chave:

Segurança do Paciente; Cirurgia Segura; Qualidade em Saúde; Complicações Cirúrgicas; Checklist

Introdução: o objetivo é investigar a existência de correlação direta entre o índice de adesão dos profissionais de saúde ao Checklist da Cirurgia Segura (CCS) e a ocorrência de complicações cirúrgicas. Examinar os índices atuais de aplicação do CCS, bem como analisar de que maneira o uso do CCS contribui com a gestão administrativa e financeira do hospital. Pesquisa transversal, documental, retrospectiva com abordagem quantitativa. Desenho não experimental e análise estatística descritiva, sendo usadas informações coletadas nos setores relacionados à segurança do paciente, nos 240 prontuários cirúrgicos *(n=240)* e no contrato firmado entre o cenário da pesquisa e a prefeitura da cidade. O valor da correlação entre o uso do CCS e a ocorrência de complicações cirúrgicas foi de 0,006, considerado baixo, pois, o coeficiente de *correlação phi (Φ)* varia entre -1 e +1. O maior índice de utilização do checklist foi 88,2% das operações realizadas e o menor, 58,8%. O checklist cirúrgico contribui sensivelmente para a gestão do hospital pesquisado, pois, quanto maior é seu uso, maior o quantitativo de recursos repassados via Sistema Único de Saúde. Apesar de a correlação encontrada entre a adesão ao CCS e a ocorrência de complicações cirúrgicas ter sido baixa, é possível defender sua utilização como uma ferramenta que proporciona maior segurança aos pacientes cirúrgicos, pois, cada item do checklist representa a chance de evitar um episódio prejudicial ao paciente submetido a uma operação. É preciso melhorar o índice de aplicação do CCS, representando ainda um desafio à gestão hospitalar.

Introduction

It cannot be said that addressing the *quality of health services* and one of its dimensions, *patient safety*, is something new. Although it is a topic that has gained relevance more recently in Brazil, historical accounts show that healthcare-related infections (HAIs) and other related (non-infectious) problems are as old as the very emergence of hospitals (325 A.D.). For many centuries, patients were treated in hospitals with precarious sanitary conditions, which aggravated their health due to the proliferation of diseases. Often, they died from an illness contracted in hospital, rather than from the one that led to their hospitalization. This situation began to worry health care workers and organizations (1).

Hippocrates (460 B.C.), considered the father of medicine, is credited with the postulate *"Primum non nocere"*, which in free translation from Latin means, "First do no harm", i.e. the concern not to cause harm to the person who needs to use the health service is already quite old, as it was also already admitted that the execution of this service could cause some kind of harm (1-2).

Following this idea of not causing harm to users in health facilities, Ernest Codman, a doctor from the United States (Massachusetts), advocated improving the conditions of health facilities in order to achieve efficient results in the treatment of patients. He created the first method for monitoring the outcome of care in order to guarantee the quality of the medical services provided. And in 1917 Codman created a set of hospital standards (minimum standards) that form the basis of the mechanisms for evaluating health services known as *Accreditation*. These minimum standards refer, for example, to the need for every hospital to have a clinical laboratory unit and an X-ray unit (3).

The work entitled "*Diseases of Medical Progress*", carried out by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in 1918, showed the frequent occurrence of *iatrogenic* diseases in healthcare centers, which are ailments caused to patients by *poor medical practice*, not stemming from their underlying disease, and are therefore *preventable*. Given this fact, the need to incorporate a *safety culture* in care institutions that sees failures and adverse events (AEs) as the consequence of a *poorly designed system* that produces bad results, and not as the result of the actions of *bad* people, was already confirmed. Therefore, it must be considered that errors result from the interaction of various factors and the whole situation must be approached holistically (integrally). It's also important to see these mistakes as a chance to learn, to improve the whole (the system) and to avoid harm by finding ways to prevent them from happening again, for example through *safe clinical practices,* risk management and root cause analysis of adverse events. Possible damages include illness, injury, disability and death (3-4).

It is clear, therefore, that there is a need for a systematic debate to improve healthcare processes, considering the numerous and rapid changes that have taken place in procedures and equipment aimed at the care area, the awareness of users about their right to access healthcare, which is considered a "good", and also society's growing questioning of the *quality* and *safety* offered by care institutions, since cases of adverse events occurring in patients are not uncommon in the press around the world (3-5).

Among the procedures needed to prevent and reduce the occurrence of EVs are the adoption of standards and procedures aimed at user safety, through good practices, and the acceptance of a *patient safety culture* by healthcare establishments. Another

action would be the compulsory inclusion of this topic in training courses for health professionals, at all levels: technical, undergraduate and postgraduate (4).

In order to build safe user care, it is necessary to understand the risks, admit that they exist, study the relationship between the health service and the occurrence of harmful incidents, and also monitor and manage episodes that could be harmful to patients (5).

At the 57th World Health Assembly in 2004, the World Health Organization (WHO) launched a program called the "Global Alliance for Patient Safety". Among the important actions of this alliance aimed at improving the care provided is the "Safe Surgery Saves Lives" campaign, the aim of which is to reduce the morbidity and mortality caused by surgical procedures, seeking to raise awareness in health units about the importance of safe surgery and the application of safe procedures in operations (6). Brazil is a member of this alliance. As a way of reducing risks and mitigating adverse events, the WHO included the use of *checklists* for *healthcare* as a whole after confirming the success of the Safe Surgery Checklist (SCC) (7).

With this in mind, the World Alliance for Patient Safety has developed the "International Safety Targets" to improve the most worrying non-conformities within healthcare institutions. Among the six goals created is *Goal 4*, which refers to ensuring that surgeries are performed on the correct site, procedure and patient (3-7).

It is in the *Surgical Center* that the most complex procedures in a health institution are carried out, because many rules must be followed. Workers are required to have up-to-date technical and scientific skills, responsibility, the ability to work as part of a team, as well as effective communication and interpersonal relationships. And the application of the checklist in surgeries in its three stages: *before induction of anesthesia; before the surgical incision; and before the patient leaves the operating room,* can help reduce surgical complications and thus contribute to patient safety (8). Complications arising from surgery can occur in the preoperative, operative and postoperative periods, and in some more critical situations, a harmful event can lead to the surgical patient's death. Considering the international context, studies show that in the United States, surgical adverse events are the third leading cause of death, surpassing even heart disease and cancer (9).

Studies on the effects of using the surgical checklist have shown that this tool prevents perioperative errors and complications, and have also found that the CCS helps to reduce the rates of complications and mortality from operations, as well as promoting greater patient safety and optimizing the work and communication of the care team (5-8).

In Brazil, the National Patient Safety Program (PNSP) was established with the publication of Ordinance No. 529 on April 1, 2013, representing recognition of the worldwide needs and the urgency that this issue requires. The PNSP includes *basic patient safety* protocols, including the *Safe Surgery Protocol*. Their aim is to *standardize* the practices carried out by care professionals in their activities, preventing and reducing the occurrence of events that result in harm to the user (10).

Given the importance that checklists have been gaining worldwide, including because they are a mechanism that measures the quality of care provided by a health organization, the aim of this research is to analyze the effectiveness of implementing the Safe Surgery Checklist, checking whether there is a relationship between its *use* and the *reduction* of postoperative complications, i.e. its objective is to investigate the existence of a direct correlation between the rate of adherence to the *Safe Surgery Checklist* and the occurrence of surgical complications in patients treated at a public teaching hospital.

Method

Study Design

Cross-sectional, documentary, retrospective study with a quantitative approach. Its design is non-experimental with descriptive statistical analysis. Data and information obtained from the hospital's patient safety departments, surgical records, considering surgeries performed between January/2022 and October/2022, and Contract No. 46/2021 signed by the hospital where the research was carried out and the municipality's management were used.

Place of Research and Period of Data Collection

The research was carried out at the University Hospital of the Federal University of Sergipe/HU/UFS, located in the city of Aracaju/SE, Brazil. This hospital is managed by the Brazilian Hospital Services Company (EBSERH). All the information was collected between June/2023 and September/2023.

