Non-protein energy supplement for malnutrition treatment in patients with chronic kidney disease

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ABSTRACT

Background and Objectives: Malnutrition, mainly caused by inadequate energy intake, predicts poor prognostic outcome in chronic kidney disease (CKD) patients. In this study, we aim to explore the effect of non-protein energy supplement in CKD stage 3b-5 (CKD3b-5) malnourished patients with or without receiving continuous peritoneal dialysis (PD). **Methods and Study Design:** 30 patients with CKD3b-5 and 20 patients who received PD were identified as malnourished according to Subjective Global Assessment (SGA), and enrolled into this clinical study. Compared with the control group which just received regular nutrition counseling, an additional non-protein energy supplement (600kcal) was given to the participants for 12 weeks in the intervention group. Before and after study, the nutritional status of patients was judged by human body composition measurement, anthropometric parameters, physical fitness test, and quality of life survey. Other biochemical indexes relating to nutrition, renal function and inflammatory response were also included for disease evaluation. **Results:** After 12 weeks of oral non-protein energy supplementation, the body weight, body fat and associated anthropometric parameters significantly increased upon intervention. Also, the participants showed enhanced physical fitness and better life quality in the intervention group. Consistently, the improved nutritional status was further confirmed by biochemical examinations. However, we did not observe a perceptible change of renal function, measured residual renal function, or general inflammatory response indices after intervention. **Conclusions:** 12 weeks of oral non-protein energy supplement could efficiently improve the nutritional status of CKD3b-5 patients and those who receive peritoneal dialysis; meanwhile, it has little effect on renal function and inflammatory response.

Key Words: oral nutrition supplement, non-protein, energy supplement, chronic kidney disease, malnutrition

INTRODUCTION

The majority of chronic kidney disease (CKD) patients suffer from protein energy wasting syndrome (PEW), a complication which is featured by multiple factors induced protein synthesis inhibition and acceleration of protein decomposition.[1] To make things worse, restriction of protein intake, intestinal malabsorption and albuminuria further exacerbate bodily protein loss in CKD patients.[2] In addition, dietary surveys showed that more than half (56.6%) of CKD stage 3-5 patients had insufficient energy intake caused by diet control or loss of appetite.[3,4] In summary, the imbalance of energy intake and consumption eventually

leads to weight loss and systemic malnutrition,[5] which subsequently causes deterioration of physical fitness,[6] immune function and life quality of the CKD sufferers.[7,8]

Malnutrition is frequently observed in end-stage kidney disease.[9] Lots of studies suggest that enteral nutritional supplement could increase total energy intake in CKD patients[10] Given that protein is not an ideal energy source under CKD conditions, strategies based on low protein or non-protein diets are eagerly demanded. Here, we aim to explore whether non-protein energy supplement could alter the nutritional status, physical fitness, life quality, renal function and inflammatory status in CKD stage 3b-5 (CKD3b-5) malnourished patients with or without receiving continuous peritoneal dialysis (PD).

MATERIALS AND METHODS

Study design

The clinic trial was conducted from July 2017 to December 2018 in Tongji Hospital (Wuhan, China). Patients were recruited from the nephrology department (CKD3b-5, n=30) or peritoneal dialysis center (PD, n=20), and all had CKD diagnosed. The nutritional assessment and counseling were performed by the same proficient dietitian. The body composition measurement, anthropometric measurement, physical fitness test and life quality survey were carried out by the same nurse. This study had been reviewed and approved by the medical ethic committee of Tongji Hospital (ethics approval number TJ-IRB20180501). Our trial was registered at ChiCTR as ChiCTR1800016536.

Inclusion and exclusion criteria

Participants were recruited complying with the following inclusion and exclusion criteria. Inclusion criteria: 1) CKD patients with an estimated glomerular filtration rate (eGFR) $\leq$ 45 mL/min/1.73m^2 (stage 3b-5) and/or receiving continuous peritoneal dialysis (regularly dialysis over six months, and the dialysis program was kept stable throughout the study duration); 2) male or female patients aged from 18 to 70 year-old; 3) malnutrition status was confirmed by a subjective comprehensive nutritional assessment (SGA) score of B or C, which represents mild or severe malnourishment;[11] 4) patients who were willing to receive the regular nutrition counseling during the experiment and sign informed consent as required. Exclusion criteria: 1) patients with severe gastrointestinal diseases, such as acute gastrointestinal bleeding, intestinal obstruction or severe digestive malabsorption; 2) patients with hyperglycemia, hyperlipidemia or type 2 diabetes; 3) pregnant or lactating women; 4) cancer, severe heart, lung, or brain disorders and other serious primary diseases; 5) patients

who were allergic or unable to metabolize any of the ingredients present in the non-protein energy supplement; 6) severe abnormal liver function (ALT level 2.5-fold higher than normal); 7) patients who had participated in other clinic trials within half a year.

