Migration Letters

Volume: 20, No: S3(2023), pp. 252-269

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)
www.migrationletters.com

Nutritional Management in the Therapeutic Care of the Complicated Diabetic Foot

Sierra-Carrero Leandro Luis[1], Carrero González Carmen Maria[2*], Ríos Estrada Mónica Itzel[3], Fabián Rosales Elena Yareli[4], Navarro Quiroz Elkin Antonio[5], Aldana-Rivera Edna Elizabeth[6], Julio Calao Digna Mercedes[7]

Abstract

Introduction: Diabetes Mellitus Type 2 (DM2) is a chronic, complex and progressive disease characterized by chronic hyperglycemia together with alterations of carbohydrate, lipid and protein metabolism as a result of a deficient insulin action Objective: To describe the nutritional management in the care therapeutics in the complicated diabetic foot. Methodology: Descriptive, retrospective and comparative study based on a systematic review of the different databases and research lines of free access and specialized health sciences, articles published in the different scientific platforms in English, Spanish and Portuguese, from North, Central and South American countries. Results: Clinical nutrition therapy is a key component of managing diabetes and hyperglycemia in the hospital setting. Maintaining balanced nutrition is important for glycemic control and for meeting adequate caloric demands in patients presenting with diabetic foot ulcers and UPD. Micronutrient deficiency is increasingly recognized as a factor in poorly healing patients with UPD, stating that inadequate micronutrition inhibits all levels of wound healing. Conclusions: Patient monitoring is necessary for proper follow-up and measurement of patient evolution. Nutritional assessment, through the development of a clinical-nutritional evaluation as part of wound management, could correct the nutritional status of the patient and an adequate feeding regimen according to the stage of evolution and clinical complications.

Keywords: *Nutritional Therapeutics, Diabetic Foot, care.*

Introduction

Type 2 Diabetes Mellitus (DM2) is a chronic, complex and progressive disease characterized by chronic hyperglycemia and alterations in carbohydrate, lipid and protein metabolism, all due to deficient insulin secretion or action or both [1]. The prevalence of

[1] Department of Medicine, Health Sciences Division, Universidad del Norte and Hospital Universidad del Norte, Barranquilla, Colombia, https://orcid.org/0000-0002-7148-5450

[2] Faculty of Health Sciences, Nursing Program. Universidad Simón Bolívar, Barranquilla,Colombia, https://orcid.org/0000-0002-4097-2694, carmen.carrero@unisimon.edu.co.

[3] Faculty of Nutrition, Centro Universitario de Tonalá, University of Guadalajara, Mexico, https://orcid.org/0000-0002-8044-7149

[4] School of Medicine, Clinical Nutrition Program. Benemérita Universidad Autónoma de Puebla, Mexico, https://orcid.org/0000-0002-4834-8618

[5] Faculty of Health Sciences, Nursing Program. Universidad Simón Bolívar, Barranquilla,Colombia, https://orcid.org/000000021718362X

[6] Faculty of Health Sciences, Nursing Program. Universidad Simón Bolívar, Barranquilla,Colombia, https://orcid.org/0000-0002-0265-7298

[7] Nursing Program Research Semillero. Faculty of Health Sciences. Simón Bolívar University, https://orcid.org/0000-0002-3925-6199

DM2 is increasing due to an aging population, changes in lifestyle, and an increased prevalence of obesity. [2,3]. DM2 is currently considered one of the main causes of premature morbidity and mortality due to its complications. The direct and indirect costs of DM2 and its complications account for a significant part of health expenditure in different countries [4].

The increase in people diagnosed with diabetes mellitus (DM) places this disease as a global health problem, according to the International Diabetes Federation (IDF) [1]. It is estimated that, in 2017, the global prevalence reached 425 million people aged 20-79 years (8.8 %); it is expected that the figures will increase to 693 million in 2045 and from what was reported by the World Health Organization (WHO), between 2000 and 2016 there was a 5 % increase in premature mortality due to diabetes, which was the direct cause of 1.6 million deaths [2]. A recent report from the WHO states that the prevalence of diabetes in adults over 18 years of age has increased worldwide from 4.7% to 8.5%. It will be the seventh leading cause of mortality in 2030 (5).

In this regard, it is estimated that, at the time of diagnosis, more than 10% of patients have risk factors for developing foot diseases, such as peripheral neuropathy or peripheral vascular disease [3].

Patients with type 2 diabetes mellitus are 25 times more at risk than the general population of losing a limb; each year, more than 1 million people lose a lower limb due to diabetes mellitus [4]. Diabetic patients consume 11% of the total health budget in the United States and about 6% of the health cost in Latin America and the Caribbean, which makes it an entity of public health interest, in addition to the impact it generates with the high burden on health morbidity and mortality indicators [6]. In Colombia, according to the National Health Observatory (ONS), diabetes reached an average mortality rate between 2009 and 2011 of 10.4 per 100 000 inhabitants, ranking among the first ten causes of general mortality, with more than 50% being preventable [7].

Diabetic foot ulcer (DFU) is a serious complication of diabetes mellitus and is associated with high morbidity and mortality levels and significant economic costs [1-3]. The WHO defines UPD as "the presence of ulceration, infection and gangrene in the foot associated with diabetic neuropathy and varying degrees of peripheral vascular disease as a consequence of the complex interaction of different factors induced by sustained hyperglycemia." Recurrence rates of (UPD) are 40% in one year and 65% in the subsequent three years after successful ulcer healing. Therefore, prevention is critical to reducing the risks to the patient and the resulting economic burden to society.

Ulcers (UPD) are the most common problem, with an annual incidence of about 2-4% in developed countries and probably even higher in developing countries [8]. Not all people with diabetes are at risk of ulceration. Key risk factors include a loss of protective sensation (PSP), peripheral arterial disease (PAD) and foot deformity. [6]

Amputation of the foot or leg occurs mainly due to events related to ischemia or infection, the latter being the main cause. Infection of the diabetic foot can involve soft tissue or bone, with the former being the most severe clinical presentation and a worse prognosis [9, 10].

The relationship between nutrition and healing has been recognized for decades, describing that proper healing requires an adequate intake of energy, protein and micronutrients [11]. Malnutrition is a determinant of the development of UPD, documenting that patient with malnutrition has a 129 % higher risk of developing them (RR 2.29, 95%CI 1.53-3.44), regardless of other predictors such as age and comorbidities [12]; a study by Banks et al. (2013), managed to show that nutritional intervention is a useful approach in the prevention of UPD, by demonstrating savings of 2.869,526 (SD 2 078 715) when patients received the nutritional intervention, compared to standard care [13]. This is why malnutrition should be identified on time to define dietary guidelines to allow adequate healing [14]. In addition to adequate nutrition and hydration, other interventions have been studied that may have significant benefits in wound healing, suggesting arginine, glutamine and micronutrient supplementation [15].

The European Pressure Ulcer Advisory Panel (EPUAP) guidelines for the prevention and treatment of UPD, published in 2019, consider nutritional therapy essential, issuing different recommendations for the dietary prescription. Before recommending supplementation, dietary intake should be evaluated, in addition to the amounts provided by fortified products such as enteral formulas [16]. However, several studies now increasingly recognize micronutrient deficiency as a factor in poor healing in patients with UPD, as several micronutrients play an important role in healing as enzyme cofactors [17, 15]. For many people with diabetes, the most challenging part of the treatment plan is determining what to eat. The American Diabetes Association (ADA) position is that there is no “one-size-fits-all” eating pattern for people with diabetes. The ADA also recognizes the integral role of nutritional therapy in the overall management of diabetes and has historically recommended that each person with diabetes be active participants in self-management, education, and treatment planning with their healthcare provider, which includes the collaborative development of an individualized meal plan [2,3].

The area of nutrition, often forgotten by technological and scientific advances, could be a key factor in improving the healing of these injuries and thus avoiding amputation. As it is known, there is a relationship between the nutritional status and the healing process of wounds and their complications. Local wound treatment is as important as daily clinical therapy and simple interventions such as a balanced diet [18]. Adequate treatment and therapeutic education for patients with diabetes mellitus at high risk of ulceration are essential to maintain quality of life and to prevent and limit lesions and recurrence [7]. The importance of an adequate nutritional assessment and dietary plan during all periods of the disease since the diabetic patient transits from malnutrition to obesity through various associated syndromes. Recognizing the importance of modifying eating habits and lifestyle implies putting into practice the three fundamental pillars for a good treatment, including a healthy eating plan (a key element in the prevention, treatment and complications of the disease), pharmacotherapy and diabetic education. Under these findings, our study aims to describe nutritional management in the therapeutic care of complicated diabetic foot.

Methodology

Professionals in medicine carried out a descriptive, retrospective and comparative study based on a systematic review of clinical nutrition and nursing of the Faculty of Health Sciences of the Simón Bolívar University, Medicine Program of the University of the North of Barranquilla and the Faculty of Nutrition of Guadalajara and the Autonomous University of Puebla, Mexico. In order to respond to the objective of describing the nutritional management in the therapeutic care of the complicated diabetic foot. A systematic search was carried out in different databases and open-access research lines specialized in health sciences, articles published from 1996 to 2020 in English, Spanish and Portuguese from different countries of North, Central and South America. The following descriptors or terms were used to search the review: Nutritional Therapeutics, Diabetic Foot. A total of 110 were identified, of which 25 studies were discarded for lacking a relation with the study categories in English, Spanish and Portuguese; for the selection of the articles, the inclusion criteria were established (articles that complied with the characteristics of the topic to be studied, that the title or abstract referred medical therapeutics of diabetes, nutrition in the patient with UPD, direct care in the UPD). The search was carried out as follows: articles found after registration in the following databases: Scielo: 25, Scopus: 20, Research Gate: 23, Pub Med: 20, Medigraphic: 2, Redalyc: 100, Web: 10, with a total of documents found: N= 110, articles discarded due to duplication: 12.

Nutritional assessment

Previous studies have assessed the Mini Nutritional Assessment (MNA) as a highly sensitive tool for the accurate detection of malnutrition and its use in diabetic patients, as recommended in the International Diabetes Federation Global Guideline for DM2 [19]

The Spanish Association of Vascular and Wound Nursing (AEVVH) emphasizes that in treating UPD, it is important to detect and correct malnutrition and dehydration employing a nutritional evaluation when assessing the patient. This should be done through nutritional tests and biochemical controls. [20]

In normal-nourished patients who do not present nutrient deficits, a nutritional plan should be established that includes a diet rich in calories, protein and arginine, vitamins with antioxidant effects (Vitamins A, B, C, D and E and minerals such as zinc, magnesium, iron and selenium) and alpha-lipidic acid [21]. In addition, all nutrients should be considered as a component of a complete diet [22].

Clinical nutrition therapy (CNT) in hospitalized patients with diabetes

In-hospital diabetes self-management may be appropriate for specific patients [23]. Candidates include adolescent and adult patients who successfully perform diabetes self-management at home and whose cognitive and physical skills are not compromised to self-administer insulin and perform blood glucose self-monitoring successfully. In addition, they must have adequate oral intake, be proficient in carbohydrate estimation, use multiple daily insulin injections or continuous subcutaneous insulin infusions (CSII), have stable insulin requirements, and understand sick day management. If (CSII) or continuous glucose monitors (CGMs) are to be used, hospital policy and procedures outline guidelines for CSII therapy [24,25].

The goals of medical nutrition therapy in the hospital are to provide adequate calories to meet metabolic demands, optimize glycemic control, address personal food preferences, and facilitate the creation of a discharge plan. Current nutritional recommendations advise individualization based on treatment goals, physiologic parameters and medication use.

Many hospitals prefer consistent carbohydrate meal plans because they make it easier to match the prandial insulin dose with the amount of carbohydrate consumed [26]. The availability of enteral formulas with lower carbohydrate (CH) and higher monounsaturated fat content with or without fiber allows flexibility of use to achieve glycemic control. Standard polymeric formulas (50/30-35/15-20) are an initial alternative because of their cost and specialized low-CH formulas. Elemental formulas are necessary in populations with digestive disorders or absorptive capacity disorders and in the case of patients with water retention problems, hypercaloric formulas are used. A post-pyloric feeding route should be considered in those patients with gastroparesis [27].

When nutritional problems in the hospital are complex, the involvement of a registered dietitian nutritionist can contribute to patient care by integrating information about the patient's clinical condition, meal planning and lifestyle habits and by setting realistic treatment goals after discharge. Orders should also indicate that meal delivery and nutritional insulin coverage should be coordinated, as their variability often creates the potential for hyperglycemic and hypoglycemic events [28].

Insulin vs. nutritional treatment (parenteral - enteral) in hospitalized diabetic patients with special situations

The regimen should include coverage of basal, prandial, and correctional needs for patients receiving enteral or parenteral feeding who require insulin. Patients with type 1 diabetes must continue to receive basal insulin even if feeding is discontinued. A reasonable estimate of basal requirements can be made from the preadmission dose of long-acting or intermediate-acting insulin or a percentage of the total daily requirement established in the hospital (usually 30 to 50% of the total daily insulin dose). In the absence of a previous insulin dose, a reasonable starting point is to use five NPH insulin/detemir subcutaneously every 12 h and 10 units of insulin glargine every 24 h [29].

For patients receiving continuous tube feeding, the total daily nutritional component can be calculated as 1 unit of insulin per 10-15 g of carbohydrate per day or as a percentage of the total daily insulin dose when the patient is being fed (usually 50-15 g of carbohydrate per day.) 70% of the total daily insulin dose). Corrective insulin should also be administered subcutaneously every six hours with regular human insulin or rapid-acting insulin such as lispro, aspart, or glulisine every four hours. For patients receiving enteral bolus feedings, approximately 1 unit of regular human insulin or rapid-acting insulin per 10 to 15 g of carbohydrate should be administered subcutaneously before each feeding. Corrective insulin coverage should be added as needed before each feeding. Regular human insulin may be added to the solution for patients receiving continuous peripheral or central parenteral nutrition, particularly if 20 units of correctional insulin have been required in the last 24 h. A starting dose of 1 unit of regular human insulin per 10 g of dextrose has been recommended [30] and should be adjusted daily in solution. Corrective insulin should be administered subcutaneously. [31,32].

Clinical nutrition therapy is a key component of managing diabetes and hyperglycemia in the hospital setting. Maintaining adequate nutrition is important for glycemic control and meeting adequate caloric demands. Caloric demands in acute illness will differ from those of outpatients. Achieving adequate nutritional balance in the hospital setting is a challenge. Anyone admitted to the hospital with diabetes or hyperglycemia should be evaluated to determine the need for a modified diet to meet caloric demands.

The general approach to modified nutrition therapy in the hospital setting is based on expert opinion and patient needs. Unfortunately, there is limited data on the best approach or method to achieve ideal caloric intake. Therefore, providers should work closely with a nutrition professional to determine their patients' best approach, method, and caloric needs [33].

All patients with diabetes or hyperglycemia should receive an individualized assessment. Most patients will generally receive adequate caloric needs with three daily meals. In addition, the metabolic need of patients with diabetes is usually provided by 25 to 35 calories/kg, whereas some critically ill patients may need less than 15 to 25 calories/kg per day [34]. Therefore, a consistent carbohydrate meal planning system could help facilitate glycemic control and insulin dosing in the hospital setting. Most patients will require 1500-2000 calories per day with 12-15 grams of carbohydrates per meal [35]. Ideally, carbohydrates should come from low glycemic index foods, such as whole grains and vegetables.

Enteral nutrition is the second best option after oral nutrition and should be preferred to parenteral nutrition in hospitalized individuals [36,37]. There are several advantages of enteral feeding over parenteral feeding, including low cost, low risk of complications, physiologic route, lower risk of gastric mucosal atrophy, and lower risk of infectious and thrombotic complications compared to the latter form of treatment [36,38].

Enteral nutrition (EN) and parenteral nutrition (PN) can prevent the effects of starvation and malnutrition [36]. The preference for using EN over PN is due to a lower risk of infectious and thrombotic complications [38,39). Standard enteral formulas reflect the reference values of macro- and micronutrients for a healthy population and contain 1-2 cal/ml. Most standard formulas contain complete proteins, lipids in the form of long-chain triglycerides, and carbohydrates. Standard diabetes-specific formulas provide low amounts of lipids (30% of total calories) combined with a high carbohydrate (HC) content (55-60% of total calories); however, newer diabetic formulas have replaced part of the carbohydrates with monounsaturated fatty acids (up to 35% of total calories) and also include 10-15 g / l of dietary fiber and up to 30% fructose [40,41]. Therefore, enteral diabetic formulas containing high- and low-carbohydrate monounsaturated fatty acids (LCHM) are preferable to standard high-carbohydrate formulas in hospitalized patients with type 1 and type 2 diabetes [40,42]. In a meta-analysis of studies comparing relatively new low-carbohydrate and (LCHM) enteral formulas with older formulas, the postprandial rise in blood glucose was reduced by 18-29 mg/dl with the newer formulas [42].

Macronutrients in type II diabetes mellitus

Macronutrient distribution includes at least 30% of total calories from fats and of these, < 7% should be saturated and up to 15% monounsaturated, with cholesterol intake < 200 mg/day. As for HC, an intake of 50-60% of total calories is recommended, mainly complex, with an intake of simple sugars < 10%. In addition, fiber intake should be 14 g per 1000 cal, with a preference for soluble fiber. Finally, protein is suggested at 15% of total calories [43].

Of the macronutrients, certain protein amino acids and fatty acids stand out; carbohydrates are the main energy source in the healing process. [21].

In the case of proteins, we find two amino acids related to the healing process: arginine and glutamine. Arginine participates in protein synthesis, cell signaling and proliferation, microvascular changes and tissue perfusion and collagen increase, in addition to increasing T cells and generating killer cells which are important factors in the immune response. Glutamine is an alternative energy source for rapidly dividing cells such as fibroblasts, epithelial cells and macrophages. In the fatty acid group, we find that they are an essential component of cell membranes that participate in tissue repair and wound healing by influencing inflammatory pathways. Omega-3 and alpha-lipidic acid have been the most studied fatty acids in the healing process, omega-3 especially intervenes in the reduction of inflammatory cytokines, reduction of platelet aggregation and intervenes in coagulation. Alpha-lipidic acid is a potent modulator of the inflammatory state of the wound [21].

Carbohydrates

Carbohydrate quality is important in terms of glycemic index and fiber, and may have other health benefits; although carbohydrate quantity is an important predictor of glycemic response [44]; there is no definitive or conclusive evidence of an ideal macronutrient ratio for all patients with DM2, but the emphasis is placed on individualization of the eating plan [45,46], it is important to include carbohydrate-containing foods, particularly cereals, fruits, vegetables, and low-fat milk in the diet of people with diabetes [46,47].

Recommendations regarding carbohydrate intake by the American Diabetes Association (ADA) 2014

1.- Monitoring carbohydrate intake, either by carbohydrate counting or experience-based estimation, remains a key strategy for achieving glycemic control.

2.- For good health, the intake of carbohydrates from vegetables, fruits, whole grains, legumes, and dairy products should be cautioned over the intake of other carbohydrates, especially those containing added fats, sugars or sodium.

Glycemic index and glycemic load, substituting foods with a low glycemic load for foods with a high glycemic load can moderately improve glycemic control.

4.-Dietary fiber and whole grains. People with diabetes should consume at least the amount of fiber and whole grains recommended for the general public.

5.-Substitution of starch by sucrose. At the same time, substituting sucrose-containing foods for isocaloric amounts of others. Although carbohydrates can have similar effects on blood glucose, consumption should be minimized to avoid displacing nutrient-rich food choices.

Fructose consumed as “free fructose” (i.e., found naturally in foods such as fruits) may result in better glycemic control compared to isocaloric intake of sucrose or starch, and free fructose is not likely to have detrimental effects on triglycerides, as long as intake is not excessive (12% of energy).

7.-The intake of any caloric sweeteners, including high fructose corn syrup and sucrose, should be limited or avoided to reduce the risk of weight gain and worsening of the cardiometabolic risk profile [2].

Glycemic index of foods

A key factor in the food type for diabetes and related to the glycemic index identifies foods that raise blood sugar rapidly. This practical tool allows the selection of appropriate foods that have a much smaller effect on blood sugar levels [48]. The glycemic index (GI) measures the change in blood glucose after the ingestion of carbohydrate-containing foods [47]. The glycemic load (GL) more accurately reflects the glycemic effect and has been defined as the product of the GI of a particular food and the available carbohydrate content. Therefore, the potential glycemic effect of a meal can be altered by changing the GI or carbohydrate content, which affects the GL [44]. The amount of available carbohydrates in the diet is also a crucial consideration. Therefore, knowledge of food types (GI) is essential for rational advice on calorie recommendation [49]. The glycemic index is ranked from 1 to 100. Foods that raise blood glucose rapidly after meals are known as high GI foods and are assigned a value of 70 or more, medium GI = 56-69%, whereas foods that release glucose slowly into the bloodstream are known as low GI foods and their values are 55 and below [50,51]. Low GI foods reduce postprandial blood glucose levels and this knowledge can be used to recommend and plan meals for people with diabetes [52-53]. The type of food with a high GI rating should not be encouraged in the dietary plan for people with diabetes. However, meals with intermediate GI can be allowed in moderation.

Fats

They are the essential component of cell membranes that participate in tissue repair and wound healing by influencing inflammatory pathways. The most studied are omega-3, which plays a role in increasing inflammatory cytokines, platelet aggregation and coagulation intermediary, and alpha-lipidic acid, which functions as a modulator of inflammation [21].

The role of dietary fat has long been studied as a modifiable variable in the prevention and treatment of diabetes and in general, the type (quality) of fat is more important than the amount (quantity) of fat intake [45]. This is consistent with recommendations to limit the intake of saturated fat, a high-fat diet, and cholesterol in the diet as stipulated by the American Diabetes Association [35,47,48,54] and the American Heart Association [55]; Fat quality is generally specified by the relative content of saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA), including the proportion or amount of essential fatty acids, i.e., linoleic acid (LA) and alinolenic acid (ALA), as well as the proportion or amount of long-chain n-3 fatty acids (n-3 LCPUFA), i.e., eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [56].

Fat is a problem for people with diabetes; the more fat in the diet, the more difficult it is for insulin to deliver glucose to the cells. Similarly, minimizing fat intake and reducing body fat help insulin do its job much better [48]. In addition, fatty acids influence glucose metabolism by altering cell membrane function, enzyme activity, insulin signaling, and gene expression [57]; and fat-containing foods can affect the rise in blood sugar and produce a lower GI than similar foods without fat [58]. Recent evidence suggests that a diet rich in healthy fats and unsaturated fatty acids, such as the Mediterranean diet, may indeed prevent the development of metabolic diseases such as type 2 diabetes mellitus but also reduce cardiovascular events [59, 54].

Proteins

Dietary proteins are important modulators of glucose metabolism [60]. However, their role in diabetes remains a matter of debate. Protein-rich foods increase insulin secretion, leading to a decrease in postprandial blood glucose concentrations [60]. On the contrary, meta-analytical studies [54, 60, 61] demonstrated that total protein and animal protein intake were associated with a high risk of DM2. In foods rich in animal protein, red meat and processed meat were associated with a high risk of DM2, whereas total dairy, low-fat dairy, and yogurt were associated with a low risk of DM2, and egg and fish were not associated with a lower risk of DM2. In plant protein-rich foods, soy was associated with a low risk of DM2 [60-62]. From an individualized approach to protein intake and among people with renal failure, the ADA recommends reducing protein intake to 0.8-1.0 g/kg per day in the early stages of chronic kidney disease (CKD) and 0.8 g/kg per day in the later stages of CKD [63, 48].

Micronutrient Nutritional Deficiencies

In patients with UPD, micronutrient deficiency is increasingly recognized as a factor in patients with poor wound healing, with inadequate micronutrients claimed to inhibit all levels of wound healing [21,64,65,66]. Despite often being seen as a high-calorie group, patients with UPD be at high risk for micronutrient deficiency. These present patient characteristics that can lead to poor nutrition since, during the wound healing process, adequate calories and nutrients are required to prevent wound complications; to achieve these nutrients, the body will have to draw on its reserves. The nutrient intake provided to maintain the body will be insufficient if an ulcer appears, resulting in a state of malnutrition. For this reason, some authors such as Gau et al. (2016), Brookes et al., Molnar et al. (2014), Gau (2016). They suggest that all patients with UPD should be considered malnourished until proven otherwise [19, 66,67].

Malnutrition is an important predictor of wound worsening and amputation [17, 19,14, 65, 66]. For example, a recent study by Brookes (2019) [66] found statistically significant differences in albumin, hemoglobin and vitamin C levels between UPD patients who underwent amputation and those who avoided amputation. Similarly, in a study by Ponce (2017)[65], 99% of patients with UPD amputation presented hypoalbuminemia.

Kulprachakarn (2017) [64] agreed that anemia is often a frequent problem in patients with UPD and added that the serum zinc level decreased significantly in patients with type 2 diabetes with foot ulcers compared to those without ulcers. Gau (2016) [19] concluded that the amputation rate is eleven times higher in a group of malnourished patients (MNA <17) than in those who are not malnourished. Furthermore, an increase of 1 point was associated with a decrease in both major and minor amputations. The mean MNA score of the patients was "at risk for malnutrition," which gradually decreased as the level of amputation increased.

In the field of wound healing, it is claimed that there are immuno-nutrients, both at the macro and micro levels, that can somehow enhance the patient's immune activity and improve the wound-healing process [68]. In addition, some micronutrients can prevent or attenuate peroxidative damage (usually produced by free radicals), which can potentially enhance healing [21, 64].

Vitamins

The intake of vitamins (A, B, C, D, E and K) and minerals (zinc, iron, magnesium, copper and selenium) is important and should be present in the diet of the patient with UPD [21, 23,69]. Vitamin A is necessary for fibroblast differentiation, increased wound tension forces, and reduced infection [21]. In addition, it enhances cellular immunity, with increased macrophage influx, inflammatory response and collagen synthesis [21,14]. This should be supplemented for 10 to 14 days; prolonged excessive intake can be toxic [14]; it has been found to stimulate epithelial growth, fibroblasts and ground substance and have an anti-inflammatory effect on open wounds. The literature supports a positive effect of supplemental vitamin A on acute wounds and the healing of fractures, burns, bowel, and radiation-induced injuries. Indeed, vitamin A appears to function as a hormone that alters the activity of epithelium, cells, melanocytes, fibroblasts, and endothelial cells through a family of retinoic acid receptors [70, 71, 72]. Wicke et al. (2000) found that vitamin A reversed the effect of steroids to decrease transforming growth factor beta (TGFb) and insulin-like growth factor-1 (IGF1) levels in the wound. In addition, it is involved in epithelial differentiation and proliferation, stimulation of angiogenesis, collagen synthesis and fibroplasia [73]. As far as vitamin B12 is concerned, it is directly related to peripheral nerve density and peripheral neuropathy [14]. Vitamin C is a potent antioxidant, performing the function of enzyme cofactor and chemical reductant in the healing process. It also participates in collagen synthesis and maintenance of the immune system with neutrophil migration and cell apoptosis [21, 74]. Vitamin C supplementation of 500 to 1000 mg/day accelerates wound healing daily in divided doses for optimal utilization. For patients with more severe wounds, such as burns over a large area, doses can be increased to 1-2 g/day [75].

They may be a good option as they are inexpensive, safe, and likely to improve healing [76]. Vitamin D has been shown to regulate the epithelial barrier’s structural integrity and transport functions, thus intervening in the healing process. Vitamin D supplementation for 12 weeks significantly reduced the duration of UPDs, their width and depth [77]. Vitamin D has various beneficial effects on UPDs, ranging from increased glycemic control to moderation of inflammation and recently has been suggested to improve diabetic foot wound healing. Vitamin E is responsible for controlling the acute response to injury and stability of cell membrane fats [21], which is also an antioxidant and regulates inflammatory reactions and cell apoptosis [21, 78]. Vitamin E supplementation for DM2 patients with low vitamin E levels and poor glycemic control significantly improved HbA1c and insulin levels (Afzali et al. 2019), stating that its excess may be detrimental to the increased risk of fibrosis and bleeding. (78) Vitamin K is an essential cofactor of coagulation factors and is involved in the hemostasis phase [21].

Minerals

As (zinc, iron, magnesium, magnesium, copper and selenium) play an important role in the nutrition of the patient with UPD. Zinc is one of the most studied minerals in the common areas of nutrition and healing. This micronutrient is a cofactor of enzyme systems involved in metabolizing other micronutrients [21, 69] and cell division, protein synthesis and collagen deposition [14, 69]. In addition, it is involved in stimulating re-epithelialization, is a potent neutrophil stimulant, is known as an antioxidant and collaborates in the maintenance of epithelial tissue hemostasis, cell division, protein synthesis and collagen deposition [69,79]. It plays an important role in the synthesis, insulin storage and altered pancreatic insulin content [79]. Few studies reported that zinc levels were significantly lower in patients with UPD than those without UPD [80]. Dorner et al. (2009) recommend zinc supplementation of up to 40 mg elemental zinc/day (176 mg zinc sulfate) for up to 10 days to improve wound healing if zinc deficiency is indicated [81], while Posthauer ME (2005) recommends higher doses, which are 220 mg zinc sulfate (50 mg elemental zinc) twice daily for two weeks [21,82]; the intake of zinc supplementation for 12 weeks among UPD patients was beneficial with effects on ulcer size parameters. Zinc supplementation resulted in a significant increase in serum zinc levels (+ 12.7 ± 4.7 vs. - 3.5 ± 4.0 mg). It was associated with significant reductions in ulcer length and width [79]. Zinc replacement with 50 mg/day in a zinc-deficient patient optimized the healing process of UPD, but only proved beneficial in people with diabetes who are deficient. [76,79]. On the other hand, iron prevents anemia, optimizes tissue perfusion, and participates in collagen synthesis; it is important for hemoglobin formation for wound oxygenation and collagen synthesis [21, 69]. As for magnesium, it is known as a potent anti-inflammatory, as it improves glycemic control and insulin sensitivity in people with diabetes. It is an essential cofactor of carbohydrate and lipid metabolism enzymes and collaborates in synthesizing proteins and tissues in the healing process [78].

Magnesium is a cofactor in more than 300 enzymatic reactions, specifically in glucose phosphorylation processes, in which ATP utilization or transfer is necessary. Its deficiency is related to insulin resistance, HC intolerance and dyslipidemia. Hypomagnesemia in patients with type 2 DM is multifactorial; it is due to poor glycemic control, alterations in insulin metabolism, oxidative stress, inflammation, glycosuria, and decreased tubular reabsorption of magnesium, among others [43]. Some studies indicate that oral magnesium supplementation improves insulin sensitivity and reduces the risk of atherosclerosis in non-diabetic subjects, even with normal magnesium levels [82]. Supplementation for 12 weeks benefits sitting size, glucose metabolism, and serum C-reactive protein levels. Subjects with low levels may respond better to supplementation [72]. Copper promotes angiogenesis and aids in synthesizing growth factors and extracellular matrix, and its deficiency leads to glucose intolerance, decreased insulin responsiveness and increased glucose, and it is associated with hypercholesterolemia and atherosclerosis [21, 43].