Research Focus Population

The population consisted of the medical records of the 4297 surgeries *performed* between January/2022 and October/2022.

Sample Selection Criteria

The sample *included* the medical records of patients who had undergone an operative procedure and *excluded* the medical records of patients seen for outpatient consultations, examinations and hospitalization for clinical treatment.

Sample Definition

The sample is probabilistic, since the population (or universe) is known and has a known and finite size, and the surgical records have the same possibility of being chosen to make up the sample. The sampling strategy used to choose the members of the sample was *systematic probability,* without replacement of the elements of the population (11).

Study Variables

The following *operational* variables were analyzed: total number of surgeries performed in the period; total number of surgeries that had complications/readmissions; rate (%) of surgeries in which complications/readmissions occurred; total number of adverse events officially reported. These variables have a *discrete scale* and the *Ratio* scale is applied, as they are quantitative data with absolute zero, so there is no negative numerical value. The following *qualitative* variables were also examined: occurrence of complication/readmission; use of the checklist; checklist completely filled in. These variables have a *Nominal scale* that only recognizes equality and inequality operations between the elements, for example, $A = A$, $A \neq B$.

Instruments Used to Collect Information

In order to collect, store, organize and analyse the information, two data collection tools were used, built by the researcher. In the first instrument, data was collected to show the current situation of the surgeries carried out within the scope of the research, and in the second, the information collected is aimed at providing data for statistical analysis. *Excel*® spreadsheet software was used to create the two instruments.

Data Collection

All the documentation provided by the hospital departments responsible for patient safety was analyzed *on site* and on working days. The first part of the data was obtained from files and spreadsheets containing the information requested, from the control and organization mechanisms and from the hospital's statistical reports. In the case of medical records, which correspond to the second part of the data, their physical version was studied, as the CCS form is also in physical format. This second piece of information was obtained through an *active search* of medical records.

To access the current monthly rates (considering the study period) of CCS utilization, the statistics report from the Health Care Related Infection Control Service (SCIRAS) was researched, considering surgeries performed between January/2022 and October/2022.

In order to understand how the application of the surgical checklist cooperates with the hospital's administrative and financial management, the clauses of the contract signed with the municipality's management were studied. The contract was made available by the Health Regulation and Evaluation Sector (SRAS). According to the contractual instrument, compliance with the *qualitative targets*, which includes the use of the CCS, totals 72 points. And according to the rate of adherence to the CCS, the hospital achieves a certain score which is distributed as follows: CCS adherence ≥ 85% = **3** points; 70% ≤ CCS adherence **<** 85% = **2** points; 60% ≤ CCS adherence **<** 70% = **1** point; CCS adherence **<** 60% = **0** point.

Thus, the score achieved through the application of the CCS contributes to the formation of the 72 points, and this score, when fully achieved, enables the hospital to receive the *total monthly* contracted amount. If it is not fully achieved in a given month, the amount received is proportional to the points achieved.

Treatment and Statistical Analysis of Data Collected from Surgical Records

To calculate the minimum necessary sample size (n) and to estimate the correlation coefficient between the variables to be correlated, a *pilot sample of 55* surgical records was used. The formula for determining the sample size in a study that correlates two nominal continuous parametric variables such as “occurrence of complication” and “use of the checklist”, for example, which can only have the results “YES” or “NO”, represented by the values 1 and 0, respectively, is shown below in figure 1:

$$nA = \frac{(1-r^2) \times (t_{\alpha;gl})^2}{r^2}$$

Figure 1. Formula for calculating the sample size in a study relating two continuous parametric variables (12)

where $gl = n_p - 2$, where:
n_A = the calculated sample, i.e. the minimum sample required;
r = correlation of the pilot sample;
t = the value of the *Student's t-test* (this is a tabulated value found in the *Student's t Distribution* Table, according to the values of the parameters α and gl);
α = significance level (which was 0.05 or 5%, it is the maximum admissible error, so the Confidence Interval - CI is 95%);
gl = degrees of freedom, since it was necessary to calculate the sample mean (X) and the sample variance (S^2);
n_p = pilot sample size (which was 55).

