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Original Article

Effects of progressive resistance exercises on quality of life and functional capacity in pediatric patients with chronic kidney disease: a randomized trail

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Abstract

Aim: To investigate the effects of progressive resistance exercises on quality of life and functional capacity in pediatric patients with chronic kidney disease. **Methods:** Thirty-two children with chronic kidney disease from both genders, age ranged from 8 to 12 years participated in this study. They were allocated randomly into two groups of equal numbers, standard medical care (SC) and exercise (EX) groups. The SC group received standard medical care with no change of their regular daily activities. The EX group received progressive resistance exercises for 60 minutes two times a week in addition to the standard medical care for six successive months. **Outcome measures:** Included the pediatric quality of life inventory and six-minutes walking test to assess quality of life and functional capacity respectively. **Results:** There were statistically significant improvements in the post-test quality of life and functional capacity in the EX group ($p<0.05$). The SC group showed significant decrease of quality of life and non-significant change was recorded regarding their functional capacity ($p<0.05$). The post-test comparison between the two groups revealed significant difference in favor of the EX group in all measured variables. **Conclusion:** Progressive resistance exercises contributed to the improvement of quality of life and functional capacity in pediatric patients with chronic kidney disease.

Keywords: Chronic Kidney Disease, Functional Capacity, Functional Resistance Exercise, Quality of Life

Introduction

Chronic kidney disease (CKD) is labeled as silent killer disorders results from irreversible kidney damage that may progress to end stage renal disease (ESRD)[1-3]. The disorder is classified to 5 stages according to Schwartz formula as: stage 1 (renal injury) estimated glomerular filtration rate (eGFR) of >90 ml/min per 1.73 m^2, stage 2 (mild) eGFR of 60-89 ml/min per 1.73 m^2, stage 3 (moderate) eGFR 30-59 ml/min per 1.73 m^2, stage 4 (severe) eGFR of 15-29 ml/min per 1.73 m^2 and finally stage 5 (ESRD) eGFR of <15 ml/min per 1.73 m^2 [4,5].

Previous studies showed that, children with CKD or those receiving dialysis demonstrate relatively poor physical functioning and quality of life performance (QoL) when compared to healthy peers[6,7]. Physical inactivity resulting in poor exercise capacity is a common consequence of CKD and is associated with increased mortality in the general population. Children with CKD demonstrate lack of physical activity, lower physical capacity that is most often affected by anemia and hypertension[8].

Daily exercise has been shown to: (1) improve the HRQOL and decrease hospitalizations in adult dialysis patients[9]; (2) improve the muscle strength, blood pressure control, lipid profile, glucose regulation and psychological profile in the general adult population[10]; and (3) improve bone health[11].

The functional strength training (functional resistance exercise) is designed to incorporate task and context specific practice in areas meaningful to each patient with an overall goal of functional independence. This training focuses mainly

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on the anti-gravity muscles and aiming at maximal carry over in daily activities. The use of resistance may be in the form of gravity, body weight, resistance bands, weight vest and free weights[12].

To stimulate strength progression, the amount of resistance should be increased as strength increases. According to the US National Strength and Conditioning Association, children should be trained at an 8- to 15-repetition maximum, which is the number of repetitions that can be completed before fatigue[13].

Various treatment protocols have studied the effectiveness of resistance exercises in adult patients with CKD receiving hemodialysis[5,14-20].

Despite the benefits of physical rehabilitation among adults and children with chronic illness, they avoid to engage in different physical activities especially pediatric population. Most of the children with CKD receive their medical treatment and follow-up with no change of their functional performance. The lack of activity and sedentary life style among these population result in reduced quality of self, functional activities in addition to behavioral and social problems and finally they become independent in most of activities of daily living. We still lack the evidence of progressive resistance exercises in pediatric population with CKD. Therefore, the primary aim of this study was to explore the effects of progressive resistance exercises on quality of life and functional capacity in pediatric patients with chronic kidney disease.

Methods

Study design: A double blinded prospective randomized trial was conducted from March 2016 to February 2018 at Abo El-Reesh hospital, Cairo University in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Ethical committee approvals of the Faculty of Physical Therapy, Cairo University, Egypt (No:P.T.RE.C/012/001463) and Abo El-Reesh hospital as well as a signed written consent form with parent acceptance for participation in the study and publication of the results were obtained before starting the study procedure.

