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Review

Nutritional assessment of patients with type 2 diabetes and chronic kidney disease: a review

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Abstract

It is a well-known fact that the prevalence of type 2 diabetes (T2DM) increases each year. It has a complex etiology that includes irreversible risk factors such as age, genetics, race, and ethnicity, as well as reversible risk factors such as diet, physical activity, and smoking. The goals of this review are to look at various studies that investigate the paths to assess the nutritional status of patients with T2DM who are also linked to chronic diseases. In patients with type 2 diabetes, malnutrition has been recognized as a serious health problem, mainly in hospitalized conditions. Therefore, we gathered information that helps the physician look into the patient's nutritional status in order to have a better outcome.

Keywords: chronic disease, clinic and para-clinic evaluation, malnutrition

Worldwide, the prevalence of diabetes is rising, with the largest increase occurring in low- and middle-income countries. In most developed countries, type 2 diabetes is currently the main cause of end-stage renal disease, and it also causes a large number of cardiovascular diseases. In countries with weaker economies, type 2 diabetes is rapidly replacing infectious diseases as the main cause of kidney disease and is competing for scarce medical resources [1]. The risk of chronic kidney disease (CKD) for people with diabetes is nearly 2 times higher than for people without diabetes. The odds ratio of CKD varies from 1.3 to 4.6, depending on the world, and this risk is exacerbated by the presence of high blood pressure [1].

As with other diseases, the clinical definition of CKD in diabetic patients is persistent albuminuria (albumin to creatinine ratio [ACR] ≥30 mg/g for at least 3 months) and/or persistent underestimated glomerular filtration rate (eGFR ≤60 mL/min/1.73 m^2), regardless of the cause.

The nutritional assessment is a complex process through which the information (clinical, laboratory, para-clinical, etc.) can be collected, classified and integrated. This is a phased process, starting with more complex procedures from basic nutritional screening to determining body composition and diagnosing abnormal metabolism of macro- or micronutrients [2]. Nutritional risk screening is a simple and fast first-line tool used to detect patients at risk of malnutrition and should be systematically performed in hospitalized patients [3].

Disorders of nutritional status are very common, with at least 40% of the world's population being affected by some form of malnutrition (malnutrition or over nutrition). Supernutrition through its most common clinical form, abdominal obesity, is a defining criterion of the metabolic syndrome, having a great impact on cardiovascular risk, often encountered in patients with type 2 diabetes [2, 4].

In addition, the predictive power of mortality may be high; for example, higher BMI and serum lipid levels associated with poor prognosis in the general population can predict improved survival of CKD, a phenomenon known as reverse epidemiology [5].

On the other hand, malnutrition (especially proteic) is a common complication of most chronic diseases, which strongly predicts repeated/long-term hospitalization, adverse evolution and high mortality. Therefore, for patients with chronic diseases, adequate nutritional treatment through nutritional means (nutrition medical intervention), especially risk detection/quantification and its subclinical manifestations are the basic goals [2]. Under nutrition has been frequently reported in patients on admission to hospital. Since this situation is not always detected in time, screening of nutritional risks on admission has been widely advocated [6].

According to this definition, malnutrition can be referred to as both over- and undernourished. Although the incidence of over nutrition among the elderly in developing countries is increasing due to the poor development of the elderly and changes in their eating habits, in general, under nutrition is still a major concern. Therefore, in this review, unless otherwise stated, malnutrition refers to under nutrition unless otherwise specified [7].

Malnutrition is a very common problem, affecting approximately 30–50% of hospitalized patients. Hospital malnutrition is associated with an increase in morbidity and mortality, a higher rate of readmission, and the need for rehabilitation support after discharge. Therefore, medical and social costs are higher. In different studies in Spain, it is estimated that among the elderly population, the prevalence of malnutrition in hospitals is between 12.5% and 78.9% [8]. It is believed that the aging process is one of the causes of malnutrition, which will eventually affect the nutritional status of the elderly. The American Society for Parenteral and Enteral Nutrition (ASPEN) defines malnutrition as acute, sub-acute or chronic nutritional conditions, in which varying degrees of over nutrition or under nutrition (with or without inflammatory activity) lead to changes in body composition and weakened functions [7].