The researcher must assume a specific value for the correlation, which can be obtained from the literature or through a pilot study, as was the case in this research, since information from 55 medical records was initially used. In addition, it is important to establish the *alpha* α level beforehand (12).

The value of n_A calculated using the above formula was 191.0005 ~ 191. However, it was decided to search a larger number of records, so a total of 240 records were searched, so *n = 240.*

In the statistical analysis, the frequencies of the variables "use of the checklist" (variable X) and "occurrence of complication/readmission" (variable Y) were studied. These are dichotomous variables, so they can only take on two values/results, and in this specific case, they take on the results "yes", represented by the value 1, and "no", represented by the value 0. Under these conditions, the most appropriate method for calculating the correlation between the variables studied in the statistical analysis of this research is the *PHI Correlation Coefficient (Φ)* also known as the *Matthews Cor* relation (13), and this correlation coefficient estimator is derived from the *Pearson Linear Coefficient* estimator, provided that the variable X is also dichotomous and has the following distribution, as shown in figure 2 below:

		Variable		
		X (Yes =1; No = 0)		
Variable	**Y** (Yes =1; No = 0)	a	b	a+b
		c	d	c+d
		a+c	b+d	

Figure 2. Contingency table of the frequency distribution of the variables analyzed (13)

Where a, b, c and d are the frequencies in the contingency table. By equating, we obtain the phi (Φ) equation below, according to figure 3, which calculates the correlation between the variables evaluated.

$$\phi = \frac{(ad-bc)}{\sqrt{(a+b)(a+c)(b+d)(c+d)}}$$

Figure 3. Correlation coefficient equation phi (Φ) (13)

The software used to calculate the correlation between the variables studied statistically was *R - Software , version 4.3.2,* widely used by statisticians and data analysts.

Ethical Considerations

The research was carried out in accordance with ethical precepts and the project was approved by the Research Ethics Committee of the Federal University of Sergipe/UFS, according to the *Consubstantiated Opinion of the Research Ethics Committee* No. 6.064.013 of May 17, 2023, in accordance with Resolution No. 466/2012 of the National Health Council, with the Certificate of Presentation for Ethical Appreciation (CAAE) registered under the number 68814223.5.0000.5546.

Results

When investigating the correlation between the use of the CCS and the occurrence of surgical complications, it was hoped that the *negative correspondence* between these two variables would be confirmed, i.e. that the *greater* the adherence to the surgical checklist, the *lower* the occurrence of complications. In practice, a negative correspondence would represent a positive situation for surgical patients. This correspondence is represented by the graph below, which shows a decreasing *function*, where cases of complications and/or readmissions decrease as the application of the checklist increases (Figure 4).

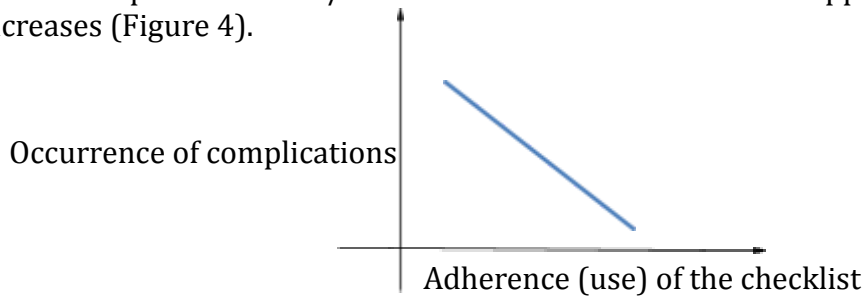

Figure 4. Graph of the relationship between the use of the checklist and the occurrence of surgical complications

With the pilot sample of 55 surgical records, the correlation value between these two variables was calculated using the PHI Correlation Coefficient (Φ), and the value was 0.08. After collecting the information from the 240 medical records, the aforementioned calculation was carried out and the result was 0.006, which shows that the correlation between the variables analyzed statistically was *low (weak)*, considering that *phi* (ϕ) varies between -1 and +1(13).

