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Nutrition and Physical Activity in Older Adults with CKD: Two Sides of the Same Coin

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Keywords
Nutrition · Chronic kidney disease · Physical activity · Physical performance · Body composition

Abstract
Introduction: Nutrition and physical activity are two major issues in the management of CKD patients who are often older, have comorbidities, and are prone to malnutrition and physical inactivity, conditions that cause loss of quality of life and increase the risk of death. We performed a multidimensional assessment of nutritional status and of physical performance and activity in CKD patients on conservative therapy in order to assess the prevalence of sedentary behavior and its relationship with body composition. ***Methods:*** A total of 115 consecutive stable CKD patients aged 45–80 years were included in the study. They had no major skeletal, muscular, or neurological disabilities. All patients underwent a multidimensional assessment of body composition, physical activity, and exercise capacity. ***Results:*** Sedentary patients, as defined by mean daily METs <1.5, were older and differed from non-sedentary patients in terms of body composition, exercise capacity, and nutrient intake, even after adjusting for age. Average daily METs were positively associated with lean body mass, muscle strength, 6MWT performance but negatively associated with fat body mass, body mass index, and waist circumference. In addition, a sedentary lifestyle may have negative effects on free fat mass, muscle strength, and exercise capacity and may increase fat body mass. Conversely, decrease in muscle mass and/or an increase in fat mass may lead to a decrease in physical activity and exercise capacity. ***Conclusion:*** There is a clear association and potential interrelationship between nutritional aspects and exercise capacity in older adults with CKD: they are really the two sides of the same coin.

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Introduction

Worldwide, one in four adults does not engage in WHO recommended physical activity, and most of the elderly people with disabilities or chronic diseases have even fewer opportunities to be physically active. In addition, changes in transport models, increased urbanization, and technologies have led to an increase in physical inactivity levels to as high as 70% in many countries.

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The "Global Action Plan on Physical Activity 2018–2030" approved by the WHO defines four strategic goals – active society, active environments, active people, and active systems – to be implemented in all countries in order to reduce the global prevalence of physical inactivity by at least 15% by 2030. The WHO action plan emphasizes the need for a systemic approach that addresses all factors that can influence physical activity: social, economic, cultural, environmental, educational [1, 2].

Physical activity has been widely shown to improve physical and mental health [3]. It is an essential tool in the prevention and treatment of obesity, diabetes and insulin resistance, cardiovascular disease and to counteract sarcopenia, which is increasing in western societies due to demographic changes.

It is also important to stress the difference between "sedentary lifestyle" and inactivity: people who meet the minimum recommended daily amount of PA can still be considered sedentary if they spend the rest of the day sitting. The effects of sedentary time are independent of physical activity levels and can be negative even in people who meet the minimum recommended level of physical activity. Sedentary activities are those characterized by an energy expenditure (EE) of less than 1.5 METs.

Chronic kidney disease (CKD) is a common disease in developed countries, affecting 10–15% of the population, with a prevalence increasing with age: CKD affects about 30% and even more people over the age of 60. CKD is often associated with comorbidities, high cardiovascular risk and a prevalence of frailty, functional impairment and mobility limitations, body composition abnormalities, and poor nutritional status. In this setting, low physical activity and exercise capacity contribute to poor quality of life and increased risk of protein-energy wasting, morbidity, and mortality [4]. In this single-center study, we performed a multidimensional assessment of nutritional status and of physical performance and activity in CKD patients on conservative therapy to assess the prevalence of sedentary behavior and the relationship with body composition.

Subjects and Methods

This is a cross-sectional study on 115 stable consecutive patients (96 males, 19 females) aged 45–80 years, affected by stage 3–5 NDCKD. Patients had no major skeletal, muscular, or neurological disabilities, or had not reported severe limitation in walking.