Participants: Thirty-two volunteer children from both genders participated in this study. The sample selection, assessment and treatment procedures were conducted at Pediatric nephrology unit, Abo El-Reesh-Hospital, Cairo University, Egypt. Sample selection was conducted by a nephrologist based on the medical and laboratory investigations and included if they were at stage 3 and 4 CKD (eGFR 15-59 ml/min/1.73m^2)[4], age ranged from 8 to 12 years, medically stable, did not yet require renal replacement therapy (no-dialysis) and willing to participate in the study and attend the treatment schedule.

Children were excluded if they had recent myocardial infarction, uncontrolled hypertension, unstable angina, severe uncontrolled diabetes, symptomatic left ventricular fibrillation, neurological or cognitive disorders with functional deficits or ssignificant cerebral or peripheral vascular disease.

Sample size estimation

To make proper inferences about the population, sample size estimation was conducted using G*Power software 3.1.9.2 (Neu-Isenburg, Germany) to guarantee proper inferences about the population. One -way ANOVA test was conducted with fixed effects, α error=0.05, actual power (1-β)=0.82, and an effect size (f)=0.51. The test revealed a total sample size of at least 28 children (14 for each group), we recruited up to 32 children (16 children for each group) to account for the possible withdrawal rates.

Randomization

Thirty-two children at stage 3 and 4 CKD were assessed for eligibility. Following the baseline measurements, children were consecutively assigned a number from 1 to 32. Then, an online Graph Pad Software was used to randomly assign 16 children to each group. All children as well as the registration clerk were blinded to the randomization process. The experimental design is shown as a flow diagram based on Consolidated Standards of Reporting Trials (CONSORT) (Figure 1).

Children in the SC group (11 boys and 5 girls) received the regular medical treatment with no change of their regular daily activities. While, those in the EX group (12 boys and 4 girls) received progressive resistance exercises in addition to regular medical treatment for 60 minutes two times a week for six successive months.

Outcome measures

Quality of life: The Arabic form of Paediatric Quality of Life Inventory (PedsQL™) generic core scale (8-12 years) was used to assess the QoL. It is composed of parallel child self-report and parent proxy-report formats. The modules contain four scales assessing a child's functioning in physical (eight items), emotional (five items), social (five items) and school (five items) domains[21]. The respondents indicated how much of a problem the child has had over the previous month with specific aspects of functioning on a 0-4 scale, with 0 indicating "never a problem" and 4 indicating "almost always a problem". The responses for each item are reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0; with higher scores reflecting better HRQOL[22,23].

Functional capacity: The six-minute walking test (6MWT) is an inexpensive, simple, practical, reliable, and valid measure of submaximal exercise capacity in healthy children[24] and children with chronic disease[25], neuromuscular disorders[26,27] or cardiopulmonary disease. The 6MWT is a useful instrument for monitoring clinical status in children and adolescents with CKD with ESRD[28] Watanabe. Children were instructed to walk around a marked hallway, 20 meters in length, as fast as possible for 6 minutes without stopping at a self-chosen

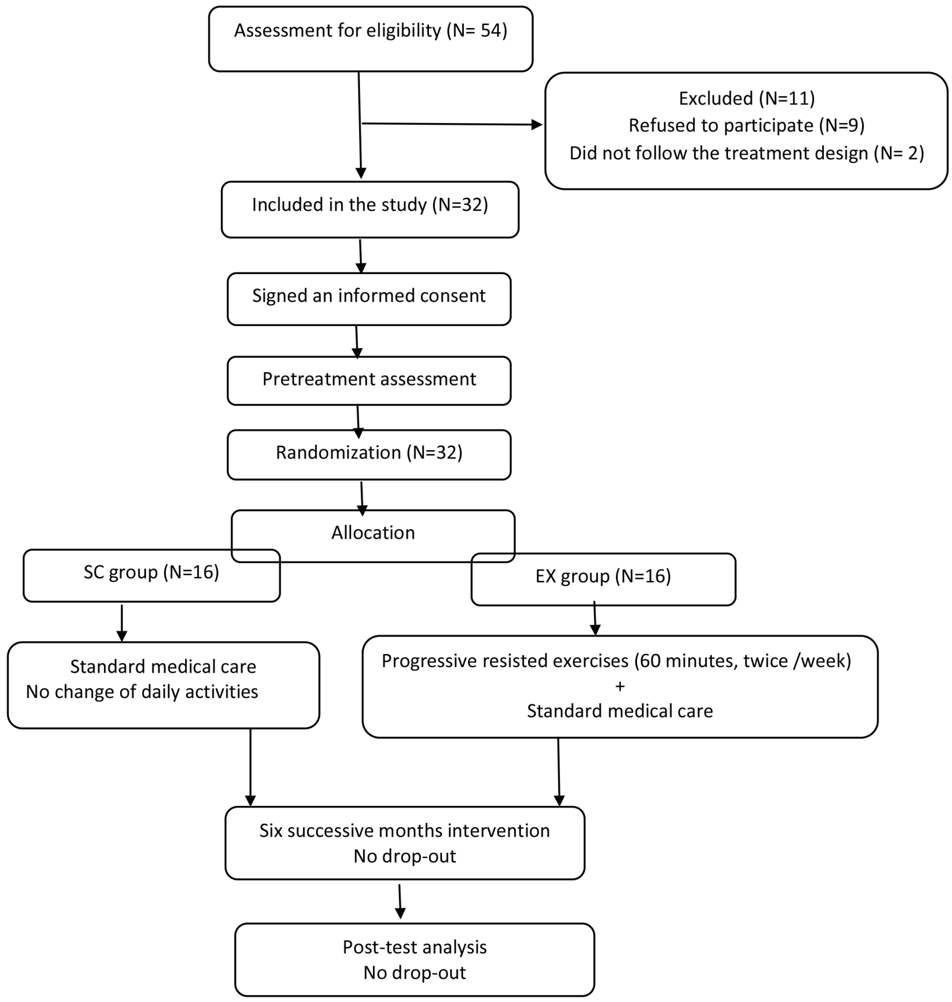

Figure 1. Flow chart demonstrates the experimental design of the study.

Table 1. List of exercise session activities[30-32].

	Intervention	Resistance
Arm exercises	Front and Lateral shoulder raise overhead shoulder press Triceps extension	Dumbbell weights
Trunk-stabilizer (Bridging)	In the hook-lying position, pressing the upper back and feet into the mat, the child should raise the pelvis, hold this position for 30 seconds and then back to initial position.	Free loads strapped around pelvis and proximal thigh
Hip flexor and ankle dorsiflexor	Stair-climbing: with upper-extremity support. For hip flexion and foot dorsal flexion, it was prioritizing the first phase of this skill (single stance), which is from the lift off of the target foot in the swing phase to its placement on the step.	Weight vest and free weight attached on proximal thigh and foot.
Knee extensor	Sit-to-stand: The child was seated in a bench and the knee and hip joints flexed at 90o. The child was instructed to get the upright position, even with upper extremity support.	Free loads around pelvis and proximal thigh
Knee flexor and ankle plantar flexor	Down stair: Walking down stair exercise was executed with upper extremity support. The child was motivated to walk backward down the step.	Free loads on distal shank and foot
Hip adductor and abductor	Lateral walk: In an upright position (parallel bars), the child was stimulated to execute lateral walk.	Free loads on proximal thigh and distal shank

Table 2. Patient physical characteristics at baseline.

Item	SC group	EX group	MD	p-value
	X̄±SD	X̄±SD		
Age (years)	10.62 ± 1.25	9.87 ± 1.36	0.75	0.11
Height (centimeter)	126.93 ± 4.75	127.81 ± 3.25	-0.8	0.54
Weight (kilogram)	29.5 ± 3.5	29.75 ± 2.23	-0.25	0.81
GFR (mL/min /1.73 m^2)	22.85 ± 7.82	21.94 ± 6.15	0.91	0.71

Level of significance at p<0.05.

Table 3. T- test for comparing baseline mean values of PedsQL™ scores and 6MWT between the two groups.