Based on the data provided by the Health Regulation and Evaluation Sector (SRAS)/HU/UFS/EBSERH, the main information on the situation of surgeries performed at the hospital, the setting for this research, is highlighted. These are: the total number of surgeries performed in the period was 4,297; the number of surgeries that resulted in complication/readmission was 443; the rate (%) of surgeries that resulted in complication/readmission was 10.3%; and the total number of adverse events officially reported was 14.

Table 1 below shows the information found after surveying the sample's medical records.

Table 1. Results found in the active search of surgical records (*n=240*)

Variable/Information	Value/index
Total surgeries *with* complications/readmission	26
Complication/readmission rate (%)	10,83%
Total surgery *with* complications/readmission and *using* the checklist	25
Total surgeries *without* complication/readmission	214
Index (%) of surgeries *without* complication/readmission	89,16%
Total surgery *without* complication/readmission and *using* the checklist	205
Total surgeries *using* the checklist	230
Overall rate (%) of checklist *use*	95,83%
Index (%) of checklist use in surgeries *with* complications/readmission	96,15%
Index (%) of checklist use in surgeries *without* complication/readmission	95,79%
Total number of surgeries with a *fully* completed checklist	132
Index (%) of surgeries with *completely* filled cheklist	57,39%
Type of surgery with the highest complication/readmission rate (%)	Hysterectomy (19,23%)

Source: prepared by the author based on data collected from the surgical records surveyed

It is important to note that in terms of absolute values, the total number of surgeries *without complications and with the use of CCS* (205 surgeries) was much higher than the number of operations *with complications and with the use of CCS* (25 surgeries).

Analyzing the current adherence to the surgical checklist by care professionals, considering the months defined for the survey, the highest rate of application of the surgical checklist was 88.2% of the operations performed and the lowest was 58.8%.

After investigating the cases of surgical adverse events reported in an official instrument by the hospital, risk situations similar to those occurring in other parts of the world were found. Examples include: an object forgotten in the patient's body; when the patient was already anaesthetized, there was a lack of essential supplies for the operation; the surgery was suspended due to a lack of equipment and/or supplies; post-operative dehiscence (opening). These are incidents that have caused or could have caused harm to the patient in their operation, which could result in readmission, prolonged hospitalization, emotional stress and disability.

A total of 64 patients had their hospitalization extended by up to two (2) days longer than expected due to some harmful event, and in the case of readmission of

patients due to some post-operative complication, the average number of days that passed between discharge and return to hospital was twelve (12) days.

With regard to the risks to which patients are exposed in the hospital studied, it was possible to see: failure to supply surgical and examination materials; failure to check the supplies and equipment needed for the operation; failure to comply with the care practices defined by the institution; lack of training for professionals in procedures that guarantee patient safety. These are threats similar to those found in the operating rooms of hospitals in other countries.

The CCS has a positive impact on hospital management, since adherence to this patient safety tool is one of the indicators of quality of care. According to the contract signed with the city, the hospital receives a monthly amount of funds to maintain itself and invest according to the rate of adherence to the surgical checklist and other indicators. Thus, the greater the adherence to these indicators, the greater the amount of resources received via the Unified Health System (SUS), since in Brazil the health service is municipalized (14).

Evaluating the CCS currently in force at the hospital studied, it was confirmed that it is in line with the surgical checklist recommended by the National Health Surveillance Agency (ANVISA), which in turn is based on the one validated by the World Health Organization (6). As well as containing the *essential* items according to the WHO, the hospital's CCS also checks other important items such as: the removal of orthoses, prostheses and adornments before surgery; confirmation of the use of the patient's identification bracelet and that of its location; and the existence of an allergy identification bracelet.

Discussion and Conclusions

The main purpose of the CCS is to reduce the rates of Adverse Events (AE) in surgeries (15). Its application increased the chances of the patient receiving surgical care with adequate and safe practices by almost 50% (16).