Patients were excluded if they had severe heart failure (NYHA class IV), respiratory insufficiency, cancer, dementia, psychiatric or neurologic diseases, inflammatory systemic diseases, Barthel Index and/or Karnowsky score <100, had been hospitalized in the previous 3 months, or refused to participate in the study. All patients received standard care including dietary support, according to their clinic and residual kidney function: 69.8% followed a 1.0–0.8 g/kg/day protein diet [5]; 30.3% followed a low protein diet (19.4% an animal-based low protein diet, 10.8% a plant-based low protein diet) [6–8]. All patients underwent a nutritional and functional assessment including anthropometry, body composition analysis (single-frequency bioimpedance analysis), dietary recall, biochemistry, physical activity, and functional testing, as described below.

Nutritional Status Assessment

Body weight was assessed on a mechanical scale with the patient wearing light clothes and no shoes. Height was measured with a stadiometer. Body mass index (BMI) was calculated as body weight (kg)/height^2 (m^2). Other measures included waist and hip circumferences, nondominant middle arm circumference (MAC), and triceps skinfold thickness (TST). TST and MAC were used to calculate the middle-arm muscle circumference and the middle-arm muscular area using specific formulas:

$$\text{Middle-arm muscle circumference} = \text{MAC} - (\text{TST} \times \pi)$$

$$\text{Middle-arm muscular area} = [\text{MAC} - (\pi \times \text{TST})]\ 2/4\pi$$

Body composition analysis was conducted using a bioelectrical impedance single-frequency analyzer (BIA/STA, Akern, Florence, Italy) with a distal, tetrapolar technique, delivering an excitation current at 50 kHz. Impedance (Z) represents the force that interferes with the flow of electric current and is given by the vectorial sum of the resistance (Rz) and the reactance (Xc): the two bioelectric parameters given by the body analyzer. The phase angle is the most immediate bioelectric index that is derived from a proportion between resistance and reactance according to this formula: phase angle = Arctang (Xc/Rz) × 180 × π.

It reflects hydration status and soft tissue cellular mass. Reduced phase angle value reflects increased extra- to intracellular water ratio as well as reduced body cell mass (BCM). BCM is derived from bioimpedance analysis and body cell mass index is consequently calculated. The phase angle is considered the best predictor of survival in CKD in conservative therapy, end-stage kidney disease on peritoneal dialysis and on maintenance hemodialysis, HIV, cancer patients, and other diseases [9–14].

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Physical Activity and Performance Assessment

The level of spontaneous physical activity was assessed by SenseWear Armband (SWA, BodyMedia, Pittsburgh, PA, USA). Patients were advised to wear the device on the upper nondominant arm, in the middle tract between acromion and olecranon processes, over the triceps muscle. They were instructed to continue with their usual daily life while wearing the device and to remove only if they shower or for water activities.

The SWA device collects physiologic data through multiple sensors, particularly a two-axis accelerometer, a heat flux sensor, a skin temperature sensor, a near-body ambient temperature sensor, and a galvanic skin response sensor, that is downloaded and analyzed using a specific software (InnerView™ Research Software, version 6.1). The integrated detections from the biaxial accelerometer and the heat-related sensors have shown to provide additional information that cannot be obtained from movement sensors alone and they have high sensitivity in detecting even little changes in EE associated with complex activities. The SWA reports actual wear time. These features provide several advantages over traditional uniaxial accelerometers for assessing physical activity.

The SWA has been validated both under laboratory conditions and under free living conditions, and it has potential advantages in accuracy when compared with traditional accelerometry-based monitors [15–18]. The validity of total EE estimates from the SWA has been supported in studies using both indirect calorimetry and doubly labelled water [19].

The metabolic equivalent task (MET) is a method for quantifying the intensity of a physical activity and the associated EE, and it is defined as the ratio of metabolic rate during a specific physical activity to a reference metabolic rate, set by convention at 3.5 mL $O_2 \times kg^{-1} \times min^{-1}$. Metabolic equivalent can be converted into kilocalories using the following equation: MET = Kcal/h/Kg bw; 1 MET is the energy expended at rest. So, two METs indicate that the energy expended is twice than that at rest and so on.