Malnutrition is an independent risk factor that can negatively affect the patient's clinical outcome, quality of life, physical function and autonomy. In order to provide timely and appropriate nutritional support, it is important to detect patients at risk of malnutrition or malnutrition early [3].

The pathogenesis of malnutrition in chronic kidney disease is complex and involves a variety of pathophysiological changes, including decreased appetite and nutrient intake, hormonal imbalance, metabolic imbalance, inflammation, increased catabolism, and abnormalities related to dialysis. Malnutrition increases the risk of morbidity, mortality and overall disease burden in these patients [9].

Anorexia is common in CKD patients and may be caused by appetite (appetite stimulation) and anorexia (appetite inhibition), accumulation of metabolic waste products, kidney failure, peculiar smell and the effect of drugs on taste buds. The cumulative effect of these factors leads to a reduction in nutritional intake. The result of the chronic inflammatory state in CKD is an increase in resting energy expenditure, which promotes protein catabolism and reduces anabolism [9].

The methods used to assess nutritional status are: clinical examination, which includes the anamnesis (including specific means of investigating dietary intake) and a thorough physical examination, including anthropometric measurements and the search for specific signs of certain nutritional deficiencies; biochemical data, which have the role of identifying/quantifying major nutritional deficiencies and to objectify to a certain extent the intake of certain nutrients; para-clinical data, especially procedures for determining body composition (with varying degrees of accuracy) [2].

Clinical Exam

Nutritional anamnesis

The physiological and pathological history of the patient constitute the first chapter in the nutritional anamnesis and address especially the presence of chronic or acute diseases that can influence the nutritional status, information about the

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chronic use of medication recommended by the doctor or self-administered (including legal/illegal drug use), vitamins, nutritional supplements, natural remedies, etc. The patient should also be asked about food allergies or known intolerances (e.g. lactose, gluten, etc.) [2].

Family history

They include two types of information: the existence of blood relatives of genetically transmitted diseases (such diseases have a family agglomeration without an absolute inheritance, for example, hypertension, type 2 diabetes, etc.) and diseases due to contagion in a familiar environment, a common way of life or exposure to the same toxins [10]. Another type of information needed in this history is family eating habits: if meals are shared, if eaten at a restaurant, gastronomy (frying fatty foods, using animal fats for cooking, eating bread, etc.); the amount and type of alcohol consumed in common at meals, etc. [2].

Socio-professional background

Includes a series of data that can be very relevant. They are varied enough to be grouped into several categories: professional, social, geographical and lifestyle of the patient (toxic consumption, eating habits (may be related to religion, occupation or place of residence) and extra-occupational physical exertion are known disease or health factors [2, 10]. Another category of data characterizes the patient's ability to understand his or her health problems as well as to adhere to a long-term TMN plan: functional and memory capacity, level of education, type of emotional response to finding out his medical condition (chronic/incurable disease, need for insulin therapy, likelihood of initiating dialysis, etc.) [2].

Dietary history. Usual intake (dietary history). The method of estimating the usual intake, also called dietary history, is a retrospective method by which the patient is asked to describe his daily "usual" intake qualitatively and quantitatively. From a technical point of view, the examiner may provide the patient with a questionnaire to complete (possibly as long as he or she is waiting for consultation), which will list the main food groups, along with a description of a "portion" of the food, accompanied by questions such as: "How many such portions are usually consumed daily/weekly?" [2].

