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A REVIEW OF THE ROLE OF EXERCISE AND FACTORS AFFECTING ITS UPTAKE FOR PEOPLE WITH CHRONIC KIDNEY DISEASE (CKD) NOT REQUIRING RENAL REPLACEMENT THERAPY

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Abstract

Chronic Kidney Disease (CKD) is a long-term progressive condition affecting 10–15% of people. The overlap of diabetes, hypertension and CKD in an aging population means that prevalence will only increase. CKD increases the risk of all-cause mortality, secondary to the elevated cardiovascular risk. It also significantly affects the patients' ability to engage in functional activities and their quality of life.

The evidence base suggests that exercise has the capacity to improve symptom burden, functional ability and mental health. The majority of the patient population are pre-dialysis yet previous research has concentrated on dialysing patients. This review will focus on the patient group not requiring renal replacement therapy (non-RRT) as this is an area where further work is urgently needed.

A large majority of people with CKD tend to be inactive despite emerging guidelines emphasising the positive effect of exercise for both people with chronic disease and healthy populations. This paper will review the evidence to support exercise to improve outcomes and quality of life and report on common barriers that patients experience and advocate the need for supported exercise interventions to help patients become more active and gain the potential resultant health benefits.

Key words: kidney disease; exercise; quality of life

Introduction

Chronic Kidney Disease (CKD) is internationally defined as evidence of kidney damage or reduced renal function for more than 3 months, with implications for health [1]. This is delineated by the evidence of pathological changes, either structurally, or by changes in appropriate blood/urine results. Renal disease is classified into 5 stages based on the estimated glomerular filtration rate (eGFR), as summarised in Table 1.

CKD is a long-term, progressive condition that affects 10% of the US population [2] and 13–14% in England [3] with no cohesive data yet published for Europe [4]. There are strong links in the pathogenesis of diabetes, hypertension and CKD [5] and the rising levels of diabetes and the aging population mean that the prevalence of CKD will only increase.

The risk of all-cause mortality increases once eGFR drops below 60 mL/min/1.73 m^2 and doubles when eGFR is between 30–45 mL/min/1.73 m [2, 6] which highlights the effect of CKD in the earlier stages. Keith [7] et al. investigated outcomes at 5 years for people with CKD 2-4 and whilst only 3.1% progressed to renal replacement therapy (RRT), 24.9% had died. These findings are in keeping with Man-

junath [8] et al. who found a 19% mortality rate at 5 year follow-up with CKD stage 3–4, but also investigated the frequency of cardiovascular events as this is one of the leading causes of mortality. 35% of the studied population suffered a cardiovascular event during the 5 year follow-up and within the subset who had previously had a cardiovascular event, 59% suffered a recurrent event. Therefore the population with non-end stage disease represent a group that warrant attention to counter cardiovascular risk and thus improve their symptom burden, disease progression and improve their quality of life.

Table1

Stages of Kidney Disease as described by National Kidney Federation Kidney Disease Outcomes Quality Initiative [1]

Stage	Description	eGFR (mL/min/1.73m^2)
1	Kidney damage but with normal or increased eGFR	≥ 90
2	Kidney damage with only mild reduced eGFR	60–89
3A	Moderately reduced eGFR	45–59
3B	Moderately reduced eGFR	30–44
4	Severely reduced eGFR	15–29
5	Kidney failure	< 15 or dialysis

An international evidence base [9, 5, 10, 11] is developing to support exercise in the management of CKD to contribute to these aims, however the majority of CKD patients remain insufficiently active to gain the health benefits of exercise [12]. Exercise can be beneficial to improve the secondary effects of CKD which patients often find reduce their quality of life. These factors include the elevated cardiovascular risk, fatigue, muscle atrophy and bone density loss, all of which can result in reduced activity levels and increased prevalence of mental health problems.

