SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Study of the effects of regular physical activity on quality of life in patients with chronic kidney disease

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I. INTRODUCTION

Epidemiological studies in recent years have shown that chronic kidney disease (CKD) is a highly prevalent global public health problem, affecting 10-12% of the world's population. According to the Global Burden of Disease, CKD was the 27th leading cause of death in 1990, rose to 18th in 2010 and is expected to be the 5th leading cause of death worldwide by 2040. An ageing population, late diagnosis, increased prevalence of chronic atherosclerotic diseases such as hypertension and diabetes are predicted to further increase the number of patients. The disease is associated with an increased risk of cardiovascular diseases such as coronary heart disease, heart failure, stroke, lower limb arterial stenosis, which increase the frequency of hospitalizations and are a cause of premature mortality. Prevention and management of the disease include appropriate management of risk factors such as hypertension and diabetes, and regular monitoring of kidney function. Lifestyle changes, smoking cessation, weight loss and proper nutrition, and increased physical activity also play an important role in effective management.

Recently, the focus of CKD management has been on the preparation for and use of renal replacement therapies. ESRD is a life-threatening condition, treatable by dialysis or kidney transplantation, that currently affects more than 2 million people worldwide. However, recent therapeutic developments offer the potential to prevent the disease, slow its progression and reduce the development of complications, thereby prolonging patients' lives. The cost of treatment is a major burden worldwide. In the United States, chronic kidney disease consumes 6.7% of the total budget, in Australia it is estimated to cost $12 billion, while in England it costs more than breast, lung, colon and skin cancer combined.

With the expansion of diagnostic and therapeutic options, CKD patients are better managed clinically, their life expectancy has improved, and the focus has shifted to the quality-of-life years gained. Health-related quality of life (HRQOL) is an important indicator of the effectiveness of these costly treatments. In addition to the technical parameters of renal care, the psychosocial characteristics of patients and the complex rehabilitation process are becoming increasingly important. Physical activity is an important and easily influenced measure of HRQOL, and its increase is a priority therapeutic option in the management of this group of patients, as it has an effect on the reduction of cardiovascular risk factors, improves health-

related quality of life, and contributes to the maintenance of independence and work capacity by maintaining and increasing endurance and muscle strength.

In the international literature, there is an increasing emphasis on quality of life and physical activity in all stages of CKD, but there are few data available on this topic in Hungary. The most commonly used questionnaire to measure quality of life has been validated in Hungarian, and several attention-grabbing publications summarizing the results of international studies on the importance of physical activity have been published. In addition to the benefits of physical activity, group outings, cycling and walking are also an incentive to change lifestyles. This is evidenced by the increasingly successful RenBikeTour, a patient-initiated cycling tour around Lake Balaton and Lake Venice, which was launched in 2012 and has since become an annual event. However, a regular, supervised, organized exercise programme for CKD patients has not been studied in the Hungarian population.

II. OBJECTIVE

The overall aim of the studies presented in this thesis was to understand physical activity and health-related quality of life in patients with end-stage renal disease (ESRD) and to develop and implement a safe and effective intervention program to improve functional capacity and quality of life.

The first step of our work was to

- We assessed physical activity and health-related quality of life in patients with end-stage renal disease treated with two different renal replacement therapies.
- We investigated whether the parameters assessed in patients treated with the more flexible PD program, which can be done at home, differed from those of patients treated with the HD program, which is done in an institution over several hours.

In the rest of our research:

- We assessed the functional capacity, pain severity and health-related quality of life of haemodialysis and kidney transplant patients on the transplant waiting list.
- We developed and implemented a safe combined exercise program for end-stage renal disease patients.
- We tested the effectiveness of the exercise program on previously assessed parameters.

- We investigated the role of our exercise program in further improving functional capacity and quality of life after transplantation.

III. METHODOLOGY

To support our research objectives, we conducted two separate studies, the methodological presentation of which is presented separately. In chronological order, the first is a quality-of-life study to assess and compare physical activity and quality of life in patients treated in HD and PD modalities, and the second is an intervention program to investigate the impact of a combined exercise training program in HD and kidney transplant patients on the transplant waiting list. We emphasize that the two studies are not sequential but contain similar methodological elements. Participants participated in the study on a voluntary basis after signing informed consent forms. The research protocol was approved by the Regional and Institutional Research Ethics Committee of the Clinical Centre of the University of Debrecen with the following ID: DE RKEB/IKEB: 5551A-2020.