It is also an enzyme cofactor involved in collagen cross-linking, erythropoiesis, immune response, growth factor induction, iron metabolism, hemoglobin synthesis, and vitamin C assimilation [69]. The maximum daily allowance is 1000 ug/day. Last but not least, selenium is an antioxidant and protector of peroxidation, being important in its supplementation in patients with UPD [21]. Selenium acts as an antioxidant, participates in signaling pathways and modifies hormone metabolism. Some studies show that glucose concentrations tend to normalize with selenium administration by modifying enzyme systems involved in hepatic glycolysis and gluconeogenesis without the need for insulin regulation, suggesting an insulin-like effect. Meanwhile, other studies show that high serum selenium concentrations are associated with a higher prevalence of DM. However, severe selenium deficiency is rare and in patients with DM increases oxidative stress, so supplementation in these cases is justifiable [43].

Currently, under extensive debate, most research indicates that micronutrient deficiencies due to inadequate intakes or low organ levels can be corrected with supplementation, considering that the above-physiologic supply of nutrients associated with wound healing does not confer an additional demonstrated clinical benefit and may negatively influence the healing response [21, 69, 64]. For this reason, before providing specific nutritional supplements, Molnar et al. (2014) suggest that appropriate assessments of the patient's overall nutritional status and reasons for malnutrition should be obtained [67].

The International Working Group on the Diabetic Foot (IWGDF) [8], in its latest PD management guideline, states that "interventions aimed at correcting nutritional status including protein, vitamin, and trace element supplementation and pharmacotherapy with angiogenesis-promoting agents should not be used in preference to the best level of care in the pursuit of improved healing." The ADA also does not specifically advocate nutritional supplementation in managing diabetes or its complications. However, they support healthy eating patterns and emphasize nutrient-rich foods in appropriate portions [80].

Recommendations

Establish a nutritional education program for patients whose objective is to establish a healthy and balanced diet and promote the cure of UPD. Caregivers should be included in this plan. These should be participants in the process, serving as support for their loved ones, which is visible in the results by improving the nutritional factor of patients.

Patient monitoring will be necessary for adequate follow-up and measurement of the patient's evolution [21].

Nutritional assessment, by developing a clinical-nutritional evaluation as part of wound management so that the patient's nutritional status could be corrected [67].

The Spanish Association of Vascular and Wound Nursing (AEVVH) emphasizes that in treating UPD it is important to detect and correct malnutrition and dehydration through a nutritional evaluation when assessing the patient. This should be done through nutritional tests and biochemical controls [20]. Verdú et al. (2011) and García Fernández et al. (2018) indicate that the risk of malnutrition is significant and should be performed both at the outpatient and inpatient level on admission and then systematically whenever there is a worsening of the wound [21,83].

The Action Guide of the PD of the Canary Islands states that the assessment should be made when the patient does not show improvement [84], and the National Consensus Conference on Ulcers (CONUEI) states that it should be made when the patient is over 65 years of age and the lesion has evolved for more than 60 days [85].

The technical document number 12 on nutrition and wounds of the national group for the study and advice on pressure ulcers and chronic wounds (GNEAUPP) dictates that the assessment should be carried out employing a validated questionnaire that should be universal, early, simple to apply, based on the best possible scientific evidence and adaptable to the clinical circumstances of the patients such as age, sex and severity of the disease [21].

Conflict of interest

The authors report having no conflicts of interest in the study's development and the manuscript's writing.

References

1. Skyler JS, Bakris GL, Bonifacio E, Darsow T, Eckel RH,Groop L. Differentiation of diabetes by pathophysiology, natural history, and prognosis. Diabetes. 2017;66:241-55. http://dx.doi.org/10.2337/db16-0806. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/27980006/

2. Araneta MR, Kanaya AM, Hsu WC, Kchang H, Grandinetti A, Boyko E, et al. Optimum BMI cut points to screen asian americans for type 2 diabetes. Diabetes Care. 2015;38:814-20. http://dx.doi.org/10.2337/dc14-2071 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/25665815/

3. Fazeli PK, Lee H, Steinhauser ML. Aging is a powerful risk factor for type 2 diabetes mellitus independent of body mass index. Gerontology. 2019:1-2. http://dx.doi.org/10.1159/000501745. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/31505500/

4. Lopez-Bastida J, Boronat M, Moreno JO, Schurer W. Costs, outcomes and challenges for diabetes care in Spain. Global Health. 2013; 9:17. Consultado 20 de junio de 2021 al 2022. http://dx.doi.org/10.1186/1744-8603-9-17.Published 2013 May (anterior 5)

5. Organización Mundial de la Salud [Internet]. Diabetes. Organización Mundial de la Salud; 2018. Consultado 20 de junio de 2021 al 2022. Consultado 20 de junio de 2021 al 2022 en: https://www.who.int/es/news-room/ fact-sheets/detail/diabetes

6. Crawford F, Cezard G, Chappell FM, Murray GD, Price JF, Sheikh A, et al. A systematic review and individual patient data meta-analysis of prognostic factors for foot ulceration in people with diabetes: the international research collaboration for the prediction of diabetic foot ulcerations (PODUS). Health Technol Assess 2015; 19(57):1- 210. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/26211920/

7. Martínez-Barbabosa I, Romero-Cabello R, Ortiz-Pérez H, Elizalde-Simón H, Gutiérrez-Cárdenas ME, AguilarVenega JM, et al. La alimentación de pacientes diabéticos tipo 2 y su relación con el desarrollo de infecciones en los pies. Rev Biomed 2014; 25(3):119–127. Consultado 20 de junio de 2021 al 2022 en: https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=53412

8. Schaper. Nicolaas C, Van Netten Jaap J, Apelqvist. Jan, Bus. Sicco A, Robert J. Hinchlife, Benjamin A. IWGDF Practical guidelines on the prevention and management of diabetic foot disease. 2019. Consultado 20 de junio de 2021 al 2022 en: https://iwgdfguidelines.org/wp-content/uploads/2019/05/IWGDF-Guidelines-2019.pdf

9. Pavón Núñez D, Cárcamo Mejía S, Flores Moreno R, Nuñez Palma J, Chacón J. J, Mendoza Talavera A, Erazo Coello A, Ortiz Avilés G, Mejía Rodríguez C, Álvarez G, Bermúdez Lacayo J. Revista Hispanoamericana de Ciencias de la Salud (RHCS), ISSN-e 2215-4256, Vol. 2, Nº. 3, 2016, págs. 215-222. Consultado 20 de junio de 2021 al 2022 en: https://dialnet.unirioja.es/servlet/oaiart?codigo=5742052

10. Lázaro-Martínez J. L, Tardáguila-García A, García-Klepzig J. L. Diagnostic and therapeutic update on diabetic foot osteomyelitis. Endocrinología, Diabetes y Nutrición (English ed.), Volume64, Issue2, 2017, pags.100-108. Consultado 20 de junio de 2021 al 2022 en: https://www.sciencedirect.com/science/article/abs/pii/S2530016417300204 (anterior 99)

11. Posthauer ME, Banks M, Dorner B, Schols JMGA. The role of nutrition for pressure ulcer management: national pressure ulcer advisory panel, european pressure ulcer advisory panel, and pan pacific pressure injury alliance white paper. Adv Skin Wound Care. 2015; 28(4):175–88. doi: https://doi. org/10.1097/01.ASW.0000461911.31139.62. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/25775201/

12. Iizaka S, Okuwa M, Sugama J, Sanada H. The impact of malnutrition and nutrition-related factors on the development and severity of pressure ulcers in older patients receiving home care. Clin Nutr. 2010; 29(1):47-53. doi: https://doi. org/10.1016/j.clnu.2009.05.018. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/19564062/

