Cardiorespiratory fitness and habitual physical activity in adult renal transplant recipients: correlations between renal function, physical performance and health-related quality of life

Abstract of the PhD Thesis

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INTRODUCTION

Chronic renal failure is a progressive and irreversible syndrome. The final stage of chronic kidney disease is called end-stage renal disease (ESRD). The number of ESRD patients is increasing all over the world. Although successful kidney transplantation is not a life-saving operation, it is the only possible treatment for patients with ESRD. Lifelong dialysis can be avoided and complete rehabilitation obtained, while improving the quality of life and increasing life expectancy. There is an imbalance between low availability of donor organs and patients on the waiting list. Therefore, it is highly important that successful long-term transplants can be assessed with the prediction of long-term graft survival.

ESRD patients have an altered/different state of health

Patients with ESRD have an altered psychological and physical status. It is typical for patients with chronic illnesses to be physically inactive. Loosing motivation and suffering from social and emotional problems is also very common among patients. Muscular atrophy is caused by physical inactivity, which also results in diminishing capillarization of skeletal muscle and the loss of maximal strength.

Cardiovascular disorders (CVD) are currently the leading cause of mortality among kidney transplant recipients. Although the rate of CVD decreases after a successful transplant, it still remains 4-5 times higher than among the healthy population. Patients also have to take into consideration the side effects of corticosteroids after a transplant, due to strong immunosuppressive therapy, which contributes to weight gain, osteoporosis, diabetes and muscle atrophy.

Changes in the skeletal system appear as osteoporosis and in increased bone fragility, which can lead to an increased risk of bone fractures. A sedentary lifestyle influences bone loss and has a negative effect on the bone system. Weight gain is one of the side effects caused by immunosuppressive therapy, which is a consequence of increased body fat in the first few months after a transplant.

Physical activity has great potential for reducing many of these risk factors and to improve physical functions and the health related quality of life. There are numerous examples to show that patients can live a normal life after a successful transplant, or even continue as an elite athlete. Most patients, however, do not even attain the quality of life expected for normal renal function.

International recommendations for physical activity for kidney transplant recipients

Physical activity has a well-known positive effect on the cardiovascular system, on muscle strength and on the state of health in general. Therefore an internationally aligned recommendation has been already developed. According to the World Health Organization (WHO) a healthy adult person should do a minimum of 150 minutes of moderate-intensity aerobic physical activity, or 75 minutes of vigorous-intensity aerobic physical activity throughout the week, in bouts of at least 10 minute durations. The American College of Sports Medicine (ACMS) developed a recommendation in 2009 which encourages healthy adults to increase their moderate-intensity physical activity to 300 minutes, or their vigorous-intensity physical activity to 150 minutes. The National Kidney Foundation created the clinical practise guidelines in 2002 based on the metabolic equivalent of a task (MET). This program recommends that ESRD patients should do at least a minimum of 30 minutes of moderate-intensity physical activity, five times a week (450 MET/week). Immediately after a transplant, patients should start walking every day for 30 minutes at low intensity.

There is a lack of scientific studies defining exact amounts and intensities for recommended physical activity for kidney transplant recipients. Scientists do not have the results of object measurements, so they can use only the estimated average data.

World Transplant Games

The World Transplant Games (WTG) is an international multi-sport event, occurring every two years since 1978. WTG is the most prestigious sports event for transplant patients who are looking for challenges through sport. WTG has an outstanding role in the transplant world, which is highlighted by the numerous scientific reviews covering physical performance, achievements and energy consumption of the transplant patients.

Health-related quality of life

Successful kidney transplants give patients the chance to achieve full rehabilitation, long-term graft survival and an increase in their quality of life. International literature points out that health related quality of life depends not only on various socio-demographic, psychosocial and physical parameters, but also on the individual's attitude towards health. It has been proven that regular low and moderate intensity physical

activity can significantly increase the health-related quality of life for kidney transplant patients. The assessment of QoL is very complex; the graft function, the possibility of rejection, re-transplantation and dialysis all have to be taken into consideration.

Although socio-demographic and socio-economic factors have a real influence on increasing QoL, the biggest effect is from the transplant itself. Socio-demographic factors such as sex, age, marital status, education level, time spent on dialysis and waiting lists, have no effect on the assessment of how patients perceive QoL.

OBJECTIVES AND HYPOTHESIS

The aim of this study was to investigate the physical and mental health of renal transplant recipients who take part in regular sport and those who are physically inactive.

We used an objective accelerometer-based method to compare the different lifestyles of the recipients. We characterized the habitual physical activity level of the Hungarian National Transplant Team.

According to the above we determined the following hypothesises:

- The members of the Hungarian National Transplant Team reached significantly higher performance during the spiroergometric test in regular sports activity.
- Active renal transplant recipients had better renal and cardiovascular function and a better musculoskeletal system.
- Habitual physical activity was significantly different between active and sedentary renal transplant recipients.
- Organized sporting activities allow for renal transplant recipients to reach the minimum level of recommended physical activity of their healthy counterparts.
- Regular physical activity results in a better quality of life for renal kidney recipients, which means a better state of mental health and a higher level of overall satisfaction.