PHYSICAL ACTIVITY AND QUALITY OF LIFE

In our study, data were collected at the Dialysis Centre of the University of Debrecen Nephrology Clinic in May 2020. Inclusion criteria included age over 18 years, at least 3 months of maintenance hemodialysis, regular hemodialysis at least twice a week for ≥ 4 hours per treatment, peritoneal dialysis for more than 3 months. All patients had to achieve the target Kt/v (1.4 once-daily Kt/v for HD recipients and 2.1 weekly Kt/v for PD recipients). In addition, regular attendance at the care facility, ability to walk and willingness to participate in the study were required. Patients who had severe mobility impairment or a cognitive or psychiatric impairment that prevented them from understanding and answering the questionnaires were excluded from the study. As a first step of the inclusion process, we reviewed the medical history of patients with chronic HD (n= 164) and chronic PD (n= 45) treated in the Dialysis Centre of the Nephrology Clinic of the University of Debrecen and selected patients who met our inclusion criteria (HD n=123, PD n=32), who were personally contacted to inform them about the study and the possibility to participate. In total, 130 patients with CKD (HD n=106, PD n=24) were included in our survey.

The data collection was face-to-face and consisted of two validated standard questionnaires and a demographic questionnaire designed by our team. After recording demographic, treatment and co-morbidity information, physical activity was measured using the International Physical Activity Questionnaire (IPAQ) short form and quality of life was

measured using the Kidney Disease Quality of Life-Short Form 12 (KDQOL- SF-12) questionnaire. HD patients completed the questionnaires during dialysis treatment, whereas PD patients completed the questionnaires at the time of reporting for treatment.

The first step in data analysis was to test the normality of continuous variables for the different strata, as normality was not met in the vast majority of cases, our data were analysed using non-parametric tests. The medians of two groups were compared using Mann-Whitney U-tests and the medians of three groups were compared using Kruskal-Wallis H-tests. Categorical data were analysed using Fisher's exact tests. Data were considered significant if the p-value of the statistical tests was less than 0.05.

EXAMINING THE IMPACT OF A COMPLEX TRAINING PROGRAMME ON FUNCTIONAL CAPACITY, PAIN AND HEALTH-RELATED QUALITY OF LIFE

Our study was conducted among members of the Debrecen Association of Renal Patients and patients (n=135) cared for at the Dialysis Centre of the University of Debrecen Nephrology Clinic between May and November 2020. Patients were informed in writing about the benefits of the training program and the possibility to participate in our study (HD n=106, RTx n=29). Patients who met the inclusion criteria and were treated in the HD program (n=25) and RTx (n=20) were classified into the intervention program volunteer (HD n=12, RTx n=9) and control (HD n=13 and RTx n=11) groups.

Eligibility criteria included age over 18 years, ability to walk, willingness to participate in the study, and at least 3 months of maintenance haemodialysis in the HD group, regular haemodialysis at least 3 times per week for ≥4 hours per treatment, Kt/V of at least 1.2, on the kidney transplant waiting list, and in the RTx group, physically fit, on stable medication for more than 6 months after kidney transplantation.

Exclusion criteria were diabetes mellitus, anaemia, any contraindication to physical exertion such as limited mobility of large joints, decompensated heart failure, untreated hypertension, major neurological dysfunction, severe peripheral polyneuropathy, combined organ transplant.

The 6-minute walk test was used to assess aerobic capacity and endurance. At the end of the test, in addition to monitoring saturation and pulse, we assessed the degree of dyspnea and leg fatigue on the Borg RPE 6-20 scale. Pain intensity was measured on a 10 cm

horizontal visual analogue scale and quality of life was measured using the Kidney Disease Quality of Life-Short Form 12 (KDQOL- SF-12) questionnaire.

MOVEMENT PROGRAMME

Participants in the treatment groups completed a 12-week exercise program, three times a week for 60 minutes at a time, including two sessions of moderate-intensity aerobic endurance training and one session of functional spinal exercise to strengthen core stabilizing muscles. HD patients exercised on non-dialysis days. Participants were divided into groups of four or five according to dialysis day, fitness level and age.