13. Banks MD, Graves N, Bauer JD, Ash S. Cost effectiveness of nutrition support in the prevention of pressure ulcer in hospitals. Eur J Clin Nutr. 2013; 67(1): 42-6. doi: https://doi. org/10.1038/ejcn.2012.140. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/23047712/

14. Haughey L, Barbul A. Nutrition and Lower Extremity Ulcers: Causality and/or Treatment. Int J Low Extrem Wounds. 2017; 16(4):238-43. doi: https://doi. org/10.1177/1534734617737639. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/29145757/

15. Neyens JCL, Cereda E, Meijer EP, Lindholm C, Schols JMGA. Arginine-enriched oral nutritional supplementation in the treatment of pressure ulcers: A literature review. Wound Medicine. 2017; 16:46–51. doi: https://doi.org/10.1016/j. wndm.2016.07.002 Consultado 20 de junio de 2021 al 2022 en: https://www.sciencedirect.com/science/article/pii/S2213909516300404 (anterior 13)

16. Munoz N, Posthauer ME, Cereda E, Schols JMGA, Haesler E. The Role of Nutrition for Pressure Injury Prevention and Healing: The 2019 International Clinical Practice Guideline Recommendations. Adv Skin Wound Care. 2020;33(3):123-136. doi: https://doi.org/10.1097/01. ASW.0000653144.90739.ad. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/32058438/ (anterior 55)

17. Ye J, Mani R. A systematic review and meta-analysis of nutritional supplementation in chronic lower extremity wounds. Int J Low Extrem Wounds. 2016; 15:296-302. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/27810941/

18. Reyero González, P. Perfil epidemiológico del paciente con diabetes en España a partir de la encuesta europea de salud en España de 2014. (Trabajo de Fin de Grado). 2018.

Departamento de Salud Pública y Materno Infantil. Universidad Complutense. Consultado 20 de junio de 2021 al 2022 en: http://147.96.70.122/web/tfg/tfg/memoria/patricia%20reyero%20go nzalez.pdf

19. Gau, B. R., Chen, H. Y., Hung, S. Y., Yang, H. M., Yeh, J. T., Huang, C. H., ... y Huang, Y.Y. (2016). The impact of nutritional status on treatment outcomes ofpatients with limb-threatening diabetic foot ulcers. Journal of diabetes andits complications, 30(1), 138-142. doi:10.1016/j.jdiacomp.2015.09.011 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/26490754/

20. Roldán Valenzuela, A., Ibáñez Clemente, P., Alba Moratilla, C., Roviralta Gómez, S.,Casajús Tormo, M.T., Pérez Barreno, D., ... y Hidalgo Ruiz, S. (2017). Guía de Práctica Clínica: Consenso sobre úlceras Vasculares y PD de la Asociación Española de Enfermería Vascular y Heridas (AEEVH). Consultado 20 de junio de 2021 al 2022 en: https://gneaupp.info/consenso-sobre-ulceras-vasculares-y-pie-diabetico-de-la-asociacion-espanola-de-enfermeria-vascular-y-heridas-aeevh/

21. Verdú J, Perdomo E. Nutrición y heridas crónicas. Documentos técnicos GNEAUPP n°12: Grupo Nacional para el Estudio y Asesoramiento en Úlceras por presión y heridas crónicas; Logroño 2011.Pp: 2-33 Consultado 20 de junio de 2021 al 2022 en: https://gneaupp.info/wp-content/uploads/2014/12/59_pdf1.pdf

22. Quain, A. et al. Nutrition in Wound Care Management: A Comprehensive Overview. Wounds. Compendium of Clinical Research and Practice. 2015 [consulted 08 Jun 2021]; 27(12), 327-335. Consultado 20 de junio de 2021 al 2022 en: https://europepmc.org/article/med/27447105

23. Shah AD, Rushakoff RJ. Patient self-management of diabetes care in the inpatient setting: con. J Diabetes Sci Technol 2015; 9:1155–1157 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/25990293/

24. Umpierrez GE, Klonoff DC. Diabetes technology update: use of insulin pumps and continuous glucose monitoring in the hospital. Diabetes Care 2018; 41:1579–1589 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/29936424/

25. Houlden RL, Moore S. In-hospital management of adults using insulin pump therapy. Can J Diabetes 2014; 38:126–133 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/24690507/

26. Curll M, Dinardo M, Noschese M, Korytkowski MT. Menu selection, glycaemic control and satisfaction with standard and patientcontrolled consistent carbohydrate meal plans in hospitalised patients with diabetes. Qual Saf Health Care 2010; 19:355–359 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/20693224/

27. McMahon MM, Nystrom E, Braunschweig C, Miles J, Compher C; American Society for Parenteral and Enteral Nutrition (ASPEN.) Board of Directors; American Society for Parenteral and Enteral Nutrition. ASPEN clinical guidelines: nutrition support of adult patients with hyperglycemia. JPEN J Parenter Enteral Nutr. 2013; 37 (1):23-36.

28. Mabrey ME, Setji TL. Patient Self-Management of Diabetes Care in the Inpatient Setting: Pro. J Diabetes Sci Technol. 2015; 9(5):1152-1154. Published 2015 Jun 19. Doi: 10.1177/1932296815590827. Consultado 20 de junio de 2021 al 2022 en: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4667327/

29. Umpierrez GE. Basal versus sliding-scale regular insulin in hospitalized patients with hyperglycemia during enteral nutrition therapy. Diabetes Care 2009; 32:751–753 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/19336641/

30. Pichardo-Lowden AR, Fan CY, Gabbay RA. Management of hyperglycemia in the non-intensive care patient: featuring subcutaneous insulin protocols. Endocr Pract 2011; 17: 249–260. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/21041168/

31. Corsino L, Dhatariya K, Umpierrez G. Management of diabetes and hyperglycemia in hospitalized patients. In Endotext. Accessed 28 October 2019. Consultado 20 de junio de 2021 al 2022 en: http://www.ncbi .nlm.nih.gov/books/NBK279093/

32. Moghissi ES, Korytkowski MT, DiNardo M, et al.; American Association of Clinical Endocrinologists; American Diabetes Association. American Association of Clinical

Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Diabetes Care 2009; 32:1119–1131 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/19429873/

33. Ketan Dhatariya, Leonor Corsino, and Guillermo E. Umpierrez. Management of Diabetes and Hyperglycemia in Hospitalized Patients. 2020. Consultado 20 de junio de 2021 al 2022 en: https://www.ncbi.nlm.nih.gov/sites/books/NBK279093/

34. Gosmanov AR, Umpierrez GE. Medical nutrition therapy in hospitalized patients with diabetes. Current Diabetes Reports. 2012; 12:93–100. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/21997598/

35. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM, Seley JJ, Van den Berghe G. Management of hyperglycemia in hospitalized patients in non-critical care setting: An Endocrine Society clinical practice guideline. Journal of Clinical Endocrinology Metabolism. 2012; 97:16–38. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/22223765/

36. McMahon MM, Nystrom E, Braunschweig C, Miles J, Compher C. Nutrition ASfPaE. ASPEN clinical guidelines: Nutrition support of adult patients with hyperglycemia. Journal of Parenteral and Enteral Nutrition. 2013; 37:23–36. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/22753619/

37. Roberts AW, Penfold S. Care obotJBDSJfI. Glycaemic management during the inpatient enteral feeding of people with stroke and diabetes. Diabetic Medicine. 2018; 35:1027–1036. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/30152589/

38. Schafer RG, Bohannon B, Franz M, Freeman J, Holmes A, McLaughlin S, Haas LB, Kruger DF, Lorenz RA, McMahon MM. Translation of the diabetes nutrition recommendations for health care institutions. Diabetes Care. 1997; 20:96–105. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/9028703/