Item	SC group	EX group	MD	p-value
	X̄±SD	X̄±SD		
PedsQL™ child self-report				
PFS	56.25 ± 4.56	56.46 ± 5.51	-0.21	0.9
EFS	63.43 ± 2.39	62.5 ± 2.58	0.93	0.29
SFS	56.25 ± 4.65	57.18 ± 3.63	-0.93	0.53
SchFS	44.37 ± 3.09	44.06 ± 4.17	0.31	0.81
Total score	55.07 ± 2.4	55.06 ± 2.55	0.01	0.98
PedsQL™ parent-report				
PFS	57.42 ± 6.23	58.98 ± 6.83	-1.56	0.5
EFS	65.31 ± 4.26	63.43 ± 3.96	1.88	0.2
SFS	58.12 ± 3.09	59.06 ± 5.83	-0.94	0.57
SchFS	46.25 ± 4.28	46.56 ± 3.52	-0.31	0.82
Total score	56.86 ± 3.23	57.14 ± 4.38	-0.28	0.83
6MWT (meter)	435.62 ± 26.57	424.37 ± 22.2	11.25	0.2

X̄; Mean; SD: Standard deviation; MD: Mean difference; PFS: Physical functioning score; EFS: Emotional functioning score; SFS: Social functioning score; SchFS: School functioning score ; level of significance at p<0.05.

Table 4. Statistical analysis of post-test PedsQL™ and 6MWT within group.

	SC group				EX group			
	Baseline (X̄±SD)	*Post-test (X̄±SD)*	*MD*	*p-value*	*Baseline (X̄±SD)*	*Post-test (X̄±SD)*	*MD*	*p-value*
PedsQL™ child self-report								
PFS	56.25 ± 4.56	54.3 ± 4.09	1.95	0.0001*	56.46 ± 5.51	69.33 ± 7.05	-12.87	0.0001
EFS	63.43 ± 2.39	62.81 ± 3.14	0.62	0.43	62.5 ± 2.58	72.18 ± 3.63	-9.68	0.0001
SFS	56.25 ± 4.65	54.68 ± 3.85	1.57	0.055	57.18 ± 3.63	70.62 ± 4.03	-13.44	0.0001
SchFS	44.37 ± 3.09	43.43 ± 2.39	0.94	0.27	44.06 ± 4.17	56.25 ± 6.91	-12.19	0.0001
Total score	55.07 ± 2.4	53.81 ± 2.22	1.26	0.003*	55.06 ± 2.55	67.24 ± 3.43	-12.18	0.0001
PedsQL™ parent-report								
PFS	57.42 ± 6.23	55.1 ± 3.02	2.32	0.02*	58.98 ± 6.83	70.9 ± 8.2	-11.92	0.0001
EFS	65.31 ± 4.26	65 ± 3.16	0.31	0.77	63.43 ± 3.96	70.31 ± 3.4	-6.88	0.0001
SFS	58.12 ± 3.09	56.25 ± 5	1.87	0.08	59.06 ± 5.83	72.5 ± 6.05	-13.44	0.0001
SchFS	46.25 ± 4.28	45.93 ± 3.27	0.32	0.75	46.56 ± 3.52	59.37 ± 4.03	-12.81	0.0001
Total score	56.86 ± 3.23	55.76 ± 2.76	1.1	0.03*	57.14 ± 4.38	68.29 ± 4.41	-11.15	0.0001
6MWT (meter)	435.62 ± 26.57	430 ± 25.03	5.62	0.07	424.37 ± 22.2	522.5 ± 32.96	-98.13	0.0001

X̄; Mean; SD: Standard deviation; MD: Mean difference; PFS: Physical functioning score; EFS: Emotional functioning score; SFS: Social functioning score; SchFS: School functioning score level of significance at p<0.05.

Table 5. T- test for comparing post-test mean values of PedsQL™ and 6MWT between control and study groups.