Nutritional intervention

All the participants were advised to use the oral non-protein energy supplement. The ones who refused the oral nutrition supplement just received the regular nutrition counseling as the control group. The Participants who received the oral nutrition supplement were provided with an additional 120ml of oral non-protein energy supplement per day for 12 consecutive weeks as the intervention group (each 100 ml containing 500 kcal energy, 0g protein, 16.7g saturated fatty acid, 13.9g medium-chain triglycerides, 24.6g monounsaturated fatty acid, 12.5g polyunsaturated fatty acid, 4.0g carbohydrate, 0.4g cellulose, 40ml water, 38.0ug vitamin K1 and 14.0mg α-TE). Specific usage: drinking directly one to two hours after each meal and the frequency was 30-40 ml three times a day. The non-protein energy supplement is produced by Fresenius Kabi Co. Ltd. (China). When severe nausea, vomiting, diarrhea and other adverse reactions occurred in the subjects, the intervention would be terminated and corresponding symptomatic treatment would be conducted.

Evaluation of interventional effects

Basic information about the participants was collected, including gender, age, body weight and body mass index (BMI). The human composition measurement, anthropometric measurement, physical fitness test and quality of life survey (SF-36 quality of life questionnaire) were administrated at the initial visit and the end of the study (12 weeks later). The results of biochemical indices relating to nutrition, renal function and inflammatory status were collected. All the measurements of human composition, anthropometry and physical fitness test were carried out under a fasting status and after the release of PD fluid for PD patients. Body composition was measured by the multifrequency bioelectrical impedance analysis (MF-BIA) using the InBody770 Body composition Analyzer (Biospace, Seoul, Korea). For the MF-BIA measurements, the patients stood barefoot on the instrument with each hand holding the handle. The phase impedance was measured by multi-frequency current (1KHZ to 1MHZ). Then the body composition was computed with the impedance value. (1) Measures for body composition: skeletal muscle, body fat, body fat percentage, visceral fat area, inorganic mass, the ratio of extra cellular water to total body water (ECW/TBW) and phase angle; (2) anthropometric parameters: waist circumference (WC), hip circumference

(HC), triceps skinfold thickness (TSF), mid-arm circumference (MAC) and calf circumference (CC); (3) physical fitness test: repeated chair stands (stand up and sit down five times) test, four-meter gait speed test, stair climb power test (height of 148.5cm) and grip strength test;[12] (4) quality of life survey (SF-36 quality of life questionnaire) including eight aspects: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health;[13] (5) biochemical examination indexes including serum albumin, total protein, prealbumin, hemoglobin, total iron binding capacity (TIBC), transferrin, serum iron, ferritin, triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen(BUN), creatinine, uric acid, HCO3-, eGFR, potassium, sodium, chloride, calcium, phosphorus, parathyroid hormone (PTH); volume, urea nitrogen, creatinine of 24h urine or 24h PD fluid; hypersensitive C-reactive protein (hsCRP) and lymphocyte count.

Data processing and statistical analysis

All data were submitted to a frequency distribution analysis by the Shapiro-Wilk test. Values with normal distribution were expressed as mean ± standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile). The comparisons against the baseline measurements within each group were assessed by paired t or Wilcoxon tests, the intergroup differences were assessed by independent samples t or Mann-Whitney U tests, and two-tailed p values <0.05 were considered statistically significant. All data were processed with SPSS software (version 23.0, IBM Company, Chicago, IL).

RESULTS

Characteristics of patients

In the CKD (3b-5) group, thirty participants were enrolled (control=14, intervention=16). In the PD group, twenty participants were enrolled (control=9, intervention=11), two participants in PD intervention group dropped out, one dropped because of gastrointestinal intolerance and another dropped due to renal transplantation surgery. Basic information of participants who completed this study including age, gender, body weight, body mass index and SGA score are shown in Table 1.

Effect of oral non-protein energy supplement on nutritional indices

Table 2 shows the mean values for body weight, body mass index (BMI), body composition and anthropometric parameters at baseline and week 12. For the control groups, there were no significant changes in the above parameters after 12 weeks. Body weight and BMI were significantly increased (p<0.01) and human composition measurement showed that the body fat, body fat percentage and visceral fat area were also significantly enhanced after intervention (p<0.05). And it is worthy of note that the average increase of body weight for CKD3b-5 or PD participants was 1.8kg. The baseline BMI levels of the participants in each group were less than 18.5 kg/m^2, and were more than this after the intervention. The value of ECW/TBW for CKD3b-5 participants was decreased significantly and come to below 0.39 after intervention. However, there were no significant differences regarding skeletal muscle, inorganic mass and phase angle for all the participants before and after intervention. As for anthropometric parameters, the values of waist circumference (WC), hip circumference (HC), triceps skinfold thickness (TSF), mid-arm circumference (MAC) and calf circumference (CC) showed various degrees of increase after intervention. For CKD3b-5 participants, there were significant increases in all of the above anthropometric parameters (p<0.05), but for PD patients, only mid-arm circumference showed a perceptible increase (p<0.01).