39. McMahon MM, Rizza RA. Nutrition support in hospitalized patients with diabetes mellitus. Mayo Clinic Proceedings. 1996; 71:587–594. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/8642888/

40. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, Hiesmayr M, Mayer K, Montejo JC, Pichard C, Preiser J-C, van Zanten AR, Oczkowski S, Szczeklik W, Bischoff SC. ESPEN guideline on clinical nutrition in the intensive care unit. Clinical Nutrition. 2019; 38:48–79. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/30348463/

41. Via MA, Mechanick JI. Inpatient enteral and parental nutrition for patients with diabetes. Current Diabetes Reports. 2011; 11:99–105. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/21170688/

42. Elia M, Ceriello A, Laube H, Sinclair AJ, Engfer M, Stratton RJ. Enteral nutritional support and use of diabetes-specific formulas for patients with diabetes: A systematic review and meta-analysis. Diabetes Care. 2005; 28:2267–2279. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/16123506/

43. Pérez-Cruz E, Calderón-Du Pont D. E, Cardoso-Martínez C, Arredondo D, Gutiérrez-Déciga M, Mendoza-Fuentes C. E, Minerva Obregón-Ríos E, Ramírez-Sandoval A. S, Rojas-Pavón B, Rosas-Hernández L. R, Volantín-Juárez F. E. Estrategias nutricionales en el tratamiento del paciente con diabetes mellitus. Rev Med Inst Mex Seguro Soc. 2020; 58(1):50-60. Consultado 20 de junio de 2021 al 2022 en: https://www.medigraphic.com/pdfs/imss/im-2020/im201h.pdf

44. Mcardle DP, Duane M, Sian R and Julie Taplin. The role of carbohydrate in diabetes management. Practical Diabetes 2016; 33(7): 237-242. [DOI:https://doi.org/10.1002/pdi.2048] Consultado 20 de junio de 2021 al 2022 en: https://onlinelibrary.wiley.com/doi/abs/10.1002/pdi.2048

45. Osama Hamdy and Mohd-Yusof BN. Nutrition in Diabetes. Clinical review article (Elsevier) 2016; 45(4): 799-817. [https:// doi.org/10.1016/j.ecl.2016.06.010] Consultado 20 de junio de 2021 al 2022 en: https://wchh.onlinelibrary.wiley.com/doi/full/10.1002/pdi.2048

46. Canadian Diabetes Association. Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes 2013; 37 (Suppl 1): S1-212. Consultado 20 de junio de 2021 al 2022 en: http://guidelines.diabetes.ca/app_themes/cdacpg/resources/cpg_2013_full_en.pdf

47. American Diabetes Association. Nutrition Principles and Recommendation in Diabetes. Diabetic Care. 2004; Vol: 27 no suppl 1536. https://pubmed.ncbi.nlm.nih.gov/14693924/

48. Mohammad Asif. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. Journal of education and health promotion 2014; 3(1): 1-5. [PMID: 24741641] [DOI:10.4103/2277-9531.127541] Consultado 20 de junio de 2021 al 2022 en: http://www.ghrnet.org/index.php/ijdr/article/view/2493/2890

49. Fasanmade AA, and Anyakudo MMC. Glycemic Indices of selected Nigerian Flour Meal Products In Male Type 2 Diabetic Subjects. Diabetologia Croatica 2007; 36(2): 33-38. Consultado 20 de junio de 2021 al 2022 en: https://www.researchgate.net/publication/287697732_Glycemic_indices_of_selected_Nigerian_flour_meal_products_in_male_type_2_diabetic_subjects

50. Ogbonna OC, Fadeiye EO, Ikem RT, Oladipo KO, Soyoye DO, Olulana TM et al. Blood glucose response on consumption of cassava varieties (Garri) in healthy Nigerian subjects. J Nutr Hum Health 2018; 2(1): 22-27. Consultado 20 de junio de 2021 al 2022 en: https://www.ifpri.org/publication/blood-glucose-response-consumption-cassava-varieties-garri-healthy-nigerian-subjects

51. Famakin O, Akindele F, Oluwole S, Adebanjo AB, and Tayo NF. Assessment of nutritional quality, glycaemic index, antidiabetic and sensory properties of plantain (Musa paradisiaca)-based functional dough meals. J Food Sci Technol 2016; 53(11): 3865- 3875. [PMID: 28035142]; [DOI 10.1007/s13197-016-2357-y] Consultado 20 de junio de 2021 al 2022 en: https://www.science.gov/topicpages/g/glycaemic+load+gl

52. Hermansen MF, Nina MBE, Lene SM, Lotte H, and Kjeld H. Can the Glycemic Index (GI) be used as a tool in the prevention and management of type 2 diabetes? Rev Diabet Stud 2006; 3:61-71. [PMID: 17487328]; [DOI: 10.1900/RDS.2006.3.61] Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/17487328/

53. Agama-Acevedo E, Islas-Herna´ndez JJ, Pacheco-Vargas G, Osorio- Dı´az P, Bello-Pe´rez LA. Starch digestibility and glycemic index of cookies partially substituted with unripe banana flour. LWT Food Sci Technol 2012; 46:177-182 Consultado 20 de junio de 2021 al 2022 en: https://jurnal.polbangtanmanokwari.ac.id/index.php/jt/article/view/48

54. American Diabetes Association. Obesity management for the treatment of type 2 diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care 2018; 41(Suppl. 1): S65-S72 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/29222378/

55. Fox CS, Golden SH, and Anderson C. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: a scientific statement from the American Heart Association and the American Diabetes Association. Diabetes Care 2015; 38(9): 1777-803. [PMID: 26246459]; [DOI: 10.2337/dci15-0012] Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/26246459/

56. Ursula S, Lotte L, Tine T, Thorhallur I, Ulf R, Matti U et al. Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: a systematic review. Food & Nutrition Research 2014; 58: 25145. [PMID: 25045347]; [DOI: 10.3402/ fnr.v58.25145] Consultado 20 de junio de 2021 al 2022 en: http://www.ghrnet.org/index.php/ijdr/article/view/2493/2890

57. Risérusa Ulf, Walter CW, and Frank BH. Dietary fats and prevention of type 2 diabetes. Prog Lipid Res 2009; 48(1): 44-51. [PMID: 19032965]; [DOI: 10.1016/j.plipres.2008.10.002] Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/19032965/

58. Eleazu CO. The concept of low glycemic index and glycemic load foods as panacea for type 2 diabetes mellitus; Prospects, challenges and solutions. Afri Health Sci 2016; 16(2): 468-479. [PMID: 27605962]; [DOI: 10.4314/ahs.v16i2.15] Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/27605962/

59. Hayley EB, Salvatore C and Carl JL. Dietary Fats and Chronic Noncommunicable Diseases. Nutrients 2018; 10(10): 1385. [PMID: 30274325]; [DOI: 10.3390/nu10101385] Consultado 20 de junio de 2021 al 2022 en:https://pubmed.ncbi.nlm.nih.gov/30274325/

60. Malik SV, Yanping L, Deirdre KT, An P and Frank BH. Dietary Protein Intake and Risk of Type 2 Diabetes in US Men and Women. American Journal of Epidemiology 2015; 183(8): 715- 728. [PMID: 27022032]; [DOI: 10.1093/aje/kwv268] Consultado 20 de junio de 2021 al 2022 en:https://pubmed.ncbi.nlm.nih.gov/27022032/

61. Shuang T, Qian X, Ruyue J, Tianshu H, Changhao S and Lixin N. Dietary Protein Consumption and the Risk of Type 2 Diabetes: A Systematic Review and Meta-Analysis of Cohort Studies. Nutrients 2017; 9(9): 982. [PMID: 28878172]; [DOI: 10.3390/ nu9090982] Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/28878172/