For example, reading, listing music correspond approximately to 1.0–1.5 METs, walking slowly corresponds to 1.5–2 METs; walking at 3 km/h or cycling at 8 km/h correspond to 2–3 METs; playing volleyball, cycling at 10 km/h correspond to 3–4 METs; walking at 6 km/h, cycling at 16 km/h, or digging correspond approximately to 5–6 METs. The measurements were carried out on a period of 3 days and include average daily METs, number of steps, the minutes spent in physical activity with intensity >3 METs/min, between 6 and 9 METs/min, or >9 METs/min. Average daily METs values may be considered as a measure of the average daily activity level; in older adults, a daily average value <1.5 METs defines a sedentary patient, 1.5–3 METs define a light activity, ≥3 METs define a moderate to vigorous activity [20].

As measured of performance, we used the 30-s sit-to-stand chair test (STS30″), 5 times sit to stand (STS5), the 6-min walking test (6MWT), and the handgrip strength test. The STS30″ is a validated test, which allows us to assess lower extremity strength in adults [21, 22]. The participant is seated in a chair with the arms crossed on the chest and hands resting against their shoulders. The score corresponds to the number of times the person can stand up from a sitting position in 30″ without the help of their arms. The STS5 takes place with the same modalities as the STS30″, but the instruction for the patient is to stand up and sit down 5 times as quickly as he/she can [23].

The 6MWT was performed according to the American Thoracic Society's guidelines [24]. The test measures the distance a subject can walk over 6 min on a hard, flat surface. After resting for 10 min, the subject walks along a path with marked turning points. The patient is allowed to self-pace and rest as needed [24].

The handgrip strength test was performed using an analog hand dynamometer (Jamar, Duluth, MN, USA). The handle of the dynamometer was adjusted to allow a good grip. The person was told to place the arm at the side, away from the body with the elbow bent at a ninety-degree angle. The test was administered on both hands. An emphasis on "squeeze as hard as you can" was used for maximum effect. We allowed three trials with each hand, right and left hand alternately, with a pause of 10–20 s between each trial to avoid excessive fatigue.

Biochemical Data

Biochemical tests included serum creatinine, blood urea nitrogen (BUN), phosphorus, calcium, albumin, bicarbonate, parathyroid hormone (PTH), hemoglobin, and hematocrit. Tests were performed using standard laboratory methods. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula [25]. Urinary sodium, phosphate, and urea were measured on 24 h urine samples. Protein catabolic rate (PCR) was calculated by the Maroni-Mitch formula to estimate dietary protein intake [26].

Statistical Analysis

Categorical data were described by absolute and relative frequency, continuous data by mean with standard deviation and median with interquartile range, as appropriate. To verify the normality of data, Shapiro-Wilk

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test was applied, as appropriate. Correlation between physical activity level and continuous variables was assessed using Pearson or Spearman correlation analysis depending on whether data were normally distributed or not. Finally, all variables resulted significant in the latter univariate analysis were analyzed together by linear regression model adjusting also for age. Comparison between sedentary lifestyle subjects and not sedentary ones was tested by *t* test for independent sample (two tailed) or Wilcoxon signed-rank test. Significance was fixed at 0.05. All analyses were carried out by SPSS v.26 technology.

Results

The 46.5% of patients had one comorbidity, the 26.4% two comorbidities, and the 18.6% three or more comorbidities. The 88.4% of patients had hypertension, 29.7% had diabetes, 22.5% had history of ischemic heart disease or heart failure, and 6.5% had a stroke.

Physical Activity and Performance Assessment

Daily average METs value was 1.28 ± 0.23 and the average number of steps per day was 6,618 ± 3,636. There were no significant gender differences in METs, number of steps, time spent on activities >3 METs or >6 METs.

