### REVIEW

# The Mediterranean diet could be an exceptional support for patients with chronic renal disease

Francesco Cacciabaudo¹, Roberta Altomare², Vincenzo Davide Palumbo².³, Giuseppe Damiano², Salvatore Fazzotta², Leonardo Gulotta², Giulia Lo Monte⁴, Francesco Maltese³, Attilio Ignazio Lo Monte².³

<sup>1</sup> "P. Giaccone" University Hospital, School of Clinical Nutrition, University of Palermo, Italy - E-mail: f.cacciabaudo@yahoo.it; <sup>2</sup> "P. Giaccone" University Hospital, School of Medicine, University of Palermo, Italy; <sup>3</sup> Department of Surgical, Oncological and Stomatolgical Disciplines, University of Palermo, Italy; <sup>4</sup> "P. Giaccone" University Hospital, School of Biotechnology, University of Palermo, Italy

**Summary.** Chronic renal disease (CKD) is a social problem affecting millions of patients characterized by loss of renal function and related to metabolic diseases. The approach from the dietary point of view to this problem could be a perfect strategy to slow down the progression of the disease and at the same time the problems of malnutrition typical of CKD. Several studies show that the Mediterranean diet (MD) may play a key role in the control of the early stages of the disease. Even if the MD showed to be the best diet for the control of metabolic diseases and for the general well-being, in the case of the patient with CKD, should be adapted in what is called the DASH diet, characterized by the typical roles of the MD but with a controlled intake of minerals and proteins.

Key words: mediterranean diet, chronic renal disease, obesity, cardiovasvascular disease, DASH diet.

## Introduction

Chronic Kidney Disease (CKD) is characterized by a physiological alteration of the kidneys, manifested by abnormal albumin excretion or decreased kidney function, quantified by measuring glomerular filtration rate (GFR), that is detectable for more than three months (1).

CKD occurs from many reasons that alter the function and structure of the kidney irreversibly. CKD is one of the biggest health problem in our society; the number of CKD patients rises every year, reflecting the growing elderly population and the increasing number of metabolic diseases (2).

The causes of CKD may be different: diabetes, hypertension and obesity are the main reasons of this disease (3).

The insulin resistance typical of the metabolic syndrome is present in mild kidney disease, and gets worse as kidney function diminishes (4).

For this reason, the first approach for patients affected by CKD is designing an optimal diet because there is an interrelationships between diet and CKD, but it is not easy to find a perfect balance. The diet plan should be balanced in all nutrients, depending on the stage of the individual patient's illness to maintain the requirements for calories (5). This is not the only problem, since the requirement for calories is also influenced by CKD; in fact, CKD results in the development of insulin resistance and eventual impairment of carbohydrates and lipids utilization. This is relevant because a high intake of protein is generally accompanied by an increase in dietary salts (6).

Up to now, many studies in CKD have focused on protein intake, in particular the guidelines have sug-

gested a protein restriction to get a modest benefit.

The Mediterranean Diet (MD) has received attention for decreasing cardiovascular risk and all the metabolic and inflammatory diseases, including the CKD. In particular, it brings improvements in blood pressure (BP), lipid profile, endothelial function, and systemic inflammation (7).

Clinical practice guidelines for adult patients with CKD have recommended dietary protein intake of 0.6-0.8 g/kg body weight per day and energy intake of 30-35 kcal/kg ideal body weight per day. However, protein restriction is only a part, though a very relevant part, of a more complex dietary management of CKD patients. Phosphate intake should be reduced (700-400 mg/day), as well as sodium intake (2-3 g/day). Dietary energy intake must cover energy requirements up to 35 kcal/kg/day for 65 years old patients (8).

## Could Chronic kidney disease induce malnutrition?

Malnutrition is defined as an alteration of nutritional status resulting from imbalanced nutrients intake; this phenomenon is very common in patients with CKD. The patients affected by CKD show reduced body weight, due to the loss of fat and muscle mass and the low levels of some plasmatic and visceral proteins (9). Various studies show high incidence of malnutrition in 23-76% of haemodialytic (HD) patients and in 18-50% of peritoneal dialysis (PD) patients. The reason of this malnutrition may be related to factors such as age, diseases and quality of dialysis therapy. In many CKD patients the reason of this phenomenon is not really clear; it may be related to a poor food intake, nausea and vomiting due to uremic toxicity, hormonal derangements, acidosis and increased resting energy expenditure and depression of the patient (10).

In CKD, malnutrition is strongly related to many inflammatory metabolic diseases such as atherosclerosis. For this reason, a rapid atherosclerosis that occurs in advanced CKD has been reported by many authors and this is probably due to different mechanisms such as inflammation, malnutrition, oxidative stress and genetic components.

Early evaluation of pre-dialysis CKD patients for malnutrition, paying more attention to their diet and correcting metabolic disorders like acidosis, may help to mitigate development of cardiovascular disease (CVD) (11).

## The role of the Mediterranean diet in several diseases

The discovery of the health benefits of the MD is attributed to the American scientist Ancel Keys who suggested a relationship among lifestyles, nutrition and CVD in different populations (12). From this study comes out, as the populations that follow a diet based on the MD present a very low incidence of metabolic and chronic diseases. The reason of this data are mainly due to the plentiful use of olive oil, bread, pasta, fish, vegetables, herbs, garlic, red onions, and other foods of vegetable origin compared to a rather moderate use of meat (13).

Many studies and clinical trials have shown that the MD reduces the risk of CVD and metabolic syndrome that are related to the CKD. In particular, it has been observed in many trials performed on patients, the decrease of abdominal circumference, an increase in high density lipoprotein (HDL), a decrease in triglycerides, a lowering of blood pressure and a decrease in the concentration of glucose in the blood and all these values are related to the reduction of many chronic diseases (14).

The typical balance of the MD maintains intestinal eubiosys whose imbalance is closely related to systemic inflammatory and metabolic diseases that, as reported, increase the incidence of CKD (15).

The MD provides the high consumption of olive oil that is very rich in monounsaturated fatty acids (MUFA); furthermore, in the traditional MD pattern, the intake of dairy products and meats is lower than in the Western diet and animal fats are mainly from goats and sheep, which provide a higher content in mediumchain fatty acids that are less atherogenic than long-chain fatty acids (16).

Results of the PREDIMED trial pointed out that a MD with relatively high fat intake (35-40%), mostly from Extra virgin olive oil (EVOO), was associated with primary prevention of CVD. Oleic acid is the main MUFA representative component and it is present in EVOO, which is also rich in polyphenols and vitamin E; these compuonds have high anti-inflammatory, antioxidant and vasculoprotective properties. Increased olive oil consumption has been consistently associated with a lower risk of all-cause mortality, car-

diovascular mortality, cardiovascular events and stroke in the general population and in individuals with manifest CVD (17).

From these observations, it is possible to say that a low-fat diet, coupled with the widespread availability of zero- or low-fat foods (e.g., milk, yogurt), is not essentially healthy; in fact, it may induce the people to have higher consumption of refined starch-and sugar-rich foods, thus contributing to excessive energy intake, overweight, obesity, and related complications (i.e., CVD). In support of this concern, there is some evidence that, compared to carbohydrates, both MUFA and polyunsatered fatty acids (PUFA) in the MD eating pattern, tend to reduce low-level density lipoprotein cholesterol (LDL-C) and triglycerides, while increasing HDL-C (18).

Worth of notice is that in the MD the most intake of fats comes from olive oil and fish that are rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and for this reason many evidences support the health benefits of a MD eating pattern against metabolic diseases (19).

Epidemiological data and various clinical trials support a correlation between moderate red wine consumption and lower risk of CVD, but also with lower risk of CKD and end-stage renal disease (ESRD) in individuals with normal kidney function (20, 21).

## Mediterranean Diet for the Chronic Kidney Disease

Traditional dietary management of CKD focuses predominantly on the quantity of calories and proteins, and the restriction of single micronutrients, with little mention of dietary quality. Emphasis on restriction of sodium, potassium and phosphorus in CKD may possibly compromise overall diet quality (22). Fruit and vegetable-rich diets such as the MD are recommended for primary and secondary disease prevention. Many evidences in patients with CKD suggests that the MD may be helpful to delay progression and prevent complications, but in the same time the scientific community has reluctance to recommend a normal MD to the CKD patient; in fact, some of the typical components of the MD pyramid could conflict with the traditional dietary restrictions of CKD (23).