Food frequency questionnaire. This is another retrospective method, which complements the dietary history and refers to the frequency with which the patient consumes the main food groups. This procedure usually insists on certain foods that have clinical significance, such as fruits, vegetables, meat, eggs or dairy products. Currently, relatively simple tools have been created that integrate the procedures of the dietary anamnesis in order to be used quickly as a screening in daily practice; they can be addressed to patients, such as the Rapid Eating Assessment for Patients (REAP) form [11], or they can be used by healthcare professionals who do not have special clinical nutrition training, such as the WAVE (Weight, Activity, Variety) guide and excess [2, 12].

Subjective global assessment (SGA) is a tool used by healthcare providers to assess nutritional status and help predict nutrition-related clinical outcomes (such as postoperative infection and/or mortality). This tool has many advantages in clinical and research environments: it is cheap, rapid to conduct; it can be effectively used by providers from different disciplines, such as nursing, nutritionist, and physician; and it is found to be reproducible in some studies, effective and reliable. Due to its advantages, SGA has been recommended by the National Kidney Foundation (NKF) Kidney Disease/Dialysis Outcomes and Quality Initiative (K/DOQI) for nutritional assessment of adult dialysis populations [13].

In the past few decades, a variety of scoring and screening systems have been established, which can be used in various clinical settings and patient populations (inpatients, communities, geriatrics, etc.). Screening should be carried out within the first 24–48 hours after admission, after which it should be screened regularly (for example once a week) in order to quickly and accurately identify those who should be referred to nutrition experts (for example nutritionists, expert clinicians) personal further evaluation. Nutrition screening should include dynamic

parameters rather than static parameters, such as recent weight loss, current body mass index (BMI), recent food intake, and disease severity [3].

One of the most commonly used nutritional risk screening tools in hospitals around the world is NRS-2002. NRS-2002 was developed by Kondrup et al. and is intended to be a generic tool in the hospital setting – that is, useful in detecting the majority of patients who would benefit from nutritional therapy [14].

The Global Subjective Nutritional Assessment (SGA) is a practical, non-invasive and inexpensive composite tool that is widely used in clinical practice [5].

Use the 4-point SGA scale to assess nutritional status. The scale consists of 6 components: three are based on the patient's weight loss history, the incidence of anorexia and vomiting, and three are based on the physician's degree of muscle wasting, the presence of edema and subcutaneous loss as mentioned before. PEW_{SGA} is defined as an SGA score> 1, and a score of 1 indicates that the nutritional status is normal. In several studies, SGA was found to be a reliable tool for assessing nutritional status, and is related to clinical features, anthropometrics, and nutritional biomarkers also shown in this study. However, due to its subjectivity, people question the effectiveness of SGA as a nutritional marker [5].

Cooper et al. who compared SGA with total body nitrogen as the gold standard for protein deposits in 76 dialysis patients reported that although SGA could differentiate severely malnourished patients from those with normal nutrition, it could not predict the degree of malnutrition [15].

Jones et al. using a compound nutritional score derived from SGA, body mass index, percentage of reference weight, triceps fold thickness, arm circumference, and serum albumin found that SGA could not reliably identify hemodialysis patients with abnormal nutrition [16]. On the other hand, Steiber et al. found that 7-point SGA is a reliable and valid tool for nutritional assessment in hemodialysis adults [17], and Cuppari et al. comparing SGA with anthropometric parameters concluded that 7-point SGA is a reliable tool for the evaluation of PEW in patients with chronic kidney disease without dialysis [18].

The most widely used are weight loss in the past 6 months, body mass index, subjective self-assessment of similar scales (SGA is used for subjective global assessment) [19], nutritional risk index NRI (15.9 × serum albumin concentration (g/dL)+41.7 × (current weight/normal weight) × 100), [3] nutritional risk score (NRS) [6], general screening tool for malnutrition (MUST) and plasma albumin concentration [20].