The nutrition-related biochemical indices at baseline and week 12 are shown in Table 3. There were no significant changes in the above indexs for the control groups after 12 weeks. The level of albumin, total iron binding capacity (TIBC) and transferrin in the CKD3b-5 group was significantly higher than before intervention (p<0.05). There were no obvious changes of the above indicators in PD participants after intervention, but the prealbumin level was lower (p<0.05) yet still within the normal range. In terms of serum lipids, except for the decreased level of high-density lipoprotein (HDL) in the PD group, the level of triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein cholesterol (HDL) in all participants were increased compared with baseline values. However, only the increases of TC and LDL in PD participants were significant (p<0.05).

Effect of oral non-protein energy supplement on physical function and quality of life

Table 4 shows the results for the physical fitness test and the SF-36 quality of life survey at baseline and week 12. The physical fitness test showed that the time taken by CKD3b-5 and PD participants for repeated chair stands, the four-meter gait speed and stair climb power tests was shortened after intervention which represented better physical fitness, but only the repeated chair stands and four-meter gait speed in CKD3b-5 participants reached statistical

difference (p <0.05). There was no significant change in the grip strength of CKD3b-5 and PD participants after intervention. The SF-36 quality of life survey consists of eight items: physical functioning (1-PF), physical role (2-RP), bodily pain (3-BP), general health (4-GH), vitality (5-VT), social functioning (6-SF), emotional role (7-RE), and mental health (8-MH). A higher score represents a better condition for that item. The result showed that the score of vitality (5-VT) in both CKD3b-5 and PD groups was significantly increased, indicating enhanced vitality after intervention. On the other hand, the score for bodily pain in CKD3b-5 participants were significantly higher than before intervention (p<0.05). There were no significant changes in the above parameters for the control group after 12 weeks. Thus, it is reasonable to conclude that non-protein energy supplement could improve the physical function and life quality of CKD3b-5 and PD participants at least in some respects.

Effect of oral non-protein energy supplement on renal function and inflammatory status

Table 5 shows the biochemical indices relating to renal function, including the level of urea nitrogen, creatinine, uric acid, HCO3- in serum, urea nitrogen and creatinine in 24h urine, and estimated glomerular filtration rate (eGFR), among which only the level of serum creatinine increased and the level of eGFR decreased substantially in PD participants after 12 weeks for both control and intervention groups (p<0.05). There was no obvious changes of serum electrolyte level (serum potassium, sodium, chlorine, calcium, phosphorus) after 12 weeks. At the same time, the level of parathyroid hormone (PTH) increased in the CKD3b-5 subjects after 12 weeks for both control and intervention groups (p<0.05), while there was no significant change of inflammatory markers, such as hypersensitive C-reactive protein (hsCRP) and lymphocyte count, which could reflect the global inflammatory status. In terms of liver function, only the AST level of CKD3b-5 participants was significantly increased after intervention (p<0.01), but was still within the normal range.

Table 6 shows the results of toxin clearance and measured residual renal function (mRRF) in PD patients. It shows that there were no significant differences in volume, urea nitrogen, creatinine level of 24h urine or 24h PD fluid at baseline and week 12. Neither the clearance rates of urea nitrogen and creatinine by residual kidney or peritoneal dialysis indicated by the urea clearance index (Kt/Vurea) and creatinine clearance rate (cCr) in PD participants showed any difference. There was also no significant change in mRRF values, which meant that the residual renal function was not affected by the intervention.

In general, our non-protein energy supplement did not affect the renal function or residual renal function and the inflammatory status of CKD3b-5 and PD patients.

DISCUSSION

Our study revealed that administering a daily oral 600-kcal non-protein energy supplement for 12 weeks significantly improved the nutritional state of under-nourished CKD3b-5 and PD participants. Also, the physical function and quality of life in these participants were improved in some respects after the intervention. However, the renal function or measured residual renal function (mRRF) and inflammatory state of the participants were not improved after administration of non-protein energy supplement in our research.

A low-protein diet could help to delay the progression of pre-dialysis CKD and restore the residual renal function of dialysis patients.[14,15] But there is little existing data examining the non-protein nutrition supplement in pre-dialysis or peritoneal dialysis CKD patients, especially for those who are malnourished. Our study revealed that the nutritional state of undernourished pre-dialysis and peritoneal CKD participants improved significantly with the application of 600 kcal non-protein nutrition. And there was a significant increase in body weight, which was mainly attributed to gaining body fat rather than skeletal muscle. The reason for this may be that the main ingredients of the non-protein energy supplements are various types of fatty acids. In line with previous studies,[15,16] our results further support the theory that high caloric nutrition supplement is needed for weight gain. As for the nutrition-related biochemical indicators, the levels of albumin, total iron binding capacity (TBIC) and transferrin increased significantly after intervention in CKD3b-5 participants, but not PD patients. The reason may lie in the improvement of protein storage in CKD3b-5 patients but not PD participants, due to a daily loss of protein through PD drainage fluid. The main ingredients of this supplement were medium-chain triglycerides and unsaturated fatty acid, which are considered beneficial for cardiovascular disease.[17,18] However, the serum lipid level of both the CKD3b-5 and the PD participants showed an increasing trend after intervention, and the TC and LDL levels of PD participants were significantly higher than before intervention, yet were still in the normal range. The increased TG level in PD participants after intervention was not statistically significant, but the average level after intervention was beyond the normal range. This may be related to the generally higher lipid levels in patients with peritoneal dialysis.[19] The above results indicated that it is necessary to periodically monitor the blood lipid level, especially in PD patients.

In this study, in order to explore whether non-protein energy supplement could improve the physical fitness of CKD3b-5 and PD patients, simple physical fitness tests were carried out on the subjects. The results revealed that only the repeated chair stands and four-meter walking speed of CKD3b-5 participants in intervention group showed significant difference, which

may be related to measurement error and the small sample size. In terms of life quality, the SF-36 quality of life survey results showed that the scores for vitality (5-VT) of CKD3b-5 and PD subjects after intervention were significantly higher than before, which means the participants generally felt more energetic, for example, they could do things for longer time or the time they felt tired reduced. In brief, the physical function and quality of life in CKD3b-5 and PD participants could be improved in some respects after the intervention of non-protein energy supplement.

It is reported that the renal function of non-diabetic CKD stage 3-5 patients with low protein and adequate energy diet was significantly better than in other diet groups.[20] One clinic study found that a 200kcal non-protein calorie containing 30g maltodextrin and 8g oil creamer could improve renal function in CKD3-4 patients.[21] However, in our study, the renal function of CKD3b-5 participants and measured residual renal function (mRRF) of PD participants was not significantly improved after non-protein energy supplement, while level of serum creatinine increased and the level of eGFR decreased substantially in PD participants after 12 weeks for both control and intervention groups. Further investigation may require a larger quantity of participants or longer study period to confirm this finding. The results verified that the non-protein energy supplement did not affect blood electrolyte level, which was consistent with the fact that it does not contain any electrolyte. However, the PTH level in CKD3b-5 subjects significantly increased after 12 weeks for both control and intervention groups, which may be associated with the progression of the disease itself. Despite being within the normal range, the AST level increased significantly in CKD3b-5 participants after intervention, which is a reminder that liver function would also need to be monitored when using this energy supplement.

Our study supported the theory that non-protein energy supplement could serve to treat malnutrition in CKD3b-5 and peritoneal dialysis patients. After administration for 12 weeks, patients achieved better nutritional status, along with improved life quality and certain respects of physical function.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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REFERENCES

1. Obi Y, Qader H, Kovesdy CP, Kalantar-Zadeh K. Latest consensus and update on protein-energy wasting in chronic kidney disease. Curr Opin Clin Nutr Metab Care. 2015;18:254-62. doi: 10.1097/MCO.0000000000000171.
2. Lodebo BT, Shah A, Kopple JD. Is it important to prevent and treat protein-energy wasting in chronic kidney disease and chronic dialysis patients? J Ren Nutr. 2018;28:369-79. doi: 10.1053/j.jrn.2018.04.002.
3. Huang MC, Chen ME, Hung HC, Chen HC, Chang WT, Lee CH, Wu YY, Chiang HC, Hwang SJ. Inadequate energy and excess protein intakes may be associated with worsening renal function in chronic kidney disease. J Ren Nutr. 2008;18:187-94. doi: 10.1053/j.jrn.2007.08.003.
4. Carrero JJ, Stenvinkel P, Cuppari L, Ikizler TA, Kalantar-Zadeh K, Kaysen G et al. Etiology of the protein-energy wasting syndrome in chronic kidney disease: a consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM). J Ren Nutr. 2013;23:77-90. doi: 10.1053/j.jrn.2013.01.001.
5. Zha Y, Qian Q. Protein Nutrition and Malnutrition in CKD and ESRD. Nutrients. 2017;9. doi: 10.3390/nu9030208.
6. Cupisti A, D'Alessandro C, Fumagalli G, Vigo V, Meola M, Cianchi C, Egidi MF. Nutrition and physical activity in CKD patients. Kidney Blood Press Res. 2014;39:107-13. doi: 10.1159/000355784.
7. Alwarawrah Y, Kiernan K, MacIver NJ. Changes in nutritional status impact immune cell metabolism and function. Front Immunol. 2018;9:1055. doi: 10.3389/fimmu.2018.01055.
8. Park JI, Baek H, Jung HH. CKD and health-related quality of life: The Korea National Health and Nutrition Examination Survey. Am J Kidney Dis. 2016;67:851-60. doi: 10.1053/j.ajkd.2015.11.005.
9. Maraj M, Kusnierz-Cabala B, Dumnicka P, Gala-Bladzinska A, Gawlik K, Pawlica-Gosiewska D et al. Malnutrition, Inflammation, Atherosclerosis Syndrome (MIA) and diet recommendations among end-stage renal disease patients treated with maintenance hemodialysis. Nutrients. 2018;10. doi: 10.3390/nu10010069.
10. Chan W. Chronic kidney disease and nutrition support. Nutr Clin Pract. 2021;36:312-30. doi: 10.1002/ncp.10658.
11. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, Jeejeebhoy KN. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr. 1987;11:8-13. doi: 10.1177/014860718701100108.
12. Painter P, Marcus RL. Assessing physical function and physical activity in patients with CKD. Clin J Am Soc Nephrol. 2013;8:861-72. doi: 10.2215/CJN.06590712.
13. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992;30:473-83. doi:

14. Ko GJ, Obi Y, Tortorici AR, Kalantar-Zadeh K. Dietary protein intake and chronic kidney disease. Curr Opin Clin Nutr Metab Care. 2017;20:77-85. doi: 10.1097/MCO.0000000000000342.
15. Bolasco P, Cupisti A, Locatelli F, Caria S, Kalantar-Zadeh K. Dietary management of incremental transition to dialysis therapy: Once-weekly hemodialysis combined with low-protein diet. J Ren Nutr. 2016;26:352-9. doi: 10.1053/j.jrn.2016.01.015.
16. Sezer S, Bal Z, Tutal E, Uyar ME, Acar NO. Long-term oral nutrition supplementation improves outcomes in malnourished patients with chronic kidney disease on hemodialysis. JPEN J Parenter Enteral Nutr. 2014;38:960-5. doi: 10.1177/0148607113517266.
17. Bhavsar N, St-Onge MP. The diverse nature of saturated fats and the case of medium-chain triglycerides: how one recommendation may not fit all. Curr Opin Clin Nutr Metab Care. 2016;19:81-7. doi: 10.1097/MCO.0000000000000249.
18. Wang DD, Hu FB. Dietary fat and risk of cardiovascular disease: Recent controversies and advances. Annu Rev Nutr. 2017;37:423-46. doi: 10.1146/annurev-nutr-071816-064614.
19. Pandya V, Rao A, Chaudhary K. Lipid abnormalities in kidney disease and management strategies. World J Nephrol. 2015;4:83-91. doi: 10.5527/wjn.v4.i1.83.
20. Chen ME, Hwang SJ, Chen HC, Hung CC, Hung HC, Liu SC, Wu TJ, Huang MC. Correlations of dietary energy and protein intakes with renal function impairment in chronic kidney disease patients with or without diabetes. Kaohsiung J Med Sci. 2017;33:252-9. doi: 10.1016/j.kjms.2017.03.002.
21. Wu HL, Sung JM, Kao MD, Wang MC, Tseng CC, Chen ST. Nonprotein calorie supplement improves adherence to low-protein diet and exerts beneficial responses on renal function in chronic kidney disease. J Ren Nutr. 2013;23:271-6. doi: 10.1053/j.jrn.2012.09.003.

Table 1. Basic information of participants[†]

Parameter	Control		Intervention	
	CKD (3b-5) (n=14)	PD (n=9)	CKD (3b-5) (n=16)	PD (n=9)
Age (years)	40±11	41±9	39±11	41±12
Sex (male/female)	7/7	3/6	7/9	3/6
Body weight (kg)	52.5 (42.3,53.4)	45.2±7.9	49.9 (45.2,53.5)	45.6±7.1
Body mass index (kg/m^2)	18.3±1.7	18.0±3.0	18.4±0.9	18.1±1.7
SGA	B	B	B	B

SGA: subjective global nutrition assessment.
[†]Body mass index was calculated from body weight and height. Values with normal distribution were expressed as mean±standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).

Table 2. Body weight, BMI, body composition and anthropometric results at baseline and week 12[†]

