Elucidating the present and future of individuals with kidney disease: a multifaceted epidemiological approach

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Chapter 09

Improving health-related quality of life after kidney transplantation using lifestyle interventions

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Abstract

Chapter 09 discusses a study by Knobbe et al., the abstract of which is given here.

Background. Robust evidence for interventions to improve health-related quality of life (HRQoL) in people who receive a kidney transplant is scarce. We aimed to assess the effects of a lifestyle intervention in this context.

Methods. We conducted a multicentre, open-label, parallel-group, randomised controlled trial among people who have received a kidney transplant. Participants from six hospitals across the Netherlands were randomly assigned 1:1:1 by an independent company into: usual care, exercise, and exercise plus diet. The exercise intervention encompassed two phases, a 3-month supervised exercise programme (twice weekly) followed by 12 months of lifestyle coaching, with 15 months of additional dietary counselling (12 sessions) for the exercise plus diet group. The primary outcome was HRQoL-domain physical functioning, assessed using the 36-item Short Form Survey at 15 months.

Findings. From Oct 12, 2010 to Nov 18, 2016, 221 participants who had received a kidney transplant (138 [62%] male and 83 [38%] female, with a mean age of 52.5 [SD 13.5] years, who were a median of 5.5 [IQR 3.6–8.4] months post-transplant) were included and randomly assigned to usual care (n=74), exercise intervention (n=77), and exercise plus diet intervention (n=70). In the intention-to-treat analyses, at 15 months post-baseline, no significant differences in HRQoL-domain physical functioning were found for the exercise group (5.3 arbitrary units, 95% CI −4.2 to 14.9; p=0.27), and the exercise plus diet group (5.9 arbitrary units, −4.1 to 16.0; p=0.25) compared with control. Safety outcomes showed no safety concerns. After 3 months of supervised exercise intervention, HRQoL-domain physical functioning improved in the exercise group (7.3 arbitrary units, 95% CI 1.2 to 13.3; p=0.018) but not in the exercise plus diet group (5.8 arbitrary units, −0.5 to 12.1; p=0.072).

Interpretation. A lifestyle intervention is safe and feasible in people who have received kidney transplants, paving the way for lifestyle intervention studies in other multimorbid populations with polypharmacy. However, improving HRQoL for people who have received a kidney transplant is challenging. The lifestyle interventions in the current study did not show significant improvements in HRQoL at the end of the study at the total group level.

Kidney transplantation is the preferred treatment for individuals with chronic kidney disease in need of kidney replacement therapy. Although both clinical outcomes and health-related quality of life (HRQoL) improve after kidney transplantation (1), baseline levels before chronic kidney disease might not be fully restored**,** and HRQoL could decline again over time owing to multiple factors such as treatment-related side-effects, progression of comorbid conditions, and progression of the underlying kidney disease (1).

Although current guidelines recommend physical exercise and a balanced diet to improve HRQoL after kidney transplantation, they appear to be predominantly based on the benefits observed in the general population rather than specific evidence for kidney transplant recipients (2). A meta-analysis of four randomised controlled trials (RCTs) found a beneficial effect of exercise on HRQoL, specifically in people who have received a kidney transplant; however, these RCTs were associated with a risk of moderate to high bias (3). Similarly, a systematic review found that a balanced diet improved HRQoL in individuals with chronic kidney disease, but no studies were identified that specifically addressed the effects of diet in people who have received a kidney transplant (4). As such, there is a paucity of high-quality evidence to support the effect of physical exercise and a balanced diet in improving HRQoL after kidney transplantation.

In a notable effort to close this knowledge gap, Tim J. Knobbe and colleagues present the outcomes of the Active Care after Transplantation (ACT) trial in *The Lancet Healthy Longevity* (5). This multicentre RCT compared an exercise intervention and an exercise plus diet intervention to usual care in people who have received a kidney transplant in the Netherlands. The exercise intervention consisted of an exercise programme for 3 months supervised biweekly, with subsequent lifestyle coaching for 12 months. The exercise plus diet intervention consisted of an additional 15 months of dietary counselling.

The primary outcome of the RCT was the physical functioning domain of HRQoL, measured using the 36-Item Short Form Health Survey (SF-36) (6). After 3 months, the exercise intervention showed a statistically significant improvement in the primary outcome, compared to that in the control group, which was not the case for the exercise plus diet intervention. After 15 months, however, both exercise and exercise plus diet interventions no longer showed a significant improvement in the primary outcome, compared with that in the control group. Therefore, although the interventions were safe and feasible, the study remained inconclusive about the long-term effects of the exercise and exercise plus diet interventions on HRQoL in people who have received a kidney transplant.

Undoubtedly, some limitations of the ACT RCT might have impeded the identification of clear long-term effects of the studied interventions. A considerable number of study participants (i.e. 44 participants; 17 control, 9 exercise intervention, and 18 exercise + diet intervention) did not fully adhere

to the interventions, which might have diluted their effect. Poor adherence to behaviours recommended in lifestyle interventions is common, which is also reported in the Kidney Disease: Improving Global Outcomes clinical practice guideline (2). The authors identified multiple barriers to adherence, such as fear of physical movement. Further qualitative research could further elucidate such barriers to adherence and provide valuable insights for designing and implementing future interventions.

Additionally, high heterogeneity in the individual response to the interventions widened the confidence intervals. Subgroup analyses showed that this heterogeneity was partly due to the differences between male and female participants, as well as between individuals younger and older than the median sample age of 54.7 years, which aligns with previous research on differences in HRQoL after kidney transplantation (7). Thus, not everyone might benefit equally from the interventions. This disparity could partly be attributed to the fact that some individuals will already have a high HRQoL after kidney transplantation, which might not improve further regardless of the intervention effectiveness, whereas other individuals might not respond to the interventions at all.

In line with the authors' suggestion, a personalised approach to exercise and diet interventions could maximise the benefit of the interventions. To identify who could benefit from an intervention aimed at improving HRQoL, a suitable prediction model could be developed to predict HRQoL at the time of transplantation. Such a prediction model could also guide recruitment to RCTs and could be used to identify individuals who can benefit the most from interventions aimed at improving HRQoL.

Counterfactual prediction modelling can be used to personalise interventions. This modelling approach allows for causal predictions about how HRQoL might change in response to changes in predictors, which is not possible with traditional prediction modelling (8). By including both the exercise and exercise plus diet interventions as predictors, it is possible to identify who would benefit more from the exercise plus diet intervention and for whom the exercise intervention alone might suffice. Additionally, predictors such as illness perceptions (a patient's beliefs about different aspects of their disease, such as illness identity and emotional control) could help to identify key areas of focus for behavioural lifestyle interventions (9).

In conclusion, the ACT RCT identified safe and feasible exercise and diet interventions but had important limitations that need to be addressed before a definitive estimate of their benefits can be made. Future research should focus on identifying the barriers to adherence to recommended behaviours in lifestyle interventions and on developing a counterfactual prediction model that identifies which individuals would benefit from these interventions and the format in which the interventions should be implemented.

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