Practically, European guidelines propose the following criteria to define severe malnutrition, in which preoperative management must be mandatory (recommendation level: A):

- loss of more than 10% of body weight in less than 6 months, or weight loss of more than 5% for a month;
- and/or body mass index <18.5 kg/m2;
- and/or SGA score of C grade;
- and/or serum albumin concentration <30 g/L [20].

Physical Exam

Determining and interpreting the usual anthropometric indices

Anthropometric measurements are considered to be part of the physical examination, are relatively simple and can be important in assessing nutritional status, especially in patients with chronic diseases, which can cause significant changes in body composition through edema or loss of muscle mass. In order to be able to compare evolving anthropometric indices, they must be measured by standardized (reproducible) procedures. The main anthropometric indices used for the diagnosis and monitoring of obesity (supernutrition), in patients with type 2 diabetes, are the BMI and AC. Another significant parameter especially for patients with chronic diseases (in which there is a risk of global and/or protein malnutrition) for those associated with CKD is weight change over a standard period, usually 6 months, expressed as a percentage of weight. initial (or "usual" weight) of the patient [2].

Alternative equations that use limb length instead of height may be valuable for

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epidemiological and clinical work, because there was no predictive equation before. Five equations that combine triceps-skinfold thickness with other anthropometrics explain >80% (male) and >77% (female) variance. The most powerful prediction is based on waist circumference and triceps skinfold thickness. Skinfold thickness measurements continue to provide good predictions of average body density, but there are significant deviations in extreme body fat and age. The most reliable prediction with the least deviation is the waist circumference adjusted for age [21].

Another important parameter is the percentage change in weight, especially for monitoring the nutritional status of patients at risk of malnutrition, such as those with chronic diseases. This index is expressed as a percentage of the patient's initial weight, or of the patient's "usual" weight. If it exceeds 10%, it is severe, and weight loss is common in the elderly, in addition to the association with CKD, and the mechanisms by which chronic diseases can induce weight loss are more often it is about reducing food intake, by decreasing appetite or for objective reasons: edentation, difficulty chewing/swallowing, pain caused by food intake, vomiting, etc. Another category of mechanisms are social: family/social disinsertion, poverty, food procurement difficulties [2].

There are many links between obesity and chronic kidney disease. There are many pathophysiological pathways (such as chronic inflammation, increased oxidative stress) and pathophysiological pathways (such as chronic inflammation, increased oxidative stress and insulin resistance, hypertension, and dyslipidemia) between obesity and chronic kidney disease [22].

The data obtained through the physical examination are valuable because they guide the nutritionist towards certain specific deficiencies, but usually require confirmation through laboratory and/or para-clinical examinations.

Biological evaluation

Laboratory and para-clinical examinations are routinely used in the practice of assessing nutritional status, having the advantage that they are objective and require only a small amount of patient cooperation. There are currently a large number of biochemical determinations that have nutritional significance; they can be classified into: tests to assess energy and protein intake, biomarkers of inflammatory syndrome, methods for estimating body composition.

Assessment of energy and protein intake/status

These biochemical tests evaluate (usually indirectly) both the dietary intake and the protein compartments of the body. These two aspects cannot be separated, because: an adequate energy intake is essential for maintaining the optimal protein status, otherwise the proteins will be used energetically (inefficiently) for energy production by gluconeogenesis; an optimal quantitative and qualitative protein intake (especially through the intake of essential amino acids) is crucial for the structural and functional integrity of protein compartments, the two major protein compartments of the body – the somatic, represented by skeletal muscle, and visceral, represented by "pool" of albumin – have different diagnostic and prognostic significance, so they should be investigated separately [2].

The rate of hepatic synthesis of most proteins used as nutritional biomarkers decreases under the effect of inflammatory cytokines, which is why they are also called "acute phase negative reagents" (albumin, transferrin); there are also proteins whose plasma levels correlate positively with the markers of the syndrome. Inflammatory, called "positive phase positive reactants" (ferritin, fibrinogen). Due to the difficulty of discriminating between the effects of the two mechanisms (intake deficit, respectively inflammation), the values of protein biomarkers should be interpreted only together with the other determinations (inflammatory markers) and in the context of clinical data [2].