62. Comerford BK and Gonca P. Protein Source on Glucoregulatory Markers and Type 2 Diabetes: Different Effects of Dairy, Meat, Fish, Egg, and Plant Protein Foods. Nutrients 2016; 8(446): 1-18. [PMID: 27455320]; [DOI: 10.3390/nu8080446.] Consultado 20 de junio de 2021 al 2022 en:https://pubmed.ncbi.nlm.nih.gov/27455320/

63. Beasley MJ and Judith WR. The Role of Dietary Proteins among Persons with Diabetes. Curr Atheroscler Rep 2013; 15(9):348. [PMID: 23881544]; [DOI: 10.1007/s11883-013-0348-2] Consultado 20 de junio de 2021 al 2022 en:https://www.researchgate.net/publication/333295637_Dietary_Management_of_Diabetes_Mellitus_with_Focus_on_Nigeria

64. Kulprachakarn, K., Ounjaijean, S., Wungrath, J., Mani, R., y Rerkasem, K. (2017). Micronutrients and natural compounds status and their effects on wound healing in the diabetic foot ulcer. The international journal of lower extremity wounds, 16(4), 244-250. doi: 10.1177/1534734617737659 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/29145756/

65. Ponce Jarrín, F. (2017). Actualizaciones en el pie diabético: estudio observacional y experimental sobre los factores de riesgo, amputación y tratamiento en la úlcera infectada del pie diabético Severo, en un hospital de especialidades de Quito (Ecuador). Departamento de ciencias biomédicas y del diagnóstico. Universidad de Salamanca. doi:10.14201/gredos.137129 Consultado 20 de junio de 2021 al 2022 en: https://gredos.usal.es/handle/10366/137129

66. Brookes, J. D. L., Jaya, J. S., Tran, H., Vaska, A., Werner-Gibbings, K., D'Mello, A. C. y Yii, M. K. (2019). Broad-Ranging Nutritional Deficiencies Predict Amputation in Diabetic Foot Ulcers. The international journal of lower extremity wounds, 00 (0), 1-7. Doi: 10.1177/1534734619876779 Consultado 20 de junio de 2021 al 2022 en:https://www.vascularfocus.com.au/research-and-press

67. Molnar, J. A., Underdown, M. J., y Clark, W. A. (2014). Nutrition and chronic wounds. Advances in wound care, 3(11), 663-681. doi:10.1089/wound.2014.0530 Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/25371850/

68. Jones, M. S., Rivera, M., Puccinelli, C. L., Wang, M. Y., Williams, S. J., y Barber, A. E. (2014). Targeted amino acid supplementation in diabetic foot wounds: pilot data and a review of the literature. Surgical infections, 15(6), 708-712. doi:10.1089/sur.2013.158 Consultado 20 de junio de 2021 al 2022 en: http://www.shieldhealthcare.com/community/wpcontent/uploads/2019/12/121119_Nutrition_A_to_Zinc_Collins.pdf

69 Carrera,C. The answer is in nature: "micronutrients: the vitamins, therapeutic agents in wounds".SciElo. 2013[Consulted 08 Jul 2021]; 12(31). Consultado 20 de junio de 2021 al 2022 en: https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1695-61412013000300017

70. Gropper SS, Smith JL, Groff JL. Advanced Human Nutrition and Metabolism, 5th ed. Belmont, CA: Wadsworth, 2009. Consultado 20 de junio de 2021 al 2022 en: https://www.worldcat.org/title/advanced-nutrition-and-human-metabolism/oclc/213355145

71. Gottschlich M. Fat-Soluable Vitamins and Wound Healing. In: In: Molnar JA, ed. Nutrition and Wound Healing. Boca Raton, FL: CRC Press, 2007: 149–171. Consultado 20 de junio de 2021 al 2022 en: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4217039/

72. Burgess C. Topical vitamins. J Drugs Dermatol 2008; 7(7 Suppl):s2–s6. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/18681152/

73. Wicke C, Halliday B, Allen D, et al. Effects of Steroids and Retinoids on Wound Healing. Arch Surg. 2000; 135(11):1265–1270. doi:10.1001/archsurg.135.11.1265

74. Moores J. Vitamin C: a wound healing perspective. Br J Community Nurs. 2013 ;(suppl):S8-S11. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/24796079/

75. Gunton, J., Girgis, C., Lau, T., Vicaretti, M., Begg, L., & Flood, V. (2020). Vitamin C Improves Healing of Foot Ulcers; A Randomised, Double-Blind, Placebo-Controlled Trial. British Journal of Nutrition, 1-21. doi:10.1017/S0007114520003815

76. Christie David, D. J., y Gunton, J. E. (2017). Vitamin C deficiency and diabetes mellitus–easily missed?. Diabetic Medicine, 34(2), 294-296. doi:19.1111/dme.13287 Consultado 20 de junio de 2021 al 2022 en: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13287

77. Razzaghi R, Pourbagheri H, Mansooreh M, et al. The effects of vitamin D supplementation on wound healing and metabolic status in patients with diabetic foot ulcer: a randomized, double-blind, placebo-controlled trial. J Diabetes Complications. 2017;31:766-772. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/27363929/

78. Afzali H, Jafari Kashi AH, Momen-Heravi M, Razzaghi R, Amirani E, Bahmani F, Gilasi HR, Asemi Z. The effects of magnesium and vitamin E co-supplementation on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial. Wound Repair Regen. 2019 May; 27(3):277-284. doi: 10.1111/wrr.12701. Epub 2019 Feb 11. PMID: 30693609.

79. Momen-Heravi M, Barahimi E, Razzaghi R, Bahmani F, Gilasi HR, Asemi Z. The effects of zinc supplementation on wound healing and metabolic status in patients with diabetic foot ulcer: a randomized, double-blind, placebo-controlled trial. Wound Repair Regen. 2017; 25:512-520. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/28395131/

80. Vas PRJ, Edmonds ME, Papanas N. Nutritional supplementation for diabetic foot ulcers: the big challenges. Int J Low Extrem Wounds. 2017;16:226-229. Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/29251542/

81. Dorner B, Posthauer ME, Thomas D. 2009. The role of nutrition in pressure ulcer prevention and treatment: National Pressure Ulcer Advisory Panel White Paper. www.npuap.org (accessed July 13, 2013). Consultado 20 de junio de 2021 al 2022 en: https://pubmed.ncbi.nlm.nih.gov/19521288/

82. Posthauer ME. Do patients with pressure ulcers benefit from oral zinc supplementation? Adv Skin Wound Care 2005; 18:471–472. Consultado 20 de junio de 2021 al 2022 en: https://www.woundscanada.ca/docman/public/wound-care-canada-magazine/2011-vol-9-no-4/440-wcc-autumn-2011-v9n4-zinc-english/file

83. García Fernández, F.P., Soldevilla Ágreda, J.J., Pancorbo Hidalgo, P.L., Verdú Soriano, J., López Casanova, P y Rodríguez Palma, M. (2018). "Qué no hacer en las heridas crónicas" Recomendaciones basadas en la evidencia (Documento técnico No. XIV). Logroño: Grupo Nacional para el Estudio y Asesoramiento en Úlceras por Presión y Heridas Crónicas (GNEAUPP). Consultado 20 de junio de 2021 al 2022 en: https://gneaupp.info/que-no-hacer-en-las-heridas-cronicasrecomendaciones-basadas-en-la-evidencia/

84. Servicio canario de la Salud. (2017). Guía de actuación Pie diabético en Canarias. Consultado 20 de junio de 2021 al 2022 en: https://gneaupp.info/guia-de-actuacion-pie-diabetico-encanarias/

85. Marinel.lo Roura, J. y Verdú Soriano, J. (Coords.). (2018). Conferencia nacional de consenso sobre las úlceras (C.O.N.U.E.I.). Documento de consenso 2018 (2ª ed). Madrid: Ergon.

Consultado 20 de junio de 2021 al 2022 en: https://gneaupp.info/conferencianacional-de-consenso-sobre-las-ulceras-de-la-extremidad-inferior-c-o-n-u-ei