The design of the exercise training program in this patient group requires great care, with the primary consideration that dialysis patients and kidney transplant recipients are at high cardiovascular risk. Therefore, determining a safe exercise intensity and monitoring heart rate during training is essential. For resistance training, the type (elastic, weight, own body weight) and degree of resistance, the number of repetitions of exercises, the required rest period should be precisely defined. For CKD patients, it is recommended to start with 50% of 1RM with 10 to 12 repetitions, which can be increased to 15 to 20 repetitions every 3 weeks, where sudden movements with high effort should be avoided. The workload may be limited by co-morbidities, side effects of medication, changes in blood count. When designing the exercise program for HD patients, special attention should be paid to the site of blood collection and protection of the arterio-venous fistula, which limits the load on the arterial side of the upper limb.

When choosing the intensity, it should be taken into account that a general feeling of weakness, high fatigue and rapid fatigue are symptoms of kidney disease, so a longer warm-up and rest period is recommended. For a training program to be effective, it must be carried out persistently over a long period of time, so that patients must be constantly motivated to make the effort necessary to increase their physical activity while bearing the burden of managing their kidney disease. Each session started with a 10-minute warm-up on an indoor bike at the lowest resistance level to prepare the body for the increasing workload and to allow the joints, muscles and nervous system to adapt to the vigorous work. After the warm-up, participants performed moderate-intensity physical activity where the desired target range was reached by the third exercise and maintained until the end of the program. During the first two weeks, the duration of aerobic training was gradually increased from 15 minutes to 30 minutes, thus achieving a steady, consistent training intensity. The class ended

with a 15-minute rest period, aimed at a continuous reduction of the heart rate to resting levels, combined with static and dynamic stretching of the muscle groups used, using breathing exercises.

Functional spinal crunches involved targeted strengthening of the muscles involved in pelvico-lumbar stabilisation, as well as improving the mobility and stability of the spine. The training consisted of two phases. In the first phase (1-6 weeks), the activation and awareness of these muscle groups (m. transversus abdominis, m. multifidus, m. rectus abdominis m. obliquus externus et internus abdominis, m. erector spinae, m. gluteus maximus) was taught. First, we practiced isometric stretching and relaxation in the supine position, then holding the stretch for 10 seconds with continuous, relaxed breathing, repeating each exercise ten times, with a one-minute break between training the different muscle groups. Then, following the principle of gradual progression, we increased progression with exercises in several postures (lying on one side, on all fours, static standing), requiring increasing concentration. The program was then supplemented with exercises on an unstable surface (sponge cushion, gymnastic ball) to improve proprioception. In the second phase (7-12 weeks), participants performed functional strengthening exercises in the form of circuit training, consisting of three sets of 15-20 repetitions, against their own body weight or weight resistance, the magnitude of which was individually determined. Suspension straps, Pilates balls and exercise baton were used as tools for variety and progression. At this stage, we aimed to strengthen all the major muscle groups (shoulder stabilizers, core muscles, hip and thigh muscles) (Figures 7-8). The exercise program was concluded with dynamic stretching, with particular attention to the muscle groups subjected to high stress, and progressive relaxation.

Data were analysed using Mann-Whitney U-tests and Wilcoxon's signed rank tests, as well as Kruskal-Wallis tests to determine differences between variables measured on a continuous scale. The majority of data were non-normally distributed, which was tested using the Shapiro-Wilk test. Results are presented with medians and interquartile ranges and their corresponding p-values. Statistical analyses were performed using Stata statistical software (version 13.0, Stata Corp., College Station, TX, USA), and a p-value less than 0.05 was considered a statistical significance signal.

IV. RESULTS

RESULTS OF THE PHYSICAL ACTIVITY AND QUALITY OF LIFE SURVEY

A total of 106 (82%) HD and 24 (18%) PD patients were included in the study, for a total sample size of 130. The study population consisted of 70 (54%) men and 60 (46%) women. The HD group consisted of 59 (56%) males and 47 (44%) females, and the PD group consisted of 11 (46%) males and 13 (54%) females. No significant ($p = 0.383$) correlation was found in the frequencies between dialysis modality and gender. We also found no significant ($p = 0.735$) difference in the median age of the two groups; the median age of patients treated with HD was 56 years (range, 46-66) and the median age of patients treated with PD was 57 years (range, 44-71). There was no significant difference ($p=0.891$) in the frequency of each activity level between the two modality groups when examining the results of the IPAQ questionnaire. Among the HD patients, 43 (41%) showed high physical activity, 38 (36%) moderate physical activity and 25 (24%) were inactive. In the PD patient group, 11 (46%) were physically active, 8 (33%) were moderately active and 5 (21%) were inactive.