Albumin

The albumin concentration in the body is affected by albumin synthesis, degradation

and distribution. Although albumin has the highest concentration of any protein in the vascular system, more than 60% of the protein exists in the extravascular space. During the period of protein consumption caused by major surgery or infection, albumin from the extravascular pool can be mobilized, so the serum albumin concentration may not drop for a long time. The rate of albumin denaturation is proportional to the size of the extravascular pool, which makes the concentration in the serum relatively constant. The long biological half-life of albumin (20 days) only allows changes in serum concentration after chronic malnutrition. Since there are many mechanisms that may cause the albumin concentration to decrease, the isolated serum albumin level may have limited value in assessing the liver synthesis rate of critically ill patients [23].

Serum albumin is not a good indicator of short-term protein and energy deficiency. However, albumin levels are a good indicator of chronic deficiency. Traditionally, albumin has been used to help determine two important nutritional states. First, it helps to recognize chronic protein deficiency when sufficient non-protein calories are consumed, leading to significant hypoalbuminemia. This may be due to the net loss of albumin in the intravascular and extravascular pools. Second, the albumin concentration may help determine a disease called marasmus. This is caused by insufficient calories rather than insufficient protein, so in marasmus, serum albumin levels remain normal, but body weight has dropped considerably [23]. Studies have classified different levels of malnutrition by using albumin levels. Serum albumin levels of 35 g/L or higher are considered normal. Albumin levels of 30–35 g/L indicate mild malnutrition; 25–30 g/L indicates moderate malnutrition; <25 g/L indicates severe malnutrition. Although hypoalbuminemia is common in most patients with diabetic nephropathy, its relationship to the severity and progression of diabetic nephropathy remains largely unknown.

The severity of hypoalbuminemia was significantly associated with an adverse renal outcome, independent of clinical and histopathological features. A study of 188 patients with type 2 diabetes and diabetic nephropathy reported that people with a lower than normal albumin level showed a 7.37-fold higher risk of progression to chronic end-stage renal disease [24].

Pre-albumin

Determining the level of pre-albumin, a hepatic protein, is a sensitive and cost-effective method for assessing the severity of the disease caused by malnutrition in patients with critical or chronic diseases. Pre-albumin levels have been shown to be correlated with patient prognosis and are an accurate predictor of patient recovery. In high-risk patients, pre-albumin levels measured twice a week during hospitalization can alert doctors of a decline in nutritional status, improve patient prognosis, and shorten hospital stays in an economy that is increasingly concerned about costs. Zinc deficiency may reduce pre-albumin levels, but vitamin deficiency does not [25].

Transferrin

Transferrin is a monomeric glycoprotein found in the biological fluids of invertebrates and vertebrates, and has the property of reversibly binding iron [26]. The main site of transferrin synthesis (but not the only one) is also the liver; the total pool is only 5 g, and the plasma half-life is 8–10 days, which is an advantage compared to albuminemia as a nutritional marker [2]. Current research shows that people with serum transferrin saturation greater than 55% have an increased risk of all-cause death [27]. In addition to its traditional role in iron metabolism, transferrin also acts as a growth factor [28].

Retinol-binding protein

Retinol-binding protein consists of 181 amino acid residues. It has been used to monitor

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short-term changes in nutritional status. Its usefulness as a metabolic marker is based on its 12-hour biological half-life and small body pool size. As a polypeptide chain, retinol-binding protein strongly interacts with plasma transthyretin, and circulates in the plasma as a 1:1 mol/L transthyretin-retinol-binding protein complex. Due to its low molecular weight, only the free form of retinol-binding protein which has no affinity for transthyretin can undergo unhindered glomerular filtration. Then, it is reabsorbed by the tubule cells and catabolized there. This may explain the extremely high serum levels of retinol-binding protein in advanced chronic renal insufficiency [23].