In the performance tests, handgrip strength was lower than the expected for age and sex in 46% of patients [27]. The performance on the 6MWT, in terms of metres walked, was significantly lower than expected for age in all patients.

In the STS5, 56% of patients reported a score lower than expected for age [28]. The performance on the STS30″ was lower than expected for age and sex in 86% of subjects [22].

The level of physical activity correlated with age, as expected, and with the presence or absence of diabetes, but not with gender or type of diet (Table 1). Physical activity level was negatively correlated with age, BMI, waist and hip circumferences, ECW and percent fat mass (FM), Charlson Index, and STS5 performance. There was a positive correlation of PA level with phase angle, BCM and free fat mass (FFM) percentages, normalized estimated PCR, 6MWT and STS30″ performance.

Multivariate statistical analysis was performed to analyze the effect of several independent variables, namely, age, BMI, handgrip strength, body composition parameter as percentage of FM and fat-free mass, and normalized PCR on physical activity level based on METs score. There was an independent significant association between physical activity level and age (β = −0.01107, 95% CI: −0.01689 to −0.005252, $p = 0.0004$) and between physical activity level and BMI (β = −0.06023, 95% CI: −0.1113 to −0.009118, $p = 0.0219$).

Subjects were classified as having a sedentary or not sedentary lifestyle based on average daily METs value, using 1.5 as the cut-off value [20]. Table 2 shows the main differences between the two groups.

The 82.6% of our patients have a sedentary lifestyle. They were older, had a higher BMI, waist and hip circumferences while the phase angle, BCM, and FFM were significantly lower than that in non-sedentary subjects.

There were no differences in renal function. The sedentary patients had higher blood glucose levels (35% had diabetes compared to 14% of the non-sedentary patients), lower LDL cholesterol levels (probably due to drug therapy), and lower serum albumin levels (Table 2). There were no differences regarding the handgrip test, while performance on the STS30″ was worse in the sedentary than in the non-sedentary patients.

The former had lower estimated protein and salt intakes, probably because they are older than the latter. In any case, the estimated average protein intake of sedentary patients resulted 0.85 g/kg bw/day, which is well in line with the most recent recommendations [29]. The type of diet prescribed was the same in both groups: normal diet in 71% and low protein diet (standard low protein/vegan diet) in 29% of sedentary patients and normal diet in the 72% and low protein diet (standard low protein/vegan diet) in 28% of non-sedentary patients.

Discussion

Overall, our study shows that CKD patients are mostly overweight/obese with a prevalence of abdominal obesity, while muscle mass and physical performance are reduced compared to the predicted values per age and sex. Our research also shows that older adult patients with CKD tend to have a sedentary lifestyle. Sedentary patients are older than not sedentary patients and this is largely expected since it is well known that physical activity decreases along with age.

Moreover, sedentary CKD patients are different from non-sedentary ones in terms of body composition, physical capacity, and nutrients intake, even when adjusted for age. This is an important consideration in the daily-life management care of CKD patients who are getting older and at risk of both malnutrition and low physical performance and activity.

The assessment of physical activity includes subjective and objective methods. The former are usually questionnaires (including IPAQ), which are easy to

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Table 1. Correlation between physical activity level, measured as average daily METs, and anthropometry, body composition, biochemical and functional parameters

	r	95% CI	*p* value
Charlson Index	−0.3788	−0.5360 to −0.1963	<0.0001
Age, years	−0.4227	−0.5660 to −0.2546	<0.0001
Body weight, kg	−0.2655	−0.4322 to −0.08112	0.0041
BMI, kg/m^2	−0.4429	−0.5827 to −0.2776	<0.0001
Waist circumference, cm	−0.4058	−0.5526 to −0.2346	<0.0001
Hip circumference, cm	−0.4035	−0.5507 to −0.2320	<0.0001
Arm circumference, cm	−0.2114	−0.3852 to −0.02314	0.0239
Phase angle, °	0.3808	0.1985 to 0.5376	<0.0001
BCM, %	0.3776	0.1950 to 0.5350	<0.0001
TBW, %	0.3423	0.1556 to 0.5054	0.0004
ECW, %	−0.3802	−0.5371 to −0.1978	<0.0001
ICW, %	0.4474	0.2215 to 0.6278	0.0002
FM,%	−0.4966	−0.6319 to −0.3320	<0.0001
FFM,%	0.4968	0.3321 to 0.6320	<0.0001
MM, %	0.5127	0.1829 to 0.7387	0.0032
BCMI, kg/m^2	0.2613	0.06759 to 0.4360	0.0071
sGlucose, mg/dL	−0.3143	−0.5001 to −0.1007	0.0036
nPCR, g/kg bw/day	0.3687	0.1299 to 0.5671	0.0025
uPhosphate, mg/day	0.2693	0.008797 to 0.4955	0.0375
Barthel Index	0.2431	0.05561 to 0.4140	0.0095
Handgrip strength, kg	0.1933	0.002486 to 0.3705	0.0411
6MWT, m	0.5552	0.4045 to 0.6766	<0.0001
STS5 rep, s	−0.3481	−0.5074 to −0.1657	0.0002
STS30″ rep, *n*	0.4308	0.2589 to 0.5763	<0.0001

Data show only statistically significant results. MAMC, middle-arm muscle circumference; MAMA, middle-arm muscle area; BCM, body cell mass; TBW, total body water; ECW, extracellular water; ICW, intracellular water; FM, fat mass; FFM, free fat mass; BCMI, body cell mass index; PCR, protein catabolic rate; nPCR, normalized protein catabolic rate; 6MWT, 6-min walking test; STS, sit to stand; MET, metabolic equivalent task; REE, resting energy expenditure; EE, energy expenditure; nEE, normalized energy expenditure.

administer but have the relevant bias of misreporting due to patient willingness or perception. The latter instead provides more precise information on quantity, i.e., number of steps or meters walked per day, or intensity (METs), using more or less complex devices (including pedometers). In this study, we used the SWA, a device that allows us to obtain quantitative and qualitative details about the physical activity of the recruited patients during their daily lives. We chose this method of physical activity assessment because it is objective, instrumental, and therefore provides more reliable data than those derived by subjective methods such as the IPAQ.

The significant association we found between low levels of daily physical activity and changes in body composition does not imply a cause-and-effect relationship, because of the study design, but it is likely that there are reciprocal influences.

In fact, it is conceivable that sedentary habits may have negative effects on FFM, muscle strength, and exercise capacity and increase fat body mass. Conversely, a reduction in muscle mass and/or an increase in FM may

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Table 2. Main features of the studied subjects based on their sedentary or not sedentary lifestyle