Parameter	Control				Intervention			
	CKD(3b-5)(n=14)		PD(n=9)		CKD (3b-5) (n=16)		PD (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
Body weight (kg)	52.5 (42.3,53.4)	52.1 (42.9,53.1)	45.2±7.9	45.0±7.5	49.7±4.8	51.5±5.6[*]	45.6±7.1	47.4±7.4[*]
BMI (kg/m^2)	18.3±1.7	18.3±1.6	18.0±3.0	17.9±2.8	18.4±0.9	19.1±1.0[*]	18.1±1.7	18.8±2.0[*]
Skeletal muscle (kg)	21.5±4.3	21.4±4.3	19.9±4.7	19.7±4.5	21.8±3.2	21.8±3.2	20.0±3.7	20.2±4.1
Body fat (kg)	8.9±1.4	9.0±1.4	7.3±2.5	7.3±2.5	9.1±2.3	10.9±3.0[*]	7.5±4.3	9.0±4.7[*]
Body fat percent (%)	18.2±3.4	18.4±3.6	18.5 (12.0,20.3)	18.4 (12.1,20.2)	18.5±5.2	21.3±5.6[*]	16.3±8.2	18.9±9.0[*]
Visceral fat area (cm^2)	41.7±8.6	41.5±9.6	38.9±8.7	38.6±8.9	42.1±9.3	49.4±11.8[*]	39.3±13.2	44.6±14.7[*]
Inorganic mass (kg)	2.76±0.39	2.76±0.38	2.34 (2.23,2.82)	2.36 (2.23,2.80)	2.77±0.33	2.78±0.39	2.59±0.35	2.61±0.46
ECW/TBW	0.391 (0.390,0.393)	0.391 (0.387,0.394)	0.397±0.003	0.397±0.003	0.390±0.008	0.388±0.007[*]	0.398±0.0.013	0.396±0.012
Phase angle (φ)	4.6 (4.3,4.9)	4.7 (4.3,4.8)	4.5±0.4	4.4±0.3	4.7 (4.2,5.2)	4.8 (4.4,5,1)	4.5 (4.4,5.2)	4.6 (3.9,4.9)
WC (cm)	70.5 (68.9,75.3)	71.3 (68.3,74.3)	70.6±5.5	70.3±5.3	72.9±4.8	75.2±5.4[*]	70.8±6.9	73.0±8.5
HC (cm)	87.6±3.8	87.5±3.4	85.1±2.9	84.9±2.5	88.2±3.0	89.7±3.3[*]	85.4±4.0	86.1±4.1
TSF (mm)	7.4±2.2	7.3±2.4	6.0 (5.0,7.5)	6.0 (5.0,7.6)	7.5±2.7	8.4±3.0[*]	6.6±3.1	7.9±3.6
MAC (cm)	23.5±1.8	23.4±1.9	22.3±1.2	22.2±1.2	23.7±1.2	24.7±1.8[*]	22.4±1.5	23.4±1.5[*]
CC (cm)	31.7±2.4	31.5±2.1	30.6±3.6	30.4±3.6	31.8±1.6	32.3±1.6[*]	30.8±2.0	31.6±2.1

BMI: body mass index; ECW/TBW: the ratio of extra cellular water to total body water; WC: waist circumference; HC: hip circumference; TSF: triceps skinfold thickness; MAC: mid-arm circumference; CC: calf circumference.

[†]Values with normal distribution were expressed as mean±standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).

[*]Significantly different (p<0.05) from baseline.

Table 3. Nutrition related biochemical tests at baseline and week 12[†]

Parameter	Control				Intervention			
	CKD (3b-5)(n=14)		PD (n=9)		CKD (3b-5)(n=16)		PD (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
Albumin (g/L)	42.1±5.3	41.3±4.7	36.7±2.9	35.5±2.6	44.4 (37.7,47.2)	45.5 (40.8,48.0)*	38.5±3.8	37.6±5.0
Total protein (g/L)	68.8±5.7	68.6±6.7	65.3 (62.6,68.3)	64.7 (63.6,66.4)	74.8 (67.5,78.4)	75.8 (71.8,80.7)	68.9±5.6	69.8±7.4
Prealbumin (g/L)	356±40	360±44	405±44	379±47*	337±82	358±71	415±52	366±46*
Hemoglobin (g/L)	106±14	99±15	97±13	92±17	101±16	101±16	94±18	89±25
TIBC (μmol/L)	45.3±4.4	46.1±3.1	49.8±5.8	51.9±5.7	48.0±10.6	51.1±9.4*	45.8±3.8	44.9±4.7
Transferrin (g/L)	2.10±0.39	1.97±0.25	2.02±0.23	2.10±0.26	2.21±0.50	2.38±0.47*	2.10±0.21	2.10±0.26
Serum iron (μmol/L)	13.9±3.9	13.6±3.5	11.1 (9.9,16.2)	11.5 (10.6,15.3)	11.0 (7.4,15.4)	13.1 (7.8,18.7)	10.9 (9.3,15.8)	11.5 (10.4,17.0)
Ferritin (μg/L)	189±46	189±51	143 (59,306)	144 (60,280)	111 (25,205)	117 (36,208)	138 (62,275)	90 (79,195)
TG (mmol/L)	1.05±0.40	1.01±0.43	1.38±0.64	1.44±0.66	1.02±0.38	1.15±0.45	1.16 (0.74,1.84)	1.56 (1.22,2.42)
TC (mmol/L)	4.01±1.10	3.89±1.10	4.25±0.94	4.28±1.20	4.00±0.58	4.29±0.77	4.50±1.03	4.89±1.06*
LDL (mmol/L)	2.44±0.57	2.29±0.66	2.12±0.73	2.15±0.76	2.17±0.32	2.36±0.39	2.36±0.77	2.65±0.81*
HDL (mmol/L)	1.29±0.36	1.30±0.34	1.21±0.26	1.23±0.28	1.37±0.43	1.47±0.41	1.33±0.30	1.29±0.37

TIBC: total iron binding capacity; TG: triglyceride; TC: total cholesterol; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

[†]Values with normal distribution were expressed as mean ± standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).

*Significantly different (p<0.05) from baseline.