This study showed that, although there was a correlation between the use of CCS by healthcare professionals and the occurrence of post-operative complications and/or readmission of patients, this relationship was low (0.006). It was possible to see this in the sample *(n=240)*, as it was expected that adherence to the checklist would be low among operations with complications, but adherence was high (96.15%). In surgeries without AE, the rate of SCC use was also high (95.79%), confirming what was expected for surgeries without harmful episodes.

These results lead to the fact that a harmful event that occurs in a surgical intervention is also related to factors other than the *lack of application* of the CCS, such as pre-existing diseases, the presentation of an allergic process by the patient or the poor application of the checklist due to the resistance of some professional to use it (17). It is true that the checklist alone cannot remedy all the flaws that occur in surgical procedures; all professionals need to be aware of the need to improve their work processes and follow the planning defined by the WHO and the hospital unit in order to achieve real improvements and safe processes in surgeries (18).

The hospital surveyed still has some problems with recording the information linked to the checklist because there is still no systematic monitoring of the use of the CCS in all the procedures carried out, which could provide more precise information on its use. For example, there is a lack of data on the rate of adherence to the checklist in

surgeries *with complications* and in surgeries *without a harmful event.* They would be very important to compare with the results found in the sample of medical records.

The hospital's surgical complication rate was 10.3% and in the sample of surgical records this rate was 10.83%. These figures, therefore, reflect the reality of the world, as they are within the 3% to 16% range in which the rates of complications resulting from surgical procedures occur around the world (3-19).

In the sample, in only 57.39% of the surgeries was the CCS *completely* filled in, a rate considered very low by the experiences already obtained, since the scientific literature advocates that 100% of the items on the surgical checklist should be checked because this completeness is fundamental to guarantee a high standard of safety in the interventions. Scientific writings argue that *no* item on the CCS can go unconfirmed/unverified (20).

During the period of surgery considered in this study, the lowest rate of adherence to the CCS was 58.8% and the highest was 88.2%. In the sample, the checklist was applied in 95.83% of surgeries, which is closer to the WHO recommendation of applying it in 100% of procedures, including less invasive ones (21).

During this period, 14 (fourteen) surgical adverse events were reported in an official instrument, a figure lower than the 26 found in the sample surveyed. It can be inferred that within the universe of 4297 surgeries, the number of cases of VS was much higher than reported. This underreporting is a reflection of various factors, such as the culture of fear that comes from individualizing mistakes, shame at being condemned by colleagues, fear of being penalized and loss of professional credibility (22).

In addition to causing physical and psychological harm to patients and their families, EVs can cause prolonged hospitalization and readmission to the hospital. In this study's scenario, 64 patients spent up to 2 days longer in hospital than expected, and 12 was the average number of days that passed between the patient's discharge and their readmission. These situations increase the expenditure of resources (financial, material, human), increasing the institution's costs, which is yet another negative consequence of an EA. The health sector is very complex and its resources are generally scarce, so existing resources need to be used rationally (23).

The risks to which the patients treated at the hospital are exposed are similar to those found in surgical centers in the rest of the world, although the political and economic conditions are better in the so-called developed countries. Harmful events to patients and their families are an important negative indicator of the quality of the health service because they compromise patient safety (24).

Adherence to the CCS has become so important at the hospital under study that it has become one of the elements contributing to its administrative and financial management. This contribution has become a way of encouraging their use. The points achieved with the application of the surgical checklist help to obtain the monthly amount contracted with the city council, in accordance with Contract No. 46/2021 signed by the parties.

Some studies have identified a lack of support from hospital management in implementing/applying the surgical checklist, but it is essential that managers set an example and encourage its use. In reality, all professionals in the care, administrative and leadership spheres must collaborate on initiatives that can mitigate the risks to which patients are exposed in surgery as well as in any hospital environment (25).