Item	SC group	EX group	MD	p-value
	X̄±SD	X̄±SD		
PedsQL™ child self-report				
PFS	54.3 ± 4.09	69.33 ± 7.05	-15.03	0.0001
EFS	62.81 ± 3.14	72.18 ± 3.63	-9.37	0.0001
SFS	54.68 ± 3.85	70.62 ± 4.03	-15.94	0.0001
SchFS	43.43 ± 2.39	56.25 ± 6.91	-12.82	0.0001
Total score	53.81 ± 2.22	67.24 ± 3.43	-13.43	0.0001
PedsQL™ child self-report				
PFS	55.1 ± 3.02	70.9 ± 8.2	-15.8	0.0001
EFS	65 ± 3.16	70.31 ± 3.4	-5.31	0.0001
SFS	56.25 ± 5	72.5 ± 6.05	-16.25	0.0001
SchFS	45.93 ± 3.27	59.37 ± 4.03	-13.44	0.0001
Total score	55.76 ± 2.76	68.29 ± 4.41	-12.53	0.0001
6MWT (meter)	430 ± 25.03	522.5 ± 32.96	-92.5	0.0001

X̄ ; Mean; SD: Standard deviation; MD: Mean difference; PFS: Physical functioning score; EFS: Emotional functioning score; SFS: Social functioning score; SchFS: School functioning score; level of significance at p < 0.05

walking speed. The time was recorded with a stopwatch, and the time was called every min. The total distance covered was measured in meters[29].

Intervention

The exercise prescription was based on the same principles as healthy children and adults including duration and type of physical activity as well as the frequency and intensity of the exercises according to the American College of Sports Medicine guidelines. The progressive resistance exercises were conducted two days per week giving an interval of 48 hours between sessions. The intensity for resistance training was determined individually at 60-75% of 1 RM. Depending up on the child exercise tolerance, each set was performed 10 gradually increased to 15 repetitions[30].

The program was directed to improve muscle strength and functional capacity and individually estimated for each child. The exercises were conducted in small groups of 4 children and each group was supervised by two pediatric physiotherapists who were instructed by the research staff to warrant the uniformity of the training program. Each session consisted of progressive resistance exercises as demonstrated in Table 1. The sessions started by warming-up and ended by cooling-down in the form of treadmill walking at zero inclination at comfortable walking speed for five minutes. The exercises included upper and lower extremities as well as trunk- stabilizer exercises[31,32]. The resistance was increased gradually in three phases. During phase 1 (first two months) the weight used was determined according to the RM. In phase two (the second two months) the weight increased by 0.25 kilogram. During the third phase (the last two months) the weight increased by 0.5 kilogram[31].

Statistical analysis

Descriptive statistics and t-test was conducted for comparison between both groups. Paired t-test was conducted for comparison between pre and post-test in each group. The level of significance for all statistical tests was set at $p<0.05$. All statistical measures were performed through Statistical package for social sciences (SPSS) version 23.0 (SPSS Inc., Chicago, IL).

Results

The baseline patient physical characteristics are presented in Table 2 showed no significant difference between the two groups at baseline assessment regarding age, weight, height and biochemical assessment. The baseline comparison of mean values of PedsQL™ and 6MWT showed no significant difference between the two groups as demonstrated in Table 3.

Table 4 shows the results of baseline and post-test within group comparison. There was significant improvement with respect with PedsQL™ subscales and total scores as well as the 6MWT in the EX group. Regarding the SC group, the results revealed non-significant change in the 6MWT and the emotional, social, and school functioning subscales of the Peds-QL™. However, significant decrease of physical performance subscale and total score of the Peds-QL™ was recorded.

As demonstrated in Table 5, there was significant difference in the post-test mean values between the two groups in favor of the EX group in respect with all measured variables.

Discussion

In this study, we attempted to investigate the therapeutic effects progressive resistance exercises in pediatric patients with CKD with respect to quality of life and functional capacity. The main findings of this study suggest that the use progressive resistance exercises twice/week along with the standard medical care have the potential to produce a significant improvement of quality of life and functional capacity in pediatric patients with CKD.

Although multiple studies have investigated the effect of strengthening exercises in patients with CKD. The majority of these studies were conducted on adult patients receiving hemodialysis[14,17,32,33], limited literature is available in pediatric patients with CKD.

Individuals with CKD have reported severe limitations of daily living activities as well as emotional difficulties including depression, anxiety, getting easily irritable, and mood swings[34]. The improvements recorded in the EX group regarding the QoL domains including the physical, social, emotional and school function could be attributed to the therapeutic effect of progressive resistance exercises. Physical activity is believed to have a direct influence on general health therefore, the use of designed, planned, structured and repetitive bodily movements can help to improve both mental and physical functioning as well as QoL. Our results are supported by the findings of several studies performed on adults with CKD which showed positive effects of exercises on physical as well as emotional aspects of QoL, and academic achievements[35-37].