This article will focus on the group of patients with CKD but not requiring renal replacement therapy (non-RRT) as these represent a discrete population, who due to the earlier stage of their disease have fewer co-morbidities and are not yet living with the effects, both physical and social, of regular dialysis or transplant. As renal disease progresses so do the concomitant co-morbidities, thus the earlier a health promotion intervention is made, the easier it is to break the cycle, where each co-morbidity fuels the progression of the others. Exercise represents a clinically and cost effective intervention that empowers the patient, but the treatment effects will only be maintained if the person is engaged and values the benefits to the extent that the effort, time and motivation of engaging in the activity are perceived as worthwhile. Thus any exercise intervention must clearly delineate these benefits and this review will discuss the merits of exercise in CKD from this perspective.

What is exercise?

Physical activity has been defined as any bodily movement using skeletal muscles that burns energy [13] whilst exercise is defined as a category of physical activity that is planned, structured, repetitive and aims to improve or maintain physical fitness [13]. These terms are often used interchangeably in the literature, but the difference between physical activity and exercise should be appreciated. Being physiccally active can be very beneficial but in order to gain the cardiovascular health benefits it is important that exercise is effective and produces an effect on the cardiac and pulmonary systems.

What are the current guidelines?

Cohesive European guidelines for the provision of exercise in CKD do not yet exist. In the UK, national standards recommend exercise but lack detail regarding the dose needed for beneficial effects, i.e. frequency, intensity or duration, due to a paucity of evidence [14, 15]. The UK Renal Association guidelines [16] recommend that people with CKD should exercise 3–5 times per week, but again there is a dearth of detail regarding intensity and duration. Smith & Burton [17] have recently suggested patient centred recommendations for both aerobic and resistance exercises, detailing frequency, duration and intensity in patient-appropriate language, aiming for 3–4 bouts of 30 minute aerobic exercise and 2–3 sessions of resistance exercise per week.

The Swedish National Institute of Public Health [18] gave more detailed recommendations (see **Table 2**) however this amount of exercise may appear daunting to the sedentary CKD patient population. Exercise and Sports Science Australia issued a position statement [19] advocating 30–45 minute sessions 4–6 times per week of aerobic exercise (RPE 11–16; 55–90% max HR) and 2 resistance sessions (60–70% 1-RM), which again may appear intimidating to a person with a sedentary lifestyle and a chronic condition.

Table 2

Recommendations for activity levels in people with CKD from Swedish National Institute of Public Health [19]

Type of exercise	**Intensity**	**Frequency** (times per week)	**Duration**
Aerobic	70% of VO_2 max	3	60 mins
Strength training	80% of 1RM	3	1–2 sets of 8–10 reps
Endurance	50% of 1RM	3	Max number of reps RPE13–15
Functional training i.e. walking, balance & co-ordination training	–	3	max walking duration & max reps other exercises RPE 13–15

Kosmadakis [20] et al demonstrated that positive results could be achieved with less exercise than these publications advise and the recent Heiwe & Jacobsen [21] meta-analysis recommend three > 30 minute exercise sessions to improve aerobic capacity, survival, strength and quality of life, although the caveat is given that the evidence to support this needs further development.

Thus an emerging consensus is evolving based on the best levels of evidence currently available but consistent European guidelines are not yet available.

What are the health benefits of exercise in CKD?

A Cochrane review of the effects of exercise training in chronic kidney disease demonstrated that exercise is an effective method, both clinically and in terms of cost, to improve the effects of this disease [5]. However much of this research was conducted in the dialysing population. Johansen & Painter [22] reviewed the research regarding exercise specifically in predialysis CKD and found a limited evidence base but could identify positive trends towards improved physical functioning for patients when the level of physical activity increased. A subsequent meta-analysis [21] investigated the research regarding exercise in CKD, separated into pre-RRT patients, RRT patients and transplant patients and concluded there was a dearth of good quality research investigating pre-RRT patients.

One of the most vital effects of exercise is the reduction of cardiovascular risk, as this is a major cause of mortality in this patient group [8]. Heiwe & Jacobsen demonstrated in the Cochrane review [5] and in their 2014 meta-analysis [21] that increasing physical exercise levels resulted in reduction in both diastolic and systolic resting blood pressure. Our own group published findings [20] from a 6 month regular walking program (30 mins, 5 times per week, using Rate of Perceived Exertion to guide intensity) with patients with CKD 4–5 not requiring RRT. Improvement gained from the exercise program included increased exercise tolerance, weight loss, improved cardiovascular reactivity, avoidance of an increase in hypertension medication and improved quality of life scores, thus the wide-ranging positive effects of exercise are illustrated.

The control of the primary factors that mediate disease progression, such as hypertension

(HTN) and diabetes mellitus (DM) is another important issue. The research into the effects in CKD and DM remain unclear and the Cochrane review found no improvement in fasting plasma glucose, fasting plasma insulin or glucose disappearance. However Yates [23] et al. did show improvements in glucose control in overweight or obese diabetic patients after 12 months of an exercise intervention, which suggests that if positive results can be achieved in patients with DM, further work is required to analyse the effects in those patients with CKD secondary to DM.

Johansen [24] et al. surveyed patients just commencing on dialysis and found that those engaging in regular exercise had fewer co-morbidities, lower BMI and fewer mental health issues, which illustrates the positive effects for this group of being more active. Beddhu [25] et al. demonstrated that mortality rates were reduced in CKD patients who had higher leisure time physical activity scores which suggests that keeping active may be the key to maintaining health.

How does increasing exercise affect functional ability?

The Cochrane review [5] evaluated 24 studies that investigated the effect of physical exercise training on aerobic capacity and found a significant causal relationship, which was confirmed in their subsequent meta-analysis [21]. The effect of this increase in aerobic capacity on functional ability is less well understood as much fewer studies have investigated this link. However, seven of the reviewed papers demonstrated an improved walking capacity with an exercise intervention, one paper evaluated stair climbing capacity, whilst three investigated capacity to engage in activities of daily living (ADL), but found no significant difference. The Cochrane review [5] sampled all stages of CKD and hence this limits the applicability of the findings to the specific pre-dialysis population, but when evaluating a health-related quality of life outcome measure, the majority of the data produced a positive result, which is an encouraging trend.

The Kosmadakis [20] et al. study demonstrated that a six-month walking program yielded improvements in exercise tolerance and equivalent improvements in a health related quality of life questionnaire. The effect of exercise to increase muscle strength in CKD is not yet fully understood and the Cochrane review of exercise found that results in strength training were at best equivocal. Kosmadakis [20] et al. demonstrated a trend towards increasing muscle mass, but no statistically significant difference and this correlates with the Cochrane review recommendation that further research should focus on combining resistance training with aerobic training.

Fatigue is a frequently cited symptom in CKD [26, 27] and exercise has been demonstrated to produce positive results in other chronic conditions. A Cochrane review in cancer-related fatigue [28] demonstrated that exercise was an effective intervention to reduce fatigue intensity, which suggests the possibility of improving the effects of this debilitating symptom with carefully prescribed exercise interventions. The interplay between depression and fatigue must not be underestimated and depression is thought to reduce the person's ability to cope with the symptom burden of chronic disease [29], which will continue the downward spiral of symptoms. This can only result in reduced quality of life for the patient and their family.

How does exercise affect mental health in CKD?

Chiang[30] et al. investigated the prevalence of depression in people with CKD and found that age-standardised depression prevalence was 20.6% in the Taiwanese CKD population. This correlates with the findings of a meta-analysis by Palmer [31] et al. of 23% in dialysing patients and 21% in CKD4-5. This compares with a normal prevalence in 7% for depressive disorders in an adult population [32]. After conducting uni-variate analysis Chiang [30] et al. found a higher occurrence of depression among the group that did not exercise regularly and an increasing prevalence with disease stage. However these findings must be interpreted with care as the multi-factorial nature of mental health conditions means that findings from one culture may not be directly transposed onto another. This data did not differentiate between stages of CKD hence caution

must be used when applying the data to the pre-dialysis population, however Chiang et al. specify that 106 of the 268 participants were in stage 3 or below and means this data may be cautiously interpreted. Abdel-Kader [33] et al. compared prevalence of depression between CKD4-5 and End Stage Renal Disease (ESRD) and found no differences, which suggests that findings from one group could be extrapolated to another, however the exclusion criteria of the study meant that the ESRD group had fewer co-morbidities than a usual dialysis patient group, which might explain this non-intuitive finding.