MATERIALS AND METHODS

Subjects

35 adult kidney transplant recipients (12 women and 23 men) participated in our study. According to their habitual physical activity levels they were divided into two groups; members of the Hungarian National Transplant Team represented the active transplant recipient group (AVTR; n=21 patients), and those who spent less than 3 hours activity per week represented the control group of the study (KVTR; n=14 patients).

Methods

The sex, age, date of transplant and age of the graft were recorded, along with the following labor parameters: urea, serum creatinine (SeCr), estimated glomerular filtration rate (eGFR), hemoglobin and hematocrit. Anthropometric measurements, such as height, weight, calculated body mass index were taken as well.

Cardio-respiratory capacity

Cardio respiratory capacity was measured through an incremental spiroergometric exercise test performed in a stationary-cycle ergometer until exhaustion. Heart rate (HR) was monitored continuously with a 12-lead electrocardiogram throughout the test. Capillary lactate concentration from the earlobe was taken before the test, at the end of the physical exertion and after 5 minutes of rest (LACr, LACmax, LACR5). Gas exchange parameters were measured during testing using breath-by-breath analysis. Maximal parameters were recorded for oxygen uptake (VO_2peak), ventilation (VE), oxygen pulse (O_2p) and load (P).

Maximal strength

The maximal strength of the quadriceps was tested by a computer-based isokinetic dynamometer. Maximal torque (Nm) and relative torque for each individual (Nm/kg) were registered. The highest value from the four trials was taken as maximal strength. Upper body strength was measured by a handgrip dynamometer. Patients had four trials with the dominant hand. The highest value out of the four was taken as maximal strength. Maximal handgrip (N) and relative handgrip (Nm/kg) were registered.

Habitual physical activity

Habitual physical activity was measured using an accelerometer-based assessment method (ActiGraph GTX3+ and Actiheart) in 24 hour monitoring, for 7 consecutive days. Data evaluation only took place between 6.00am and 8.00pm. We differentiated the moderate to vigorous physical activity (MVPA) and sedentary (SED) intensity according to the international recommendation for physical activity.

Health-related quality of life

The World Health Organization Health-Related Quality of Life (WHO-HRQOL-Bref) questionnaire was used to self-evaluate health status domains. The WHO questionnaire contains 2 general and 24 transplantation-specific items in four domains. The four domain scores (physical health, psychological health, social relationships and environmental factors) are all scaled in a positive direction with higher scores indicating a higher quality of life. Cronbach's alpha coefficient was used to test the reliability of the questionnaire. Cronbach's alpha was higher than 0.7 for two domains and for the other two it was 0.68 and 0.63, respectively. Recipients who had domain scores greater than the *mean plus 1 SD* were categorized as having high QoL and were given code 1 for active and code 2 for sedentary. Recipients who had domain scores within the range of *mean plus or minus 1 SD* were categorized as having normal QOL and were given code 3 for active and code 4 for sedentary. Those who had domain scores less than the *mean minus 1 SD* were categorized with poor QOL and were given code 5 for active and code 6 for sedentary.

Statistical analysis

All data analyses were performed using Statistica 13.0 (SatSoft GmbH, Hamburg, Germany) and Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) programs. Either the Shapiro-Wilk test or a non-parametric test was used for normality. Descriptive statistics (mean values and standard deviations) were calculated for the total sample as well as for active and sedentary control group. Two-paired *t*-test and Mann-Whitney-U tests were performed for the total sample set in order to compare the mean values of the active and sedentary control groups. A correlation matrix was used to compare the total sample and the two groups. The chi-square test was performed to assess the prevalence rate of the QoL categories. One-way ANOVA or Kruskal-Wallis

ANOVA was used to compare the parameters in the different HRQoL categories. The level of significance was set to $p < 0.05$.

RESULTS

Demographic and anthropometric results

The ratio of male to female subjects was 2:1 for kidney transplant recipients in the total sample and in the groups. There were no significant differences between the active and sedentary groups in regards to age, the main anthropometric parameters and BMI (kg/m^2). There was a significant difference in body fat percentage between the two groups. Active kidney transplant recipients had a lower fat percentage than the sedentary recipients ($p<0.05$).

Graft function

There were no significant differences in the graft age between the two groups. The average graft age of the active recipient group was two years older than the sedentary control group. The active recipient group was characterized by a significantly lower urea level ($p<0.05$). According to the eGFR level, there were no significant differences between the active and the control groups. However, the active group had a better eGFR function with roughly 10 $ml/min/1.7m^2$ more than the control group. Moreover, there were significant differences in the haemoglobin levels between the two groups ($p<0.05$).

Cardio-respiratory capacity

There were significant differences in almost all of the physiological parameters during the spiroergometric test. The active recipients reached significantly higher performance levels ($p<0.01$) than the control group. The maximal performance of the active group was at about 200 Watts, which meant a difference of 1 Watt/kg in relative values ($p<0.01$). The active kidney recipients reached their performance with a significantly higher heart rate ($p<0.01$), minute ventilation ($p<0.05$), oxygen uptake ($p<0.01$) and lactate concentration ($p<0.05$). The difference in the maximal oxygen uptake between the two groups was about 600 ml, which meant a 20% higher aerobic capacity for the active recipient group.