As a result of the quality-of-life analysis, a significant difference ($p=0.004$) was found in the mean PCS score by dialysis modality, as the mean PCS score was 4 (1-5) in the HD group and 5.5 (4-6) in the PD group. There was no significant difference ($p=0.445$) for MCS, however, the median value of MCS was 5 (4-6) in the HD group and 5 in the PD group, but the interquartile range (5-5) was considered narrower compared to the HD group.

Significant correlations were found when physical activity categories were analysed in terms of the PCS and MCS quality of life categories. The results found that the median PCS was significantly ($p<0.001$) higher in the high physical activity category with a median value of 5 (4-6) and lower in the moderate physical activity category with a median value of 4 (2-5) and in the inactive category with a median value of 2 (0-4). The same significant ($p=0.005$) correlation was found when comparing MCS category scores for physical activity. The highest median value was observed in the high physical activity group with a median value of 5 (4-6), and lower in the moderately active and inactive categories with median values of 5 (4-5) and 4.5 (2-5), respectively.

PCS and MCS values were also analysed by stratifying by dialysis modality for physical activity. A significant ($p=0.014$) difference in PCS scores was found when comparing the HD and PD groups, as the median PCS score was 5 (3-5) in the HD group and 6 (5-6) in the PD groups within the high physical activity category. People with PD also had significantly ($p=0.078$) higher PCS scores in the moderate physical activity category, as the median score in the PD group was 5-5 (3.75-6) compared to a median score of 4 (2-5) in the HD group.

The same relationship was also observed in the inactive stratum, as the median score for PCS was 2 (0-4) for HD patients compared to 4 (2-4) for the PD group. There was no significant ($p<0.05$) difference in MCS mean scores when comparing HD and PD groups for physical activity categories for the high ($p=0.829$), moderate physical activity ($p=0.244$) and inactive ($p=0.886$) groups. The median MCS score for PD patients was 5 (5-6), compared to 5 (4-6) in the HD group. The same trend was observed for moderate physical activity patients, as the median score for PD patients was 5 (5-5) and for HD patients was 5 (4-,5,75). In the physically inactive group, the median MCS was higher in the PD group, with a value of 5 (2-5), compared to 4 (3-5) in the HD group, but the difference was not significant.

STUDY OF THE IMPACT OF A COMPLEX TRAINING PROGRAMME ON FUNCTIONAL CAPACITY, PAIN AND HEALTH-RELATED QUALITY OF LIFE RESULTS

The HD training group consisted of 6 men and 6 women, with a mean age of 49 years (46-55) and a duration of hemodialysis of 43 months (30-55). The HD control group consisted of 8 men and 5 women, with a mean age of 52 years (47-58) and a mean time on haemodialysis of 39 months (26-51). The RTx training group included 4 men and 5 women, mean age 49 years (45-59), time since transplant 84 months (72-104), and the RTx control group included 5 men and 6 women, mean age 50 years (47-58), time since transplant 81 months (72-98).

For the 6-minute walk test, the initial median value in the 12-person HD training group was 440 (395-463), which increased significantly ($p=0.002$) to 489 (448-508) after training. In the 13-person HD control group, the initial median value was 432 (389- 471), which changed to 430 (390-470) during the study period, showing a decrease in walking distance, but this association was not significant ($p=0.461$). The median value for the 6-minute walking test for the 9 RTx patients in the training group increased significantly ($p=0.008$) from 495 (462-510) to 542 (508-555). In the control group of 11 RTx patients, no significant ($p=0.118$) increase was found, but the initial median value of 441 (399-561) increased to 445 (409-555) over the course of the programme. No significant difference in baseline values was found between patients in the training and control groups either within the HD group ($p=0.849$) or the RTx group ($p=0.621$). After the 12-week training program, the median score of patients in the HD training group was significantly ($p=0.030$) higher compared to the control group. There was no significant ($p=0.081$) difference in post-test

median values between patients in the RTx group. The median change at the individual level was 46 (43- 51) in the HD exercise group and 2 (-3-5) in the control group, with a significant ($p<0.001$) difference between the two groups. The median increase at the individual level was 55 (47-66) in the RTx training group and 3 (-2-9) in the control group, with a significant ($p<0.001$) difference between the two groups. A significant ($p=0.023$) difference was observed when comparing the delta of those exercising in the HD group with the delta of those exercising in the RTx group, indicating that the median value was lower in the HD group. A significant difference was observed for the initial ($p=0.010$) and post-training ($p=0.011$) median values when comparing the HD and RTx groups without stratification. However, the median increase between groups was not significantly different ($p=0.367$).

For pain, the initial median score in the HD group was 6 (5.5-7) in the 12-person training group, which changed significantly ($p=0.002$) to 3 (3-4) by the end of the study. In the 13-patient HD control group, the initial median score was 6 (4-6), which changed to 5 (4-6) by the end of the study period, showing a non-significant association ($p= 0. 083$). In the RTx group, the initial median score for the 9 patients who completed the training was 4 (3-4), which changed to 2 (1-2) by the end of the program, showing a significant change ($p= 0.008$). The 11 participants in the RTx control group had a baseline median score of 4 (1-5), which became 4 (1-5), a non-significant change ($p= 0.157$). In terms of pain, no significant difference was found in the baseline scores of patients in the HD group ($p= 0.084$) and the RTx group ($p= 0.621$) between the training and control groups. After the 12-week training programme, patients in the HD group showed a significant improvement ($p=0.001$) compared to the HD control group. We also found a significant improvement ($p=0.003$) in patients in the RTx group compared to the RTx control group. The median change at the individual level was -3 (-3.5-2) in the HD training group and 0 (0-0) in the control group, with a significant ($p<0.001$) difference between the two groups. The median change measured at the individual level was -2 (-2--1) in the RTx training group and 0 (0-0) in the control group, with a significant ($p=0.008$) difference between the two groups. When comparing the delta of the training participants in the HD group and the delta of the RTx group, there was no significant ($p=0.051$) difference between the two groups. Significant differences were observed for the initial ($p=0.001$) and post-training ($p=0.003$) median values when comparing the HD and RTx groups without stratification. However, the median increase between groups was not significantly different ($p=0.215$).

For quality of life, the initial median score in the 12-person HD training group was 8.5 (7-10.5), which changed to 10.5 (9-12) by the end of the study, showing a significant correlation (p=0.006). In the HD control group of 13 patients, the initial median score was 10 (7-11), which changed to 9 (7-11) at the end of the study period, a non-significant association (p=0.317). In the RTx group, the initial median score was 10 (7-10) for the 9 patients who completed the training, which changed to 10 (10-11) at the end of the program, a non-significant association (p=0.041). The initial median score for the 11 participants in the RTx control group was 10 (9-11), which became 10 (9-11), a non-significant change (p=0). No significant difference in baseline quality of life scores was found between patients in the HD group (p=0.721) and those in the RTx group (p=0.150) who trained and those in the control group. After the 12-week training program, there was no significant difference (p=0.121) between the median score of patients in the HD training group and patients in the HD control group, nor was there a significant difference (p=0.809) between the median score of patients in the RTx training group and patients in the RTx control group. The median change at the individual level was 1.5 (0-3.5) in the HD training group and 0 (0-0) in the control group, with a significant difference (p<0.001) between the two groups. The median change at the individual level was 1 (0-3) in the RTx training group and 0 (0-0) in the control group, with a significant (p=0.014) change between the two groups. Comparing the delta of those who trained in the HD group with the delta of those who trained in the RTx group, there was no significant (p=0.913) difference between the two groups. In terms of quality of life, no significant difference was found between the initial (p=0.319) and post-training (p=0.272) median scores when comparing the HD and RTx groups without stratification. The median increase between groups was also not significant (p=0.883).