Pop-Jordanova & Polenakovic [34] investigated the prevalence of depression in the dialysis patients in Republic of Macedonia and found significantly increased occurrence compared to the rest of the population. They also found that the prevalence correlated with number of years of dialysis, age and educational level. This paper found an exceedingly high prevalence rate (90.63%) compared to that seen in other fields/research and it must be considered that a measuring error may have occurred, especially when some of the symptoms of depression, e.g. fatigue and appetite suppression, may occur as a direct result of the CKD [29]. The Palmer [31] et al. meta-analysis found similar significant variability in measuring rates, varying from 1% to 95%, which they felt was due to different diagnostic threshold values and to the cross-over of somatic symptoms between CKD and depression.

The Cochrane review [5] reviewed the evidence regarding the effect of exercise to improve the level of depression in CKD. The data was found to be heterogeneous and deemed not appropriate for meta-analysis, but recommended a program of between 3 and 10 weeks of supervised mixed cardio-vascular and resistance exercise to reduce the symptoms of depression. This recommendation was made with the caveat that further research was necessary before more detailed recommendations could be made. Although the evidence reviewed by Heiwe & Jacobsen gave a mixed picture of results, when this is considered with the tentative findings of Chiang [30] et al., this represents an area worth further investigation.

Cardiac rehabilitation, an exercise intervention, has demonstrated significant reductions in anxiety and depression levels in Coronary Heart Disease (CHD) patients [35, 36]. A reduction in anxiety prevalence among people with CHD from 13% to 8% and reductions in depression prevalence from 26% to 9% was demonstrated. It is suggested that similar positive results may be achievable in CKD with an equivalent exercise and education intervenetion. Exercise is a treatment administered by the patient and hence has a significant role in the empowerment of the patient, which in itself improves the patients' feelings of control and allows them to more actively engage in their treatment.

An educational programme [37], which included a session on the value of exercise, demonstrated that by improving anxiety levels in a dialysing population, the patient recorded measures of symptom frequency and severity also decreased. The patient group also reported improved quality of life scores. Although this research was conducted amongst Swedish patients as they started dialysis, it supports the suggestion that a programme of exercise, supported by an educational element has the capacity to significantly improved quality of life for this patient group.

Putting this into practice

Take-up of exercise among people with CKD is poor and Goodman & Ballou [38] found that 52% of patients reported not doing even any mild exercise, whilst Delgado & Johansen [39] found that only 17 of 100 participants with CKD followed the American College of Sports Medicine (ACSM) guidelines[40] of >150 minutes of moderate physical activity per week. Both of these pieces of research were conducted with US patients receiving dialysis and thus it must be considered that there may be differences in other national populations and to people in earlier stages of CKD. Hull [12] et al. surveyed > 500 people with CKD not requiring RRT and found that 80% were not achieving the activity levels advised by clinicians, thus the same problem can be seen in earlier disease stages.

Johansen [24] et al. measured the self-reported activity levels of 1547 individuals new to dialysis and found that male activity levels were below the 25th percentile levels of healthy

men, whilst the female activity levels were less than the equivalent 1st percentile. This demonstrates that significant losses have already been made to physical functioning when patients commence dialysis and suggests that an exercise intervention earlier in the disease process would have merit.

A significant part of this problem is the patchy availability of services to facilitate exercise for this population. However we must also acknowledge the low levels of patients' physical activity and seek to understand the barriers to engagement that exist for these people. It is only by clearly understanding the problem from the person's perspective that we can hope to encourage participation in physical activity.

What affects people's ability or willingness to engage in exercise?

Potential barriers to exercise in CKD in the UK were postulated by Smith & Burton [41] to fall into three main categories; those experienced by the population as a whole (especially social issues i.e. time, cost, family commitments, lack of motivation, fatigue, preconception that exercise is unpleasant); those experienced by anybody with a chronic health condition (risk of increasing symptoms, belief that sick people should be resting) and barriers specifically related to renal disease (anaemia, muscle fatigue and increased pain). Goodman & Ballou [38] investigated the barriers and motivators to exercise in US haemodialysis patients, as shown in Table 3.