	Sedentary lifestyle (n = 95)	Not sedentary lifestyle (n = 20)	p value
Age, years	72.0 (67.0, 77.0)	65.5 (51.8, 71.8)	0.0002
BMI, kg/m^2	28.2 (25.9, 30.9)	26.3 (23.8, 28.4)	0.0077
Waist circumference, cm	103±10.2	96.9±9.4	0.0192
Hip circumference, cm	105±7.9	101±5.2	0.0151
Arm circumference, cm	30.2±2.8	28.9±2.6	0.0710
Triceps skinfold, cm	1.2 (0.9, 1.5)	1.2 (0.73, 1.85)	0.8990
MAMC, cm	26.1±2.8	24.7±3.1	0.0522
MAMA, cm^2	54.2±13.1	49.1±11.7	0.1190
Phase angle, °	4.7 (4.1, 5.4)	5.2 (4.9, 6.1)	0.0051
BCM, %	46.8±5.9	51.3±4.4	0.0039
TBW, %	52.9±5.1	55.9±5.0	0.0298
ECW, %	52.2±5.6	48.0±4.1	0.0037
ICW, %	47.9±6.0	54.0±4.5	0.0055
FM, %	30.8±7.0	24.7±6.9	0.0013
FFM, %	69.2±7.0	75.3±6.9	0.0013
BCMI, kg/m^2	9.2±1.6	10.2±1.3	0.0263
eGFR, mL/min/1.73 m^2	31.4±12.8	30.6±13.2	0.8016
sSodium, mEq/L	141±2.5	141±2.4	0.7913
sPotassium, mEq/L	4.7±0.5	4.8±0.6	0.4055
sCalcium, mg/dL	9.3±0.5	9.4±0.4	0.5603
sPhosphate, mg/dL	3.3±0.6	3.3±0.8	0.9333
sBicarbonate, mEq/L	24.5±2.9	23.8±2.6	0.4307
sGlucose, mg/dL	99.0 (87.0, 114)	87 (82, 102)	0.2650
HbA1c, %	6.3 (5.9, 7.0)	6.4 (6.2, 7.0)	0.6830
sUric acid, mg/dL	6.4±1.6	5.5±1.0	0.0258
sCholesterol, mg/dL	177±35.3	185±29.1	0.4463
HDL cholesterol, mg/dL	47.5 (39.0, 58.8)	58.5 (35.5, 64.5)	0.5577
LDL cholesterol, mg/dL	105±31.1	111±31.8	0.5708
Iron, µg/dL	67.0 (59.5, 85.5)	82 (69, 94)	0.4496
Ferritin, ng/mL	89.3 (63.9, 153)	92.3 (73.6, 194)	0.5432
Transferrin, mg/dL	233 (211, 260)	212 (162, 220)	0.0327
PTH, pg/mL	81.4 (57.3, 132)	116 (66, 153)	0.7977
25OH-vitamin D, ng/mL	22.0 (15.2, 27.2)	23.1 (15.3, 30.4)	0.2398
sTotal protein, g/dL	7.2 (6.7, 7.6)	7.0 (6.8, 7.3)	0.0434
sAlbumin, g/dL	4.2±0.3	4.2±0.4	0.7067
Hemoglobin, g/dL	13.4±1.7	13.7±1.7	0.3694
Hematocrit, %	40.2±4.6	41.2±4.4	0.4076
uUrea, g/day	18.5±6.5	17.3±6.3	0.5601

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Table 2 (continued)

	Sedentary lifestyle (n = 95)	Not sedentary lifestyle (n = 20)	p value
PCR, g/day	68.4±21.8	65.4±19.6	0.6471
nPCR, g/kg bw/day	0.8±0.2	0.9±0.2	0.4969
uSodium, mEq/day	129±50.8	148±50.4	0.2118
uPhosphate, mg/day	510 (420, 734)	554 (411, 698)	0.8538
Appetite test score	30 (28, 32)	30.0 (29, 32.8)	0.4353
MIS	0 (0, 2)	0 (0, 1)	0.2537
Charlson Comorbidity Index	7 (6, 8)	5.5 (4.0, 7.0)	0.0372
Barthel Index	103.7±1.3	105±0	0.4479
Karnowsky score	99.7±0.3	99.5±0.5	0.7973
Handgrip, kg	28.8±8.1	29.6±8.0	0.6745
6MWT, m	330±88.9	408±59.7	0.0003
STS5, s	13.0 (11, 17.5)	11 (8.0, 12)	0.0066
STS30″ stands, *n*	11.3±3.0	13.8±2.8	0.0010
Steps, *n*	5,288 (3,764, 6,726)	9,199 (7,497, 13,080)	0.0000
METs	1.2 (1.1, 1.3)	1.6 (1.5, 1.75)	0.0000
REE, kcal/day	1,322±241	1,244±237	0.2042
EE, kcal/day	1,805±798	1,927±738	0.6237
nEE, kcal/day/ibw	26.2±12.2	31.3±7.1	0.2290
Energy intake, kcal/day	1,702±300	1,907±431	0.0802
nEnergy intake, kcal/kg ibw	24.5±3.8	28.4±7.4	0.0193

MAMC, middle-arm muscle circumference; MAMA, middle-arm muscle area; BCM, body cell mass, TBW, total body water; ECW, extracellular water; ICW, intracellular water; FM, fat mass; FFM, free fat mass; BCMI, body cell mass index; PCR, protein catabolic rate; nPCR, normalized protein catabolic rate; 6MWT, 6-min walking test; STS, sit to stand; MET, metabolic equivalent task; REE, resting energy expenditure; EE, energy expenditure; nEE, normalized energy expenditure; ibw, ideal body weight.

lead to a reduction in physical activity and exercise capacity.

The most relevant question is not which came first but the potential relationship between nutrition and physical performance. They are really two sides of the same coin.

Then, in clinical practice, we can implement physical activity and exercise programs not only to increase functional capacity but also to improve body composition and nutritional status. Conversely, in the presence of inadequate dietary intake, nutritional support tailored on the patient's habits, clinical parameters, and kidney function is essential to improve body composition and even functional capacity. The combination of nutritional intervention and physical exercise is expected to counteract the vicious cycle that leads to a decline in quality of life and activities of daily living and ultimately to PEW [30, 31].

Very recent data from the 2007 to 2016 National Health and Nutrition Examination Survey showed that CKD patients with a sedentary lifestyle had a higher risk of all-cause and CVD-related mortality. In this case, sedentary lifestyle was defined as a period of inactivity >6 h per day (defined as sedentary time) [32].

Sarcopenia is quite prevalent in CKD patients. It is defined as reduced muscle mass, muscle strength, and physical performance, and it is a strong predictor of increased risk of hospitalization and all-cause mortality [33]. Nutritional therapy alone or in combination with a personalized exercise program may be a useful tool for the prevention or treatment of sarcopenia in CKD and dialysis patients [34]. It is recommended that older people (>65 years) engage in moderate intensity (i.e., of about 3–6 METs) physical activity for at least 150 min per week,

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or vigorous intensity (i.e., >6 METs) physical activity for at least 75 min per week [35, 36].

In our study, patients who did both moderate or vigorous physical activity were quite rare. The reasons for low physical activity reported by most patients are diverse, ranging from fatigue to lack of time and general laziness, which affects not only patients with CKD but also the general population. The aging process is a determining factor, as shown in this study, but it cannot be a limiting factor [37].

The future holds a population characterized by older people with more comorbidities and disabilities, and this means that we need to introduce neuromuscular rehabilitation programs as soon as possible, integrated with appropriate nutritional therapy, which is essential for effective exercise interventions. Educational programs should be implemented to explain the effects of exercise to encourage inactive CKD patients to start exercising.

Several international working groups are currently addressing the issue of the contribution of physical inactivity to the burden of disease in patients with chronic renal failure [38, 39]. Evidence exists that a rehabilitation program designed as a combination of personalized exercise and nutritional therapy for patients with renal, cardiac, and pulmonary impairments can not only improve exercise capacity and quality of life but also have a positive effect on survival. The new concept of this comprehensive rehabilitation for patients with CKD aims to add life to years and years to life [40].

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Pisa University Hospital (protocol code: 66006, date of approval: November 6, 2014). Written informed consent was obtained from participants to participate in the study.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Author Contributions

Conceptualization: C.D., D.G., and A.C.; methodology and validation: C.D. and A.C.; software and writing – original draft preparation: C.D.; formal analysis: E.L. and C.D.; writing – review and editing: A.C., D.G. V.P, N.P. M.R.R., and E.L.; and supervision: A.C. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author (A.C.).

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