V. DISCUSSION

V.1. ASSESSING PHYSICAL ACTIVITY AND QUALITY OF LIFE

During the pre-dialysis period, it is of great importance to educate patients and provide them with credible information about the different renal replacement modalities, giving them the choice of finding the right treatment, increasing their awareness, ensuring compliance with the therapy and thus the long-term effectiveness of the treatment. Our published findings on the relationship between quality of life and physical activity broaden the scope of patient education, contributing to informed decision-making to ensure that the treatment plan meets the preferences of the patient, relatives and health care staff. HD and PD can affect patients' physical activity to different degrees. The time required for HD treatment, travelling to

treatment, arriving for appointments, feeling tired and weak after the procedure can reduce patients' activity levels on dialysis days. While the flexibility and continuity of PD treatment provides a more even electrolyte and fluid balance in the body, less fatigue, potentially higher physical activity levels. These facts presuppose the activity, better functional capacity and physical resilience of patients treated in the PD program. Recently, international studies have focused on the impact of two very different dialysis modalities in this direction. Painter and colleagues, who were the first to compare physical activity and physical function in young (mean age 49 years) patients treated in chronic PD and HD programs, have shown that the two main areas of interest are the physical activity and physical function of patients on chronic PD and HD. PD patients performed better in the six-minute walking distance and walking speed tests, but physical activity levels measured by questionnaires were low in both groups of patients. The authors found no statistically significant difference in physical activity between patients treated with the two modalities. Cobo and colleagues, who conducted their study using a pedometer, found that 63% of PD patients and 71% of HD patients lead sedentary lifestyles with very low physical activity. Cupisti and colleagues studied the physical activity levels of PD patients over 60 years of age on a PD program and non-dialysis CKD patients. They found reduced physical performance in both groups compared to the non-renal population. However, when comparing the results of PD patients and CKD patients, there was no difference, suggesting that the initiation of PD treatment is not the main cause of the decline in physical activity (46). The importance of physical activity is highlighted in a summary paper by Zhang et al. who, examining the association between physical activity and mortality in HD patients, found that the risk of mortality was lower in patients who performed regular physical activity, and in this light, given the significant costs associated with HD treatment, it is necessary to address the physical inactivity of this patient group. The international literature shows low physical activity levels in end-stage renal disease patients regardless of dialysis modality, which is consistent with our own study, one of the main findings of which is that in our study population, physical activity levels were low in both HD and PD patients, and there was no statistically significant difference between the two modalities.

In terms of quality of life, a recent meta-analysis summarising the results of 21 studies found that patients treated in the PD program had significantly better quality of life compared to patients treated in the HD program in the subscales of physical functioning, emotional functioning and participation in social relationships. Hiramatsu et al. found improved scores

for PD patients on all scales of quality of life, whereas the quality-of-life scores of patients treated in the HD program did not change from the beginning of the study. In contrast, in Shdaifat et al's study, the physical component summary (PCS) score for quality of life was similar for HD and PD, while the mental component summary (MCS) score was higher for HD. In the present study, we found a significant difference between PCS scores, with higher PCS scores for patients treated in the PD program, but no significant difference for MCS scores.

Overall, our results showed that physical activity levels measured by the IPAQ questionnaire correlated with patients' quality of life. Patients treated in the HD program had significantly lower levels of physical activity and worse quality of life than patients treated in the PD program. Higher physical activity levels in both regimens resulted in better quality of life, which is in line with international data. Quality of life PCS and MCS scores were also analysed by stratifying physical activity by dialysis modality. At high, moderate and inactive physical activity levels, patients treated in the PD program scored significantly higher in the PCS category of quality of life. The same relationship was observed for MCS scores, although there was no significant difference. This confirms that higher physical activity can lead to better quality of life and that patients treated in the PD modality have better outcomes compared to patients treated in the HD modality.

V.2. STUDY OF THE IMPACT OF A COMPLEX TRAINING PROGRAMME ON FUNCTIONAL CAPACITY, PAIN AND HEALTH-RELATED QUALITY OF LIFE

Increasing physical activity is a priority area for lifestyle change in people with CKD, with a growing number of studies demonstrating the benefits of exercise programs in reducing cardiovascular risk factors and pain, improving functional capacity, muscle strength and quality of life. In terms of type of exercise, resistance training, aerobic exercises, combined (aerobic + resistance) training have been the most commonly used, but several studies have also used electrical stimulation, stretching, and respiratory training. Assessing, maintaining and improving functional capacity is a primary rehabilitation goal in this group of patients at high cardiovascular risk. Studies of the effects of exercise programs in CKD patients have also focused on reducing cardiovascular risk factors, with methodologies focusing on long-established forms of exercise training with proven efficacy in cardiac rehabilitation. A specific form of exercise for patients treated in the HD program is aerobic exercise during haemodialysis treatment, usually on a bicycle attached to the treatment bed. The reason for the large number of studies using this methodology is that patients can be tested in a safe,