The importance of the MD comes from the balance among all the nutrients but even if a lot of

evidence recommend this diet for special needs, in CKD, some values in nutrients should be readapted (for example protein intake in the MD aligns with a controlled protein diet for CKD – 0.8 g/kg/day). An interesting aspect is the source of protein, which in the MD comes predominantly from vegetables, fish and white meat. Red meat and processed meats are less often consumed, which may convey a lower amount of dietary sodium, phosphate and potassium. Such habits have been associated with lower risk of CKD and ESRD in individuals with a normal kidney function (22). In some studies have been showed the benefits of plant-based versus animal-based protein in patients with CKD, slowing or even blocking the progression of the disease (24, 25).

The Mediterranean diet for CDK treatment may become DASH

The Dietary Approaches to Stop Hypertension (DASH) provides high intakes of fruit, vegetables, legumes, and nuts, moderate amounts of low-fat dairy products, low amounts of animal proteins and sweets; sodium reduction is part of this diet (26). Although the DASH diet was originally designed for blood pressure (BP) reduction, several characteristics, such as higher intakes of whole grain and lower intakes of red and processed meat, are similar to the MD; this may suggest that the DASH diet may be the adapted version of the MD for CKD patients. The DASH diet also improves low-density lipoprotein cholesterol control, insulin sensitivity and reduces the risk for coronary heart disease, heart failure and stroke, all highly important treatment targets for patients with CKD.

For all these reasons, the DASH diet is strongly considered as a MD modified for electrolyte and protein intake suggesting that it may be safe for these specific patients (27).

BP control is a mainstay of treatment for patients with CKD to prevent both the progression of CKD and its associated CVD-related complications.

The National Kidney Foundation - Kidney Disease Outcome Quality Initiative (KDOQI) guidelines do not recommend the DASH eating plan for individuals with "advanced" CKD (defined as eGFR < 60 ml/min/1.73m²). KDOQI guidelines suggest that non-dialysis patients with advanced CKD should limit

protein intake to 0.6 - 0.75 g/kg/day. Reasons cited for this recommendation include observational studies that show an associated reduction in the generation of nitrogenous wastes products and inorganic ions with protein restriction (28).

It is well known that a reduced intake of protein is recommended for CKD patients since it diminishes uremic symptoms, improves hyperkalemia, hyperphosphatemia, and calcium or sodium balance control, protects against oxidative stress which may aggravate progression of CKD, and delays the initiation of dialysis (29).

The DASH diet may be safe in any case for preventing Hypertension and in the population at risk for kidney diseases.

In general there are many evidences that the patients following the DASH diet experience a lower prevalence of metabolic complications and may be most likely to experience slower progression of CKD with adequate BP control (30).

On the other hand, there are many instances when the DASH eating pattern may not be appropriate for patients with CKD. This occurs for individuals who have already experienced metabolic complications or are at high risk for their development. That is, if a patient has high-normal or elevated serum potassium and phosphorus values, the DASH eating pattern should not be initiated (28). A larger study of patients with lower kidney function is clearly needed to definitively establish the efficacy and safety of the DASH diet in this population, considering the risk of hyper-kalemia (30).

#### **Conclusions**

A proper nutritional regimen is important for patients with CKD, and the MD which is rich in fruits, vegetables, fish, cereals, whole grains, fibers and polyunsaturated fatty acids but low in saturated fatty acids, could be beneficial for this category of patients.

Malnutrition often occurs in CDK patients, causing metabolic inflammatory diseases, such as atherosclerosis, and the development of complications that may induce patient early death.

For this reason, choosing accurately the dietary

plan is really important, because it could improve the patient's quality of life.

The re-adaptation of the MD in the DASH diet makes this regimen even more appropriate and safe for the treatment of those patients in an initial or intermediate CKD. In fact, the adjustment of nutrients such as proteins, sodium and potassium, make this diet an ideal therapeutic approach for these patients.

Finally, the DASH diet has a positive effect on blood pressure and those markers of mineral metabolism and kidney function. Further studies are necessary to confirm the therapeutic and safe effects to be adopted worldwide as treatment for the patient in CKD.

### References

- 1. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Prim Care 2008; 35(2):329-44.
- 2. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet. 2017; 389(10116):1238-52.
- 3. Spinelli G, Tomasello G, Damiani F, Damiani P, Lo Monte AI. Endoscopic findings in chronic renal failure: review of literature. Acta Med Mediterr 2012; 28(3):261.
- Liao MT, Sung CC, Hung, KC, Wu CC, Lo L, Lu K C. Insulin Resistance in Patients with Chronic Kidney Disease. J Biomed Biotechnol. 2012: 691369.
- 5. Nashar K, Egan BME. Relationship between chronic kidney disease and metabolic syndrome. Diabetes. Metab Syndr Obes. 2014; 7: 421–435.
- Mitch WE, Remuzzi G. Diets for patients with chronic kidney disease, should we reconsider? BMC Nephrology. 2016; 17:80.
- 7. Khatri M, Moon YP, Scarmeas N, Gu Y, Gardener H, Cheung K, Wright CB, Sacco RL, Nickolas TL, Mitchell SV. The Association between a Mediterranean-Style Diet and Kidney Function in the Northern Manhattan Study Cohort. Clin J Am Soc Nephrol. 2014; 7; 9(11): 1868–1875.
- Aki K, Yasushi O, Reibin T, Toshiyuki A, Sonoo M, Toyoko O, Atsushi A, Ken S. Association between Low Dietary Protein Intake and Geriatric Nutrition Risk Index in Patients with Chronic Kidney Disease: A Retrospective Single-Center Cohort Study. Nutrients. 2016; 8, 662.
- Chung S, Koh ES, Shin SJ, Park CW. Malnutrition in patients with chronic kidney disease, Open J Int Med 2012; 2:89-99.
- 10. Stenvinkel PO, Heimbürgerb O, Lindholm B, Kaysen GA, Bergströmm J. Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). Nephrol Dial Transplant. 2000; 15(7):953-60.
- 11. Adejumo, O, Okaka, E. Malnutrition in pre-dialysis chronic kidney disease patients in a teaching hospital in Southern

- Nigeria. Afr Health Sci. 2016; 16(1):234-241.
- 12. Feinleib M. Seven countries: a multivariate analysis of death and coronary heart disease JAMA. 1981; 245(5):511-512.
- 13. Menotti, A, Keys, A, Blackburn, H, Kromhout, D, Karvonen, M, Nissinen, A, Pekkanen, J, Punsar S, Fidanza F, Giampaoli S, Seccareccia F, Buzina R, Mohacek I, Nedeljkovic S, Aravanis C, Dontas A, Toshima H, Lanti M. Comparison of multivariate predictive power of major risk factors for coronary heart diseases in different countries: results from eight nations of the seven countries study, 25-year follow-up. J Cardiov. Risk, 1996; 3; 69-75.
- 14. Altomare R, Cacciabaudo F, Damiano G, Palumbo VD, Gioviale MC, Bellavia M, Tomasello G, Lo Monte AI. The Mediterranean Diet: A History Of Health. Iranian J Publ Health, 2013; 42(5): 449-457.
- 15. Sinagra E, Tomasello G, Cappello F, Leone A, Cottone M, Bellavia M, Rossi F, Facella T, Damiani P, Zeenny MN, Damiani F, Abruzzo A, Damiano G, Palumbo VD, Cocchi M, Jurjus A, Spinelli G, Lo Monte AI, Raimondo D. Probiotics, prebiotics and symbiotics in inflammatory bowel diseases: state-of-the-art and new insights. J Biol Regul Homeost Agents. 2013; 27(4):919-33.
- Widmer RJ, Flammer AJ, Lilach OL, Lerman A. The Mediterranean Diet, its Components, and Cardiovascular Disease, Am J Med. 2015;128(3):229-38.
- 17. Violi F, Loffredo L, Pignatelli P, Angelico F, Bartimoccia S, Nocella C, Cangemi R, Petruccioli A, Monticolo R, Pastori D, Carnevale R. Extra virgin olive oil use is associated with improved post-prandial blood glucose and LDL cholesterol in healthy subjects. Nutr Diabetes. 2015. 5(7): e172.
- 18. Russo GL. Dietary n 6 and n 3 polyunsaturated fatty acids: From biochemistry to clinical implications in cardiovascular prevention. Biochem Pharmacol 2009;15:937-946.
- Mekki K, Bouzidi-Bekada N, Kaddousb A, Bouchenaka M. Mediterranean diet improves dyslipidemia and biomarkers in chronic renal failure patients. Food Funct 2010;1:110-115.
- 20. Ix JH, Sharma K. Mechanisms Linking Obesity, Chronic Kidney Disease, and Fatty Liver Disease: The Roles of Fetuin-A, Adiponectin, and AMPK. J Am Soc Nephrol 2010;21:406-412.
- 21. Moreno-Luna R, Muñoz-Hernandez R, Miranda ML, Costa AF, Jimenez-Jimenez L, Vallejo-Vaz AJ, Muriana FJ, Villar J, Stiefel P. Olive Oil Polyphenols Decrease Blood Pressure and Improve Endothelial Function in Young Women with Mild Hypertension. Am J Hypertens 2012;25:1299-1304.

- 22. Bellizzi V, Cupisti A, Locatelli F, Bolasco P, Brunori G, Cancarini G, Caria S, De Nicola L, Di Iorio BR, Di Micco L, Fiaccadori E, Garibotto G, Mandreoli M, Minutolo M, Oldrizzi L, Piccoli GB, Quintaliani G, Santoro D, Torraca S, Battista FV. Low-protein diets for chronic kidney disease patients: the Italian experience. BMC Nephrol. 2016;17(1):77.
- 23. Huang X, Jiménez-Moleón JJ, Lindholm B, Cederholm T, Ärnlöv J, Risérus U, Sjögren P, Carrero JJ. Mediterranean Diet, Kidney Function, and Mortality in Men with CKD. Clin J Am Soc Nephrol. 2013; 8(9):1548-1555.
- 24. Chauveau P, Aparicio M, Bellizzi V, Campbell K, Hong X, Johansson L, Kolko A, Molina, P Sezer S, Wanner C, Wee PM, Teta D, Fouque D, Carrero JJ. Mediterranean diet as the diet of choice for patients with chronic kidney disease. Nephrol Dial Transplant. 2017; 1–11.
- Gorayaa N, Wessona DE. Dietary management of chronic kidney disease: protein restriction and beyond. Curr Opin Nephrol Hypertens. 2012; 21(6):635-40.
- 26. Fung TT, Hu, FB, Wu K, Chiuve SE, Fuchs CS, Giovannucci E. The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets and colorectal cancer. Am J Clin Nutr; 2010; 92(6):1429–35.
- 27. Tyson CC, Lin PH, Corsino L, Batch BC, Allen J, Sapp S, Barnhart H, Nwankwo C, Burroughs J, Svetkey LP. Short-term effects of the DASH diet in adults with moderate chronic kidney disease: a pilot feeding study. Clin Kidney J. 2016; 9(4): 592–598.
- 28. Tyson CC, Nwankwo C, Lin PH, Svetkey LP. The Dietary Approaches to Stop Hypertension (DASH) Eating Pattern in Special Populations. Curr Hypertens Rep; 2012.14(5):388-389.
- Rysz J, Franczyk B, Ciałkowska-Rysz A, Gluba-Brzózka A. The Effect of Diet on the Survival of Patients with Chronic Kidney Disease. Nutrients. 2017; 9(5): 495.
- 30. Tyson CC, Kuchibhatla M, Patel UD, Pun PH, Chang A, Nwankwo C, Joseph M, Svetkey L, P. Impact of Kidney Function on Effects of the Dietary Approaches to Stop Hypertension (Dash) Diet. J Hypertens 2014;3.pii:1000168.

Correspondence:

Francesco Cacciabaudo

"P. Giaccone" University Hospital, School of Clinical Nutrition, University of Palermo, Italy

E-mail: f.cacciabaudo@yahoo.it