Review Article

Chronic kidney disease and sports participation by children and adolescents

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Abstract: Individuals suffering from chronic kidney disease (CKD) deal with major morbidity and mortality including poor exercise tolerance. A variety of factors including anemia, poor muscle mass, cardiovascular changes and limited physical activity contribute to exercise intolerance. Studies suggest that early initiation of aerobic and resistance training improves the muscle function, ability to tolerate exercise and quality of life in CKD patients. A thorough medical examination and exercise testing are recommended before initiating an exercise regimen in individuals with CKD. Though current recommendations suggest a qualified approval to contact sports in patients with solitary kidney, a proper risk assessment and counselling must be provided detailing all the risks involved. Special care must be taken to avoid infection or damage to the peritoneal dialysis catheter and hemodialysis vascular access sites. Collision sports should be avoided in individuals with kidney transplant, ectopic kidney or with other urological abnormalities (severe hydronephrosis or ureteropelvic junction obstruction) with high risk of injury.

Keywords: Chronic kidney disease (CKD); glomerular filtration rate (GFR); aerobic exercise; resistance exercise; solitary kidney; hemodialysis; peritoneal dialysis; kidney transplant; exercise prescription; contact sports

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Introduction

Chronic kidney disease (CKD) is a public health issue with increasing prevalence with each passing year affecting about 12 to 14 % of the population in USA (1,2). The epidemiological information on CKD is mainly obtained from the adult end stage renal disease (ESRD) data (3). As most renal diseases remain silent especially in the initial stages, the reported incidence and prevalence may be an underestimation. Based on the report from United States Renal data system (USRDS) there were about 661,648 prevalent cases of ESRD with about 21,000 new reported cases every year (4). The unadjusted incidence rate was 363 per million/year with a prevalence of 2034 per million in the U.S population. The projected prevalence is close to 20 million for all stages of CKD. There were 17,600 kidney transplants, in USA, in 2013 with about 86,695 candidates in the transplant waiting list (4).

The exact prevalence of childhood CKD is not known, but it is estimated at 82 cases per million and about 15 ESRD cases per million based on data from various national registries (5-7). Though pediatric ESRD contributes to only about 2% of the total ESRD burden, the mortality rate in adolescents is about 30% to 150% higher than in the general population (6,8). The expected remaining life time for an adolescent under 14 years on dialysis is only 20 years indicating the need for specialized care in this population (6,8).

Definition

CKD is a heterogeneous group of disorders with altered structure and function of the kidneys. The clinical manifestations vary widely based on the underlying etiology with acute and life threatening presentation such as rapidly progressive glomerulonephritis to the more chronic insidious loss of renal function as seen with diabetes and hypertension. Based on kidney disease: improving global outcomes (KDIGO) guidelines, CKD is classified into 5 stages taking into account the quantitative loss in glomerular filtration rate (GFR) and the degree of albuminuria (9). The progression on CKD from stage 1 to stage 5 is based on renal function. GFR is the most widely used measure to assess renal function. According to the KDIGO 2012 clinical practice guidelines a GFR of 90 mL/min/1.73 m^2 indicate a normal or high renal function (stage 1); whereas, a GFR of less than 15 mL/min/1.73 m^2 indicates renal failure (stage 5) (9). Persistent albuminuria is generally categorized as, normal (less than 30 mg/g); moderately increased (30–300 mg/g); and, severely increased (more than 300 mg/g) (9). A definition of CKD to include morphological abnormalities and duration of kidney disease has been proposed by the National Kidney foundation (NKF) that includes the following criteria (10,11):

(I) Kidney damage for ≥ three months, as defined by either structural or functional abnormalities of the kidney, with or without decreased GFR. Such kidney damage can manifest as, pathological abnormalities; or markers of kidney damage, including abnormalities of the blood or urine, or abnormalities in imaging tests;

(II) GFR of less than 60 mL/min/1.73 m^2 for ≥3 months, with or without kidney damage.

The calculation of GFR is based on serum creatinine levels. Serum creatinine levels is influenced by muscle mass and can be falsely low in advanced stages of CKD due to tubular secretion and hence overestimating GFR. Despite the limitations, serum creatinine remains a widely used marker to calculate GFR, though newer markers such as cystatin C has been gaining more popularity. The Ckid (CKD in children) study came up with a modified Schwartz formula to calculate GFR using creatinine and is defined as eGFR =0.413 × height in centimeter/serum creatinine (12). The GFR varies with gender, age, body size and increases from infancy to adulthood. Normative data varies widely with age (13). For instance, in a new born infant, the GFR at birth is between to 25 to 50 mL/min/1.73 m^2 and increases up to normal adult value of > 90 mL/min/1.73 m^2 by around 2 years of age (13). This age based changes in GFR need to be taken into account when staging for CKD in younger children.

The term physical fitness encompasses several basic tenets. These include an individual's ability to perform daily functions with sufficient energy, alertness, and without undue fatigue (14). Physical activity is differentiated from physical fitness as a concept. Physical activity is associated with contractions of muscles, movement of body, and an increased utilization of energy above individual's basal level (14). The concept of exercise or exercise training differs from those of physical fitness and physical activity. Exercise involves physical activity; however, it is further qualified by the fact that exercise is a structured, planned, and purposeful activity that is performed on a regular basis over a long time.

Etiology

The etiology of ESRD varies with age. Hypertension and diabetes mellitus are common causes for CKD in adults. In children, the causative factors are different. Based on data from the North American Pediatric Renal Trial and Collaborative Studies (NAPRTCS) structural anomalies such as renal aplasia/dysplasia/hypoplasia contribute the majority of ESRD in younger children while glomerular diseases such as FSGS predominate in older children (15).

Renal physiology in CKD related to exercise

Renal blood flow (RBF) reduces during exercise with the magnitude of decrease directly proportional to the intensity of physical activity (16-19). The degree of intravascular hydration can affect the changes in RBF with more decline noted in a dehydrated state when compared to an initial hyper hydrated status (20-22). During exercise, there is a preferential shunting of blood to the exercising skeletal muscles explaining the decline in RBF. There is a small increase in the GFR initially, followed by a decline especially with increased exercise intensity. The levels of intrarenal paracrine hormones such as renin, angiotensin, prostaglandins and other modulators of salt and water excretion such as atrial natriuretic peptide all increase proportionally with the intensity of exercise affecting renal tubular function to achieve electrolyte and volume homeostasis.

Exercise tolerance in CKD

Maximