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Physical activity in kidney transplant recipients: benefits, barriers, interventions

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Abstract

Kidney transplant recipients are reported to have low levels of physical activity compared to the general population. This population is burdened by high prevalence of both traditional and non-traditional cardiovascular risk factors. Physical activity has multiple known health benefits, including reduction of cardiovascular disease risk factors, which are the most common cause of morbidity and mortality in this group. Sedentary lifestyle has been associated with poorer long-term graft outcomes and inferior quality of life. Lack of specific guidelines regarding exercise post-transplantation has been cited as one of the barriers to physical activity, alongside comorbidities and immunosuppressive drugs' side effects. Exercise interventions, leading to improved physical functioning both pre- and post-transplant, have been demonstrated to lead to improved muscle strength, overall physical functioning, as well as cardiorespiratory performance. Currently available data on physical activity in kidney transplant recipients and its role in long term management of these patients remains limited, but promising results regarding its impact on long-term outcomes highlight the need for further research and development of more precise guidelines and educational programmes for both healthcare professionals and kidney transplant recipients.

Keywords: physical activity, exercise intervention, kidney transplantation, kidney transplant recipients, cardiovascular disease

Introduction and Objectives

Physical activity (PA) is a possible intervention in kidney transplant recipients (KTRs), with the potential to improve their cardiovascular disease (CVD) risk-factor profile, mortality, as well as overall quality of life, as its impact in the general population has been widely proven(1, 2). Although empirical evidence concerning KTRs is limited in scope, exercise has been demonstrated to have positive effects post-transplantation and should be considered in long term management of KTRs.

PA is defined by the World Health Organization (WHO) as any bodily movement produced by skeletal muscles that requires energy expenditure(3). For adults, WHO recommends at least 150-300 minutes of moderate intensity moderate-intensity aerobic physical activity, or at least 75–150 min of vigorous-intensity aerobic physical activity, or an equivalent combination of both throughout the week in order to achieve health benefits, as well as muscle-strengthening activities involving all major muscle groups at least twice a week(3).

Clinical practice guideline for the care of KTRs recommends that patients follow a healthy lifestyle and exercise(4), but it doesn't further discuss the topic. At present, no precise guidelines regarding PA in KTRs have been developed.

Prevalence of physical activity is low in patients with chronic kidney disease (CKD), especially hemodialysis patients(5, 6). Kidney transplantation, the renal replacement treatment of choice in end stage renal disease (ESRD), has been found associated with improved PA levels(7). Nonetheless, sedentary lifestyle is common in KTRs.

Despite the growing interest in inclusion of exercise in the therapeutic process of KTRs, its impact on morbidity and graft-related outcomes remains uncertain. The purpose of present review is to outline current knowledge regarding possible benefits of PA in KTRs, as well as discuss existing barriers and exercise interventions that might be implemented in post-transplantation management.

Methods

A literature review was conducted using PubMed with search terms like "physical activity in kidney transplant recipients", "kidney transplantation outcomes", "obesity in kidney transplant recipients", "cardiovascular risk in kidney transplant recipients", "solid organ transplantation", "exercise interventions" and related variations. The focus was on clinical trials, double-blind randomized controlled trials, meta-analyses, systematic reviews, and other review articles. Priority was given to articles published within the last five years to ensure that the review captured the most up-to-date research in this rapidly evolving field. Case reports were not included in the review.

Impact on CVD and mortality

Kidney transplantation has been shown to reduce CVD-related morbidity and mortality compared with hemodialysis patients(8). Nevertheless, KTRs have up to 10 times the rate of fatal cardiovascular incidents of the general population(9). Well-established risk factors for CVD, such as hypertension, diabetes mellitus, dyslipidemia, obesity and metabolic syndrome are common in KTRs(9-12) and are associated with impaired long-term graft function and pose a risk factor for graft failure(13, 14).

Sedentary lifestyle is a known risk factor of CVD(2). Physical inactivity is associated with a higher incidence hypertension, obesity, dyslipidemia and other CVD risk factors in the general population(15). It has also been associated with higher overall mortality(15).

Physical inactivity has been proven to be associated with increased mortality risk in dialysis patients(16).

Literature on the topic of the relationship between PA and CVD risk factors and cardiac death in KTRs remains limited in scope. A study of 540 KTRs has demonstrated that low level of PA is associated with history of cardiovascular disease and cardiovascular deaths(17). It was found that cardiovascular mortality was respectively 11.7 and 1.7% in the least and the most physically active tertile, while all-cause mortality was 24.4 and 5.6% according to these tertiles(17). Kang et al.(18) have also found that lower levels of PA were positively related to higher CVD risk in a study of 4043 participants. Another study of 650 KTRs has also demonstrated that higher levels of PA were associated with a lower risk of cardiovascular and all-cause mortality(19).

In a study of 10,875 KTRs, whose physical function was examined using the SF-36 questionnaire, worse physical function was associated with higher mortality(20). In patients with the highest physical function, the 3-year mortality was at 3%, while in patients with lower physical function was at 14%(20). Another study of 64 older KTRs compared their graft and health outcomes with patients aged 18-59 years and found that pretransplant inactivity and poor functional capacity were associated with inferior outcomes(21).

Impact on quality of life (QoL)

Physical activity is associated with higher life satisfaction and happiness levels in adults(22). In KTRs, physical performance, which is an important determinant of health and QoL, can be impaired in aspects such as muscle strength(23). Mazzoni et al.(24) assessed health-related quality of life in a group of 118 physically active KTRs, 79 sedentary KTRs and 120 active healthy control subjects using the SF-36 questionnaire. Active KTRs scored higher than their inactive counterparts in multiple SF-36 scales, including Physical Functioning, General Health, Social Functioning and Mental Health(24). Another survey study of 32 participants(25) has demonstrated that greater participation in walking, higher levels of overall PA and less time spent sedentary was associated with better QoL. Regular physical activity was found to be positively associated with QoL and aerobic fitness(26).

In a small randomized control trial, Kastelz et al.(27) have studied the effects of a 12-month exercise rehabilitation program consisting of 2 day/week, 60-minute personalized, one-on-one, resistance-based exercise trainings compared with standard care alone. The study found that the exercise intervention had a positive impact on employment, global physical and mental health, with intervention group showing greater improvements(27).

Impact on allograft function

The impact of PA on kidney function appears to be positive(28-30). In healthy subjects, increasing PA levels might potentially reduce the odds of developing CKD by 18%(30). Villanego et al. (31) have concluded in their study have found that PA has no negative impact on renal function in non-dialysis CKD patients, in fact some studies suggest that higher levels of PA might be associated with a slower rate of eGFR loss(29, 32).

In a study of 88 recent KTRs, who had been followed over the period of one year, Gordon et al.(33) found that lifestyle factors, such as greater PA and a history of non-smoking, were associated with improved graft function at the 6 month mark, with eGFR approximately 8 mL/min/1.73 m² higher in physically active patients. The suggested mechanisms include improved perfusion and oxygen delivery to the kidney graft due to improved cardiovascular function and delayed development of atherosclerosis(33).

A large retrospective study analyzing the impact of PA on graft function of 6,055 Italian KTRs over a 10-year follow up period demonstrated that active patients maintained higher eGFR values in the long term, especially patients aged more than 50 years(34). Out of 6,055 patients, 51.6% were active, and it was found that male, non-overweight, younger patients were more likely to be physically active(34). The study serves as confirmation of the positive impact of PA on long-term graft function preservation.

Impact on obesity and weight gain

Obesity in KTRs is frequent as it mirrors its growing incidence in the general population(35, 36). Analysis of literature shows that obesity has been associated with inferior transplant outcomes, increased mortality and higher risk of graft failure(37, 38). It is also a widely known CVD risk factor and a risk factor for the development and progression of CKD(39). Due to multiple factors, such as sedentary lifestyle, dietary intake and immunosuppressive medication, KTRs are prone to weight gain(36).

Regular PA is one of the easiest to implement strategies in weight maintenance. It has been shown that KTRs that are physically active have lower body mass index (BMI)(18). Another study found that 44% of patients with obesity had low PA levels(40). Heng et al.(41) in a study of 19 non-diabetic male KTRs determined that patients who had gained weight had lower adjusted energy expenditure and reduced spontaneous PA.

Barriers

It appears that PA levels among KTRs are relatively low(5, 34). Barriers to PA in this population can be divided into those pre-dating transplantation and those which arise post-transplant.

Many KTRs were previously dialysis patients, and in this population findings such as anemia, uremia, skeletal muscle atrophy, mental health issues, and comorbidities such as CVD or diabetic neuropathy may act as barriers to physical activity(42, 43). Moreover, the long hours spent on dialysis each week cause the hemodialysis patients to be less active on a daily basis than the general population(44). Some of these factors might be corrected by a kidney transplant, though some, such as bone and muscle changes, remain present post-transplant.

Immunosuppressive drugs, with their multiple side effects, might also form a more or less direct barrier to PA. Corticosteroids are associated with osteoporosis, reduced bone mass and increased risk of fractures, and thus can indirectly lead to inactivity(42). Corticosteroids and calcineurin inhibitors might cause skeletal muscle atrophy. Calcineurin inhibitors have also been associated with neurotoxic adverse events, such as tremor, neuralgia and peripheral neuropathy(45).

Billany et al.(46) conducted a phenomenological study in which 13 KTRs with no major contraindications to exercise were interviewed. Among other factors, participants were concerned about lack of guidance from health care professionals, potential harm exercise might cause to the graft, and lack of access to sports facilities(46) as potential barriers to PA. In another survey study, KTRs cited lack of motivation, preference for other activities, bad weather and fatigue as factors detracting from PA(47).

Many physicians don't feel confident in performing physical activity counselling in the solid organ transplant recipients, citing lack of time and lack of exercise guidelines as barriers in counselling(48). Conversely, well-established exercise programmes have been identified as one of the crucial factors in lung transplant recipients having greater PA levels than KTRs(49).

Interventions

At present, there are no precise, widely-accepted guidelines on inclusion of PA in the managements of a KTR. Kidney Disease: Improving Global Outcomes (KDIGO) recommends that KTRs maintain a healthy lifestyle(4).

Fear of movement, often associated with history of cardiovascular and cerebrovascular events and inferior physical functioning, has also been found to be positively correlated with physical inactivity(50). In order to improve physical activity, optimal management of comorbidities is necessary.

In some patients, adjustment of immunosuppressive regime may contribute to increase in PA(51). A randomized control study analyzed the impact of rapid steroid withdrawal on muscle structure and has found that it lead to significant improvements in muscle structure, which might contribute to better muscle function and exercise capacity(52).

Over the last decade there's been a growing interest in developing exercise training that would address KTRs specific needs and result in better long term health outcomes.

A recent meta-analysis of randomised clinical trials studying the impact of exercise interventions on patients pre- and post-transplantation offers more detailed recommendations for this patient population(53). Baker et al.(53) recommend that KTRs should aim for 150 min of moderate to vigorous PA a week or 75 of vigorous PA, both aerobic and resistance exercise. The study also recommends that appropriately trained staff (e.g., physiotherapist, sport scientist, cardiac rehabilitation specialist, other healthcare professionals with additional training) takes part in creation of a structured exercise routine based on patient's individual goals, pathophysiology, level of experience and graft status(53). For some patients, especially those with less experience with exercise, supervision might result in better compliance and higher motivation levels(46, 53).

It is important to assess the patient's physical activity levels in the pre-transplant phase. Simple screening tools such as the PAVS can be used(53). Regular exercise programmes can be set up for patients awaiting transplantation(54, 55). The concept of "prehabilitation", meaning short term exercise-based programmes introduced prior to major surgery, has been found to be safe and associated with improved peri-operative outcomes(56). In KTRs, prehabilitation has been associated with improved cardiorespiratory and physical function, as well as decreased duration of post-operative hospital stay(54). In a study of 15 candidates for kidney transplantation, the participants were enrolled in an 8-week-long exercise intervention supervised by an exercise physiologist(57). The prehabilitation programme was safe, feasible

and acceptable, with 60% completion rate, and most participants found it beneficial to their overall health(57). Another study of 18 kidney transplant candidates found that a programme consisting of weekly physical therapy sessions and at-home exercises resulted in improved physical activity and high satisfaction(58). Due to limited research available, it remains unclear which type(s) of exercise are the most beneficial in the pre-transplant phase.

Conclusion

Kidney transplantation is considered the gold standard for long term treatment of end stage renal disease. Compared to hemodialysis, it's associated with lower mortality(59) and improved quality of life(60). Although the research on the impact of PA on specific risk factors associated with graft function and other health outcomes remains limited in scope, it appears that inclusion of PA in guidelines for long term management of a transplant patient could be a positive influence on CVD risk factors and an important preventive measure of cardiovascular mortality, whose prevalence in this group remains high.

KTRs commonly lead a sedentary lifestyle. The lack of additional measures, such as specific guidelines or widespread exercise programs, is an obstacle that contributes negatively to levels of PA in this group. Further research focused on strengthening the body of evidence reporting the effectiveness of PA in improving long term transplant outcomes, development of specific exercise recommendations for different age groups and adjusted to local socioeconomic conditions will be fundamental in supporting health care professional in more informed and efficient introduction of PA in their management of KTRs.

Disclosures

Author Contribution Conceptualization, MS, and SP; methodology, KC; software, JP; check, AR, KS and AS; formal analysis, MN; investigation, GP; resources, MS; data curation, MN; writing - rough preparation, MS; writing - review and editing, MS; visualization, SP; supervision, GP; project administration, MN;

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