After analyzing the CCS currently applied in the hospital studied, it was found that it complies with WHO and ANVISA recommendations and with the current needs detected, such as *confirming the correct identification of the patient, the surgical site and*

the procedure. Thus, there is no need to include other items or propose improvements. However, new situations that have not yet been dealt with may arise in the future, which makes it important to frequently monitor this security instrument in order to meet the needs of each era.

It is true that the items on a surgical safety checklist may, in some cases, fail to prevent harm to the surgical patient, as it may be linked to a factor that is difficult to predict. On the other hand, several studies have proven the benefits of this list, as it has been associated with a statistically significant reduction in mortality and length of stay. It is common to find experiences in the scientific literature which also show that the implementation of the surgical checklist promotes changes in the surgical culture (26).

A study similar to the one carried out at HU/UFS/EBSERH confirmed that the Safe Surgery Checklist is efficient in verifying the essential items of an operation, bringing a higher level of safety to the surgical patient. However, the low level of adherence to this instrument, its incomplete completion, inefficient communication between care professionals and deficiencies in team training have compromised the desired results, and the implementation of the SCC has not resulted in significant improvements in the communication and participation of surgical workers (27).

There are some limitations to this study, such as the fact that it was carried out in a single hospital, which makes it difficult to generalize its results. In many cases, the professional's handwriting was illegible, so there could be some mistake in interpreting the information accessed. Another weakness is that it is not possible to know if there is missing information or if the data is incomplete. These are inherent limitations of retrospective studies, so we are forced to rely on what was entered on the *Nursing Care Record (RAE)* title form, the CCS form, and the medical record as a whole. Omission or incompleteness of information may interfere with the results of the study.

Despite these weaknesses, the research has strengths, such as the fact that it alerts us to the importance of studying the subject of *patient safety* in health professional training courses, especially in the medical field, since the medical profession has shown greater resistance to the use of CCS in surgeries, because they don't believe in its effectiveness. In addition, the way in which adherence to the checklist contributes to the administrative and financial management of the hospital studied was analyzed in detail. This is a very important issue, since the health service is very expensive, and for a hospital to offer all the care services with the quality required and demanded by society, it needs a fairly large volume of financial resources. Another strong point was the *opportunity for improvement* identified in terms of the need for the hospital to carry out more direct, detailed and organized monitoring of the application of the CCS in all the surgical interventions carried out. This study may encourage more targeted tracking of the surgical checklist in order to record precise and in-depth information on its use and on the various situations linked to its use and what happens in surgeries.

In view of the information and evidence acquired through this study, it was possible to see that the importance of applying the checklist as an *error prevention* tool is clear within hospitals. Proof of this is that in the context of this research, other checklists are used in various environments and at various times during care, not just in operating rooms. It's important to note that the surgical checklist is low-cost and the average time to apply it during the three phases of surgery is three minutes.

Although the *correlation* between the use of the CCS and the occurrence of complications was weak, since the rate of its application was also high in surgeries that *resulted in a harmful event*, it must be understood that EVs, especially surgical EVs, are caused by various factors, so the use of a surgical process checklist can result in a

reduction in harm to patients, but the checklist cannot yet be considered a definitive element in this reduction. However, according to all the scientific literature researched, it is possible to *defend* its application because it has been verified that each item on this list represents the chance of avoiding a harmful episode for the person being assisted, and this tool, in addition to providing a higher level of safety for surgical patients by standardizing activities and avoiding reliance on memory, at the very least provides an opportunity to reflect on safe practices in surgeries.

It is true that the hospital studied needs to improve adherence to the CCS in order to reach 100% of procedures performed, as recommended by the WHO, but this is still a challenge for its management, as achieving this rate also depends on raising awareness among professionals and a continuing education program on the subject of patient safety and the proper application of the surgical checklist.

We hope that this research will encourage the development of new studies in other hospitals in the city, both public and private, with different realities, investigating the effect of the safe surgery checklist, because it would be very valuable for society as a whole to know in greater depth the extent to which the SCC reduces the occurrence of post-operative complications.

Thanks

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Conflicts of Interest

The authors declare no conflicts of interest in relation to this scientific text.

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