Maximal strength

There were no significant differences in the maximal strength of the knee extensor between the two groups. The maximal handgrip showed no differences either.

Habitual physical activity

The study groups showed significant differences in time spent being sedentary ($p<0.01$) and the time spent doing moderate to vigorous physical activities (MVPA) ($p<0.01$). The active kidney transplant recipient group spent an average of 351 min (5.84 hours) in the MVPA intensity during the 7 days, while the control recipient group spent less than half of that (2.97 hours). The difference between the two groups was significant (AVTR: 350.31±148.1 vs. KVTR: 178.15±93.6 min/7days; $p<0.01$). Time spent in the sedentary intensity below 1.5 MET, was also significantly different between the two groups (AVTR: 72.33±6.1 vs. KVTR: 78.86±5.8 hours/7days; $p<0.01$).

The chi-sqaure test did not show significant differences between the active and control groups according to the recommended physical activity, which should be at least 150 minutes in MVPA intensity per week. All of the active kidney recipients reached this level of activity, but less than the half of the control group did.

Correlations of kidney function

The relationship between the eGFR level and age was significant in the total sample ($r= -0.46$; $p<0.05$). Kidney function in older recipients was worse. There was also a significant correlation between the graft age and eGFR level ($r= -0.44$; $p<0.05$). The less time since the transplant, the better kidney function the recipient had.

There was no significant correlation between habitual physical activity and the graft function. In the total sample the correlation between the graft function and performance was significant ($r= 0.54$; $p<0.05$). A higher eGFR level correlated significantly with a higher maximal oxygen uptake ($r= 0.49$; $p<0.05$).

One-way ANOVA did not show a significant difference between groups that were based on their level of CKD. However, active recipients reached a higher oxygen uptake than their control counterparts and better kidney function resulted in higher performance. A significant correlation was found between eGFR and VO_2peak in the control group ($r= 0.69$; $p<0.05$).

Better kidney function showed significant correlation with maximal and relative hand grip values ($r= 0.45$; $p<0.05$ and $r= 0.51$; $p<0.05$, respectively).

Correlations of Health-related quality of life

According to the total score in the four domains of *Quality of Life* (physical health, psychological health, social relationships and environment), physical health and environment had the highest and lowest values. The two groups, however, showed a different pattern: active recipients reached the highest score in physical health (82.9%) and the lowest in environment (73.86%). On the contrary, the control recipients had the highest score in environment (75.1%) and the lowest in the physical health (65.57%). Less than 30% of the kidney transplant recipients were in the "Low" quality of health category, despite their level of physical activity. In all four domains there were a greater number of active recipients in the "High" category than control recipients.

CONCLUSIONS

Habitual physical activity of kidney recipients in the Hungarian Transplant Team was higher than the control group because of regular and organized sports activities. They spent significantly more time in MVPA intensity and significantly less time in Sedentary intensity during the 7 days of testing. Not only did they reach this intensity, but they exceeded the recommended amount of physical activity for a healthy adult population. As a result, during the spiroergometric test, the active recipients reached significantly higher performance levels and better aerobic capacity than the control group.

The small difference between the two groups in the knee extensor tests and the hand grip tests validates the benefits of complex, specialized, individual strength training for transplant recipients. There is a need for individually tailored training programs for kidney recipients coupled with an internationally aligned recommendation for the exact amount of physical activity required after a kidney transplant.

According to this study, the independent role of eGFR for kidney function has been proven. Independent of physical activity, eGFR correlated significantly with performance and aerobic capacity. Furthermore, better cardio respiratory capacity correlated with better eGFR values apart from the amount of physical activity. Better kidney function was accompanied always by higher oxygen uptake in the three different

groups, based on the level of CKD. The difference in oxygen uptake was more than 0.5 l between the groups. Moreover, in all three groups, active recipients had higher aerobic capacity than the control recipients.

Although the members of the Hungarian Transplant Team had significantly higher performance, it did not always mean a better quality of life. Active transplant recipients reached higher total scores in all of the domains, but the main contributors of this result have not been identified. It has not been proven that regular physical activity can decrease post transplant symptoms.

As a result of this study it is strongly recommended that transplant recipients should follow a structured aerobic training program, coupled with strength training, in order to improve their cardio-respiratory capacity. It is also recommended for recipients to take part in spiroergomteric tests regularly, in order to keep their physical capacity in check. After a transplant, recipients should start taking part in physical activity programs as soon as possible, if it is available as part of their rehabilitation program. They have to be informed about their illness and the state of their health regularly. Physical capacity can be drug-free therapy which not only improves their physical capacity, but also helps to develop their quality of life.

In light of these results there is a need for close cooperation between recipients, transplant-specific physicians, transplant centres, sports professionals and therapists. Kidney transplantation helps itself for recipients to regain their earlier lifestyle. The operation in connection with regular physical activity gives recipients an opportunity not only to reach a state of health before kidney transplantation but to reach the functionality and quality of life equal to their healthy counterparts.

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