monitored, institutional setting in large numbers at a time, so that the practical benefits and potential risks of exercise can be well detected. A disadvantage is the limited amount of applicable training material. Patients treated in the HD program can also undergo a training program on non-dialysis days, the effects of which have been described in previous chapters.

In the present study, we measured functional capacity using the 6-minute walk test, in line with Kohl et al. who found that the test, in addition to being a reliable measure of functional capacity, has prognostic value in the lifespan of CKD patients. Their results showed that for every 100 m increase in walking distance measured with the 6MWT, a 5% reduction in the risk of death was observed. In our study, walking distance measured by the 6-minute walk test increased significantly in the HD training group after the training program, indicating an improvement in functional capacity. However, our results show a small decrease in the HD control group, which is noteworthy and indicates the need for interventions. In RTx patients, walking distance increased significantly in the exercise group, while it also increased, although not significantly, in the RTx control group. This result indicates better functional capacity in kidney transplant patients and is consistent with the results of a study by Zhang et al. in kidney transplant recipients who also found an improvement in gait test scores as a result of an aerobic exercise program. In our case, when comparing the 6-minute gait test scores of the full HD and RTx groups, the RTx group showed better functional status at the first assessment. Our results are in agreement with the outcome of a meta-analysis by Theodorakopoulou et al. showing that RTx patients had significantly better functional reserve than patients on dialysis. No significant difference was found in mean (delta) scores, indicating similar improvements between patients in the HD and RTx groups, i.e. the program was useful for improving physical function at both stages of the disease.

A common complication of HD is musculoskeletal, neuropathic and muscle spasm pain, while kidney transplant patients typically report spinal, joint and muscle pain leading to reduced quality of life and sleep quality. Patients often cite pain as a limiting factor to their physical activity, for which non-pharmacological therapies such as exercise therapy can be used with good results in addition to pharmacological options. The Visual Analogue Scale has been widely used to collect quantitative data in subjective conditions where patients may find it difficult to accurately describe their pain levels, thus allowing objective measurement and monitoring of patients' conditions and the effectiveness of treatments. Although few studies have investigated the effectiveness of exercise programs in relieving

pain in CKD patients, their data have shown positive results. In a study of HD patients by Gerogianni and colleagues, aerobic exercise programs significantly reduced musculoskeletal pain. In a study involving forty-three patients with chronic kidney disease who performed aerobic and resistance exercises on non-dialysis days, they found that musculoskeletal pain was reduced, and general health and vitality improved. In our study, we found a significant reduction in pain severity in both the HD and RTx training groups, while there was no change in the control groups, suggesting that our exercise program is effective in both groups of patients. For the overall sample, members of the HD group reported higher baseline pain levels than members of the RTx group. Measuring quality of life is of paramount importance in the management of chronic diseases such as CKD. By measuring it, healthcare professionals involved in treatment can better understand the individual needs and preferences of the patient, which improves the efficiency and quality of care, and the focus of care is not only on the relief of clinical symptoms but also on the patient's satisfaction and general well-being. In our study, quality of life scores improved significantly in the HD treatment group, whereas in the HD control group, scores decreased slightly; however, this was not statistically significant. The same trend was also observed in the RTx group, as the median did not change in the treatment group, but the change in interquartile ranges (in 50% of the sample) was more favourable (7-10 at baseline versus 10-11 after intervention), whereas there was no change in the control group. Our results confirm literature data showing that increasing physical activity has a beneficial effect on quality of life at all stages of CKD, regardless of the training method used. The effectiveness of the exercise program is indicated by the significant median change in quality of life in both the HD and RTx training groups. We found no significant difference in quality of life between the two groups in our study population, which differs from the reported literature showing significant improvement in quality of life after transplantation. In conclusion, our intervention programme is equally effective and efficient in both groups of patients with end-stage renal disease. The participating patients achieved significantly higher scores in functional capacity, pain and health-related quality of life. The introduction of movement therapies into nephrological practice in Hungary is both necessary and timely.