The results of the current study may be attributed to the type of exercises which included a group of exercises which consisted of a group of loaded multi-joint functional resisted exercises (sit-to-stand, half knee rise, step up) that were designed to incorporate the fundamental tasks required for the daily living performance during walking, stair climbing and general mobility. This comes in accordance with Lee et al[38], who stated that, sit-to-stand, lateral step-ups, front step-ups, walking up and down stairs, high-kneeling and lateral walking are effective methods to enhance motor performance and functional capacity.

The mechanism whereby the resistance exercises improve QoL and physical performance are reported by Liao et al[39]. They stated that, training programs targeting large muscles such as strengthening exercises help to improve the efficiency of the aerobic energy- producing systems and therefore improve cardiorespiratory endurance or fitness. Furthermore, Sietsema et al[40], mentioned that resistance training can contribute to increase in maximal oxygen carrying capacity and exercise tolerance in patients with CKD.

Many researchers proposed that the strengthening exercises are believed to increase muscle mass, endurance, cardiopulmonary efficiency and muscle strength in individuals with CKD. Other benefits also include increased confidence, social wellbeing, improved body image, and all are believed to improve physical activities and QoL as a result of enhanced psychological well-being and improved physical functioning[5,16-18,20,33].

Our results confirm those already reported by Song and Sohng[17], who investigated the effects of a 12 weeks progressive resistance training on body composition, physical fitness and QoL of patients on hemodialysis. They reported significant improvements in physical fitness and QoL. They also added that progressive resistance training can be utilized as part of a regular care plan for patients with CKD.

Cheema et al[41], studied the effect of a 12 weak of high-intensity, progressive resistance training administered during routine hemodialysis treatment in patients receiving hemodialysis. They reported statistically significant improvements in muscle attenuation, strength and cross-section area.

Likewise, Chen et al[16], conducted a randomized pilot trial on 50 elderly participants receiving hemodialysis. The results of their study revealed that, the strength training exhibited significant improvements in muscle strength, leisure-time physical activity and self-reported physical function and activities of daily living.

Our results are consistent with the study of Watson et al[42], who studied the effect of 8-week progressive resistance exercise program in adult patients with CKD stages 3b to 4. They found significant improvements in muscle anatomical cross-sectional area, muscle volume and strength, as well as exercise capacity. They also added that, this type of exercise is well tolerated by patients with CKD and confers important clinical benefits.

Furthermore, Headley et al[43] explored the effect of 12 weeks of resistance training in patients with CKD who were on hemodialysis. Their findings showed an improvement in muscle strength, endurance, exercise tolerance and slow down muscle wasting in CKD.

Regarding the SC group, significant reduction of the physical functioning and QoL total scores may be attribute to the limited physical activity and sedentary life style. This comes in accordance with previous studies which reports that patients with CKD have reduced levels of physical functioning, which, along with low physical activity, predict poor outcomes in patients with CKD[40,44-47].

Likewise, studies have shown the negative impact of the CKD and the treatment have on the cardiorespiratory and musculoskeletal systems and the QoL among those patients. These studies reported that CKD is a chronic illness affecting physical and mental health[48-51], functional independence, overall well-being and social interaction[52]. Furthermore, the condition results in reduced functional capacity and muscle strength in these patients[53-55].

Our study had some limitations which require cautious interpretation of our data. Firstly, the study was conducted to investigate the effect of a designed intervention program in a small sample of children. Secondly, the sample selected represented children with stage three (moderate) and four (sever) CKD. Thirdly, limited studies were conducted on pediatric patients with CKD. Thus, the improvements we observed may not be reproducible in a larger, more representative cohort. Despite these limitations, our data suggest that strengthening exercises are effective in improving QoL and functional capacity in pediatrics with CKD.

Conclusion

Progressive resistance exercises have been shown to be an effective therapeutic method to improve QoL and functional capacity in pediatric patients with CKD. Further rigorous studies including are warranted to determine the effect of the suggested program in different age groups, children with ESRD, those who receive hemodialytic or peritoneal dialysis and children with kidney transplantation. Follow up studies are recommended to investigate if the program can yield further improvements in QoL and functional capacity and/or other medical and psychological benefit.

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