Retinol-binding protein (RBP)-4 is a recently discovered adipocytokine associated with insulin resistance. Compared with healthy subjects, the level of RBP-4 in diabetic patients was significantly higher. RBP-4 is significantly positively correlated with triglycerides, systolic blood pressure and urine albumin excretion, and significantly negatively correlated with high-density lipoprotein cholesterol and blood flow-mediated vasodilation [29]. The results are consistent with these findings and may indicate that the degree of obesity (reflected by BMI) is the main determinant of RBP-4 levels [29].

Serum creatinine

Serum creatinine is the most commonly used biomarker of renal function. In the steady state, serum creatinine can be used to evaluate the glomerular filtration rate by adjusting the kidney disease diet (MDRD) or the Chronic Kidney Disease Epidemiology Collaborative Research (CKD-EPI) formula. Serum creatinine is not only considered to be one of the main criteria for the acute kidney assessment of homeostasis and CKD, it also impairs it [30].

The concentration of creatine and creatine phosphate is highest in the skeletal muscle of mammals. Therefore, under steady-state conditions, especially when on a vegetarian diet, the main source of creatinine is skeletal muscle [30].

In healthy individuals, the kidney is the main way to eliminate creatinine. Creatinine has a low molecular weight and does not bind to albumin. [30] Therefore, it is filtered freely at the level of the glomerulus. Creatinine does not have a specific biological function; it is continuously released from muscle cells and excreted by the kidneys being reabsorbed only to a small extent [31].

Other para-clinical investigations

The most accurate estimation of the body composition is of great importance for the evaluation of the nutritional status, because the relative changes of the body compartments significantly influence the diagnostic value of the other nutritional parameters.

Body composition can be assessed by direct and indirect methods. Direct methods address molecular or cellular levels, are precise, but usually invasive and laborious. In practice these methods are used for research purposes [2].

In the early days, body composition analysis was based on anthropometry, which evaluated skinfold thickness (estimating the amount of subcutaneous fat) and/or around the mid-arm or thigh (as a measure of skeletal muscle mass). This method is extended to the evaluation of various parts of the human body through reliable and effective body density measurement of underwater weighing. More advanced methods include dilution technology (D_2O to evaluate whole body water; NaBr to evaluate extracellular water), dual X-ray absorption method (DXA; measurement of bone mineral content, lean soft tissue and fat mass) [32]. MRI or computed tomography (CT; based on ionizing radiation and X-ray attenuation) are used to accurately assess the entire body and regional organ (i.e. skeletal muscle, brain and visceral organs) and tissue masses. In addition to MRI, magnetic resonance spectroscopy measures ectopic fats (e.g. liver, muscle, and pancreas fat). More recently, quantitative (without imaging) magnetic resonance imaging has been introduced to assess adipose tissue (and total body water) with high accuracy [32].

There is currently no universally accepted or comprehensively validated approach to assessing a patient's nutritional status. Moreover, clinical trials have repeatedly shown that no clinical, physical or laboratory examination can adequately predict nutritional risk. It is important for doctors to know both objective and subjective measures of basic body needs and functional capacity [33].

Due to their global ability to assess nutritional needs, clinical assessment systems have gained popularity in clinical practice. However, each has its own limitations, stressing the importance of the need for further evaluation of the effectiveness of these instruments [6]. When used properly, these tools lead to the early identification of patients at risk and allow for rapid intervention, which not only provides better care but also reduces costs [34].

Malnutrition continues to be an independent risk factor that negatively influences patients' clinical outcomes, quality of life, body function and autonomy. However, when equipped with the right clinical tools, the doctor is more likely to provide safe and effective nutritional intervention and ultimately lead to improved clinical outcomes.

Conflict of Interest

The authors declare no conflict of interest.

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