Table 3

Barriers and motivators in US haemodialysis patients as described by Goodman & Ballou [38]

Barriers	Lack of motivation Lack of interest Fear of falling Lack of access to exercise facilities
Motivators	Belief in one's ability to be physically active Wanting to feel better Wanting to have decreased anxiety Having less pain High expectations from family and/or friends Feeling healthy Knowing the value of increased exercise Enjoying how exercise feels

Several of these factors could be perceived as overlapping, for example "lack of motivation" and "lack of interest" and "wanting to feel better" and "wanting to have decreased anxiety". Some of the statements encompass both physiological and psychological meanings e.g. "feeling healthy" and hence the respondents could rate the statement differently depending on how they interpret the statement. This ambiguity may be a source of error in the data.

Similar research[39] was conducted in the US in 2012 and 98% of respondents to a questionnaire felt a sedentary lifestyle represented a health risk and that increasing exercise was beneficial. An interesting approach used during this piece of research was that they quantified how many barriers applied to each participant, demonstrating the multi-factorial nature of the problems patients encounter when engaging in exercise. More than 20% of participants endorsed eleven or more barriers. The most commonly described barriers were fatigue, dyspnoea, lack of motivation, pain, lack of time on dialysis days, co-morbidities and fear of injury.

In China, Zheng [11] et al. published the Dialysis Patient Perceived Exercise Barriers and Benefits Scale questionnaire (DPEBBS) to assess patient perceived benefits and barriers looking at 24 aspects of exercise behaviour. The factors affecting attitudes to exercise are shown in the following Figure 1. However much of this tool was specifically designed to understand the perspective of the dialysing population and hence the data loses significant validity when considering pre-dialysis people. Cultural differences between the Chinese and European populations must be appreciated and these findings must be used cautiously when considering the European pre-dialysis population.

All the data discussed above relates to dialysing patients, however emerging themes can be seen from this international data. As yet unpublished data from our group has investigated patient perceptions regarding exercise in pre-RRT CKD and found barriers to exercise included concerns regarding other co-morbidities, frailty, fear of injury, fatigue and reduced motivation [26] and thus it can be seen that there are common themes between stages of CKD.

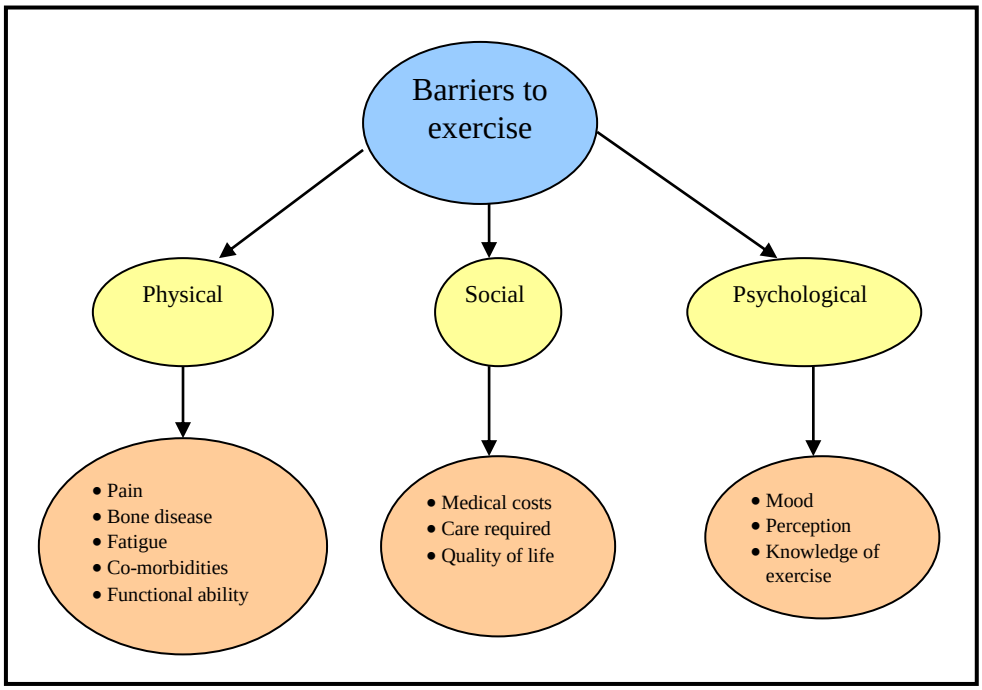


Figure 1 – Barriers to exercise in Chinese Haemodialysis as described by Zheng [11] et al.

This data demonstrates that the value of physical activity to improve health and quality of life in CKD cannot be underestimated and as Health Care professionals we need to change our culture so that physical activity levels are discussed at every consultation. Patient engagement is key and so the conversation should include the benefits of being more active and encouraging patients to set appropriate goals using enjoyable and functionally important activities. Assisting patients to identify barriers and mechanisms to conquer these stumbling blocks are also important topics to discuss, whilst emphasising that exercise should be moderate, regular and sustainable and that any small increase is a positive step.

Conclusion

This review has demonstrated that CKD is a growing global problem that comprises primary and secondary problems that affect the person's physical and mental health and their ability to engage in functional activities. Exercise has been demonstrated to be a clinically and cost effective intervention to improve these problems, however physical activity levels in the patient population remain inadequate.

Factors that may positively influence people with CKD to engage in more physical activity vary for each individual, but emerging themes occur in the literature. These include health benefits, improved functional ability based on improved aerobic capacity and improved mental health. The evidence to support the role of exercise to achieve improvements on each of these issues has been reviewed. There is a lack of direct evidence that has focussed on the pre-dialysis patient group, but trends can be seen in dialysis research and in other chronic illness groups that suggest the potential for positive results.

As Health Care Professionals we need to understand the patient's perspective to facilitate their engagement in exercise and reap the potential manifold benefits of increasing the activity levels of this group.

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Резиме

ПРЕГЛЕД НА УЛОГАТА НА ВЕЖБАЊЕТО И ФАКТОРИТЕ ШТО ВЛИЈААТ НА НЕГОВАТА ПРИМЕНА КАЈ ЛИЦА СО ХРОНИЧНА БУБРЕЖНА БОЛЕСТ (ХББ) ЗА КОИ НЕ Е ПОТРЕБНА БУБРЕЖНА ЗАМЕНСКА ТЕРАПИЈА

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Хроничната бубрежна болест (ХББ) е долгорочна прогресивна состојба која зафаќа 10–15% од населението. Совпаѓањето на дијабетесот, хипертензијата и ХББ кај населението што старее значи дека преваленцијата само ќе се зголемува. ХББ го зголемува ризикот за сите причини за смртност, секундарно во однос на покачениот кардиоваскуларен ризик. Таа, исто така, значително влијае на способноста на пациентите да се вклучат во функционалните активности и нивниот квалитет на животот.

Базата на докази укажува дека вежбањето има капацитет да ги подобри симптомите на оптоварување, функционална способност и ментално здравје. Поголемиот дел од популацијата на пациенти се во преддијализна состојба уште пред истражувањето да се концентрира на пациентите на дијализа. Овој преглед ќе се фокусира на групата пациенти за кои не е потребна бубрежна заменска терапија (не-БЗТ), бидејќи ова е област за која е итно потребна понатамошна работа.

Голем дел од луѓето со ХББ имаат тенденција да бидат неактивни и покрај новите насоки што го истакнуваат позитивниот ефект од вежбањето и за луѓето со хронични болести и за здравата популација. Овој труд ќе ги разгледа податоците за поддршка на вежбањето со цел да

се подобрат резултатите и квалитетот на животот и извештајот за заедничките бариери што ги доживуваат пациентите и да се поддржат во потребата од интервенции за вежбање за да им се помогне на пациентите да станат поактивни и да се здобијат со потенцијални здравствени придобивки што произлегуваат од тоа.

Клучни зборови: болести на бубрезите, вежбање, квалитет на животот.