IMPORTANT FINDINGS AND CONCLUSIONS OF OUR STUDY

- We found that physical activity in the study population was low and independent of dialysis modality, but that patients treated in the PD program had a better quality of life than patients treated in the HD program in terms of both physical and mental components.

Incorporating these findings into a predialysis patient education program could lead to more informed decision making when choosing a modality.

- Our results suggest that higher physical activity leads to better quality of life regardless of dialysis modality. This confirms that good physical fitness has a positive impact on patients' self-esteem, so there is a need to raise awareness of the effectiveness of physical activity and to provide more information on exercise in this patient group.

- Combining aerobic endurance training with core stabilization training is a new method in the exercise therapy of chronic kidney disease patients

- Our results show that our exercise program for end-stage chronic kidney disease patients is feasible and effective in increasing functional capacity, reducing pain and improving quality of life.

VI. SUMMARY

Chronic kidney disease (CKD) is a progressive disease affecting an increasing number of people worldwide, and the economic burden of its treatment is significant. It is a disease with many complications, high cardiovascular risk and mortality, and its management is increasingly focused on the psychosocial well-being of patients, in addition to the clinical management of underlying causes and complications. Low physical activity, which is easily controlled by non-pharmacological therapies, has an impact on the poor quality of life that is also characteristic of this group of patients.

The first study in this thesis focuses on physical activity and quality of life in CKD patients receiving dialysis treatment in HD and PD modality CKD patients. The results showed low levels of physical activity in both HD and PD patients, with no significant differences between the two groups. However, PD patients had significantly higher PCS scores ($p=0.004$), indicating better physical health. Higher levels of physical activity correlated with better quality of life in both groups.

The remainder of the thesis examines the effects of a 12-week exercise program of combined aerobic and core stabilisation exercises for HD and kidney transplant patients on the transplant waiting list. The 45 CKD patients enrolled were divided into intervention and control groups (HD n=25, n=12 intervention, n=13 control; RTx patients n=20, n=9 intervention, n=11 control). The results showed significant improvements in the

intervention groups for both HD and RTx patients in 6-minute walk distance ($p=0.002$ and $p=0.008$), pain severity ($p=0.002$ and $p=0.008$) and quality of life ($p=0.006$ and $p=0.041$) compared to the control groups. The results suggest that structured exercise programs can significantly increase functional capacity, reduce pain and improve quality of life in CKD patients, supporting their inclusion in nephrology practice.

Our experience has shown that with appropriate communication and comprehensive education, CKD patients can be encouraged to participate in exercise therapy. By introducing safe, supervised and guided exercise programs, in close teamwork involving a specialist nephrologist, nurse and physiotherapist, physical activity can be increased in this patient group, leading to an improvement in quality of life.

VII. PUBLICATIONS

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Subject: PhD Publication List

Candidate: Enikő Király
Doctoral School: Doctoral School of Health Sciences

List of publications related to the dissertation

1. **Király, E.**, Szőllősi, G. J., Jenei, Z., Kárpáti, I.: Association between physical activity and quality of life in haemodialysed and peritoneal dialyzed patients in Hungary.
   Ren. Fail. 46 (1), 1-6, 2024.
   DOI: http://dx.doi.org/10.1080/0886022X.2024.2324079
   IF: 3 (2023)
2. **Király, E.**, Szőllősi, G. J., Jenei, Z., Balla, J., Kárpáti, I.: Effects of a combined aerobic and core stabilization exercise training program on functional capacity, pain, and health-related quality of life in hemodialysis and kidney transplant patients.
   Ren. Fail. 46 (2), 1-7, 2024.
   DOI: http://dx.doi.org/10.1080/0886022X.2024.2370439
   IF: 3 (2023)

List of other publications

3. **Király, E.**, Kárpáti, I.: A fizikai aktivitás megőrzésének és fejlesztésének lehetőségei: hemodialízis- és peritoneálisdialízis programban kezelt krónikus betegeknél.
   Mozgásszervi Továbbk. Szle. 3 (2), 60-62, 2020.

DEBRECENI EGYETEM Egyetemi és Nemzeti Könyvtár

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