Table 4. Results for physical fitness test and SF-36 quality of life survey at baseline and week 12[†]

Parameter	CKD (3b-5)(n=14)		PD (n=9)		CKD (3b-5)(n=16)		PD (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
Repeated chair stands (s)	7.49 (5.76,8.57)	7.31 (7.19,8.26)	8.91±2.30	8.96±1.72	7.67 (5.68,10.1)	6.35 (5.54,7.66)[*]	8.94±2.40	7.72±2.57
4m-gait speed (s)	4.43±1.00	4.50±0.76	4.26 (3.90,4.99)	4.32 (4.00,5.12)	3.82 (3.47,4.82)	3.62 (3.41,4.02)[*]	4.45±0.71	4.08±0.55
Stair climb power test (s)	3.38 (2.72,4.21)	3.69 (3.23,4.45)	4.58 (3.78,5.47)	4.56 (4.04,5.25)	3.50 (2.69,4.38)	3.24 (2.60,3.79)	4.65±1.29	4.10±0.73
Grip strength (kg)	29.2±6.10	29.4±6.05	24.4±1.27	24.3±4.35	29.4±10.2	30.2±9.9	24.4±7.6	24.3±7.3
1-PF (Physical Functioning)	85.0 (83.8,90.0)	85.0 (80.0,90.0)	80.0 (75.0,87.5)	75.0 (75.0,87.5)	85.0 (81.3,90.0)	85.0 (85.0,93.8)	85.0 (77.5,90.0)	85 (80,90)
2-RP (Role-Physical)	0 (0,56.3)	0 (0,31.3)	25.0 (0,25.0)	25.0 (0,25.0)	0 (0,37.5)	0 (0,68.8)	0 (0,37.5)	0 (0,37.5)
3-BP (Bodily Pain)	74.0 (54.3,100)	74.0 (63.3,95.5)	94.0 (41.0,100)	94.0 (41.0,100)	78.0 (62.5,100)	100 (65,100)[*]	94.0 (52.5,77.5)	94.0 (51.5,100)
4-GH (General Health)	30.0 (20.0,40.5)	30.0 (20.0,40.5)	30.0 (25.0,40.0)	30.0 (27.5,40.0)	31±15	33±13	32±8	33±10
5-VT (Vitality)	55.0 (45.0,60.0)	55.0 (45.0,56.3)	65.0 (62.5,75.0)	65.0 (57.5,75.0)	56±22	69±14[*]	65.0 (57.5,77.5)	75.0 (67.5,80.0)[*]
6-SF (Social Functioning)	37.5 (37.5,87.5)	37.5 (37.5,87.5)	37.5 (37.5,75.0)	37.5 (37.5,75.0)	62.5 (37.5,96.9)	62.5 (37.5,96.9)	37.5 (37.5,75.0)	37.5 (37.5,75.0)
7-RE (Role-Emotional)	33.3 (33.3,100)	33.3 (33.3,100)	66.7 (37.5,100)	66.7 (37.5,100)	100 (0,100)	83.4 (8.33,100)	100 (50,100)	100 (50,100)
8-MH (Mental Health)	68.0 (52.0,84.0)	68.0 (52.0,84.0)	80.0 (72.0,80.0)	80.0 (72.0,80.0)	68.0 (56,84)	68 (57,84)	74.7±8.2	74.7±8.2

[†]Values with normal distribution were expressed as mean ± standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).
[*]Significantly different (p<0.05) from baseline.

Table 5. Liver function, biochemical indices relating to renal function, inflammatory status at baseline and week 12[†]

Parameter	Control				Intervention			
	CKD (3b-5)(n=14)		PD (n=9)		CKD (3b-5)(n=16)		PD (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
ALT (U/L)	12 (10,14)	14 (11,16)	13±3	14±4	10 (6,17)	11 (7,20)	11 (8,16)	10 (8,17)
AST (U/L)	15±3	15±3	16 (12,20)	13 (12,21)	14 (12,15)	18 (13,22)[*]	15 (11,20)	18 (12,22)
BUN (mmol/L)	18.4±6.8	18.8±8.2	18.6±6.9	19.4±6.2	14.1 (8.7,19.0)	14.7 (10.5,21.4)	15.3 (11.6,25.1)	13.5 (12.7,22.2)
Scr (μmol/L)	354±192	390±185	705±169	743±170[*]	307±133	344±175	855±232	980±264[*]
Uric acid (μmol/L)	361±122	392±116	354±112	366±95	369 (302,410)	375 (307,416)	367 (296,393)	390 (360,450)
HCO_3^- (mmol/L)	24.6 (21.1,26.5)	23.0 (20.8,26.9)	25.0±1.6	25.2±1.6	21.9 (20.4,23.6)	24.1 (21.4,25.8)	25.2±4.7	26.3±2.9
eGFR (ml/min/1.73m^2) [‡]	17.1 (11.8,23.4)	15.2 (10.1,22.2)	5.1±0.9	4.9±0.9[*]	19.9 (11.7,28.9)	18.3 (11.0,28.3)	5.2±1.9	4.4±1.6[*]
24h Urine volume (L)	1.66±0.44	1.65±0.45	0.32 (0,0.36)	0.25 (0,0.34)	1.71±0.56	1.72±0.51	0.10 (0,0.38)	0 (0,0.68)
24h UUN (mmol)	143±58	147±67	16 (0,19)	11 (0,19)	150 (117,184)	166 (112,203)	5 (0,17)	0 (0,23)
24h Ucr (mmol)	7.36±3.28	7.27±3.26	0.68±0.59	0.64±0.61	7.11 (6.51,7.88)	7.56 (6.37,8.67)	0.48 (0,1.09)	0 (0,1.99)
Potassium (mmol/L)	4.63±0.61	4.72±0.53	4.31±0.71	4.34±0.83	4.84±0.59	5.01±0.44	4.42±0.92	4.05±0.71
Sodium (mmol/L)	141 (140,142)	141 (138,142)	138±3	140±5	140±2	140±2	138±3	139±3
Chlorine (mmol/L)	102±4	101±4	96±3	96±3	105 (103,108)	103 (101,106)	96±4	96±4
Calcium (mmol/L)	2.34 (2.24,2.45)	2.33 (2.28,2.47)	2.40±0.15	2.35±0.14	2.33 (2.29,2.35)	2.33 (2.23,2.38)	2.42±0.28	2.48±0.31
Phosphorus (mmol/L)	1.35±0.44	1.49±0.53	1.83±1.02	2.13±1.36	1.21 (1.02,1.42)	1.21 (1.10,1.49)	1.78±0.79	1.59±0.53
PTH (pg/mL)	129 (99,158)	137 (113,220)[*]	364±111	395±101	121±50	155±66[*]	238 (158,368)	226 (171,484)
HsCRP (mg/L)	0.5 (0.3,5.2)	0.7 (0.3,5.4)	2.3±0.8	3.9±2.5	0.3 (0.1,2.5)	0.3 (0.2,0.7)	0.9 (0.3,3.6)	1.0 (0.5,9.0)
Lymphocyte count (10^9/L)	1.33 (1.19,1.40)	1.31 (1.16,1.35)	1.02 (0.98,1.45)	1.00 (0.72,1.57)	1.16 (1.04,1.67)	1.11 (1.00,1.38)	1.20±0.44	1.19±0.28

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; Scr: serum creatinine; eGFR: estimated glomerular filtration rate; UUN: urine urea nitrogen; Ucr: urine creatinine; PTH: parathyroid hormone; HsCRP: hypersensitive C-reactive protein.

[†]Values with normal distribution were expressed as mean±standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).

[‡]Calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

[*]Significantly different (p<0.05) from baseline.

Table 6. Toxin clearance and residual renal function in PD participants at baseline and week 12[†]

Parameter	PD control (n=9)		PD intervention (n=9)	
	Baseline	Week 12	Baseline	Week 12
24h Urine volume (L)	0.32 (0,0.36)	0.25 (0,0.34)	0.10 (0,0.38)	0 (0,0.68)
24h UUN (mmol)	15.6 (0,19.4)	11.4 (0,18.8)	5.0 (0,17.4)	0 (0,23.4)
24h Ucr (mmol)	0.68±0.59	0.64±0.61	0.48 (0,1.09)	0 (0,1.99)
24h PD fluid (L)	6.93±2.54	7.37±2.32	8.20 (4.70,8.62)	8.35 (6.89,8.59)
24h PD urea nitrogen (mmol)	96.2±37.5	96.2±38.1	96.2±37.5	96.2±38.1
24h PD creatinine (mmol)	4.56±2.39	4.94±2.15	4.56±2.39	4.94±2.15
Weekly residual renal Kt/V_{urea}	0.20 (0,0.24)	0.17 (0,0.23)	0.11 (0,0.61)	0.05 (0,0.61)
Weekly peritoneal Kt/V_{urea}	1.65±0.50	1.64±0.54	1.65±0.50	1.64±0.54
Weekly Kt/V_{urea}	1.98±0.35	1.93±0.51	1.98±0.35	1.93±0.51
Residual renal cCr (L/W)	9.52±12.94	9.77±14.75	4.27 (0,16.78)	3.03 (0,19.22)
Peritoneal cCr (L/W)	34.8±14.5	34.7±10.2	34.8±14.5	34.7±10.2
Total cCr ($L/W/1.73m^2$)	54.2±7.1	53.8±13.5	54.2±7.1	53.8±13.5
mRRF ($ml/min/1.73m^2$)	0.67±0.53	0.61±0.50	0.22 (0,1.14)	0 (0,1.80)

UUN: urine urea nitrogen; Ucr: urine creatinine; PD: peritoneal dialysis; Kt/Vurea: urea clearance index; cCr: creatinine clearance; mRRF: measured residual renal function.

[†]Values with normal distribution were expressed as mean±standard deviation, and values displaying skewed distribution were expressed as median (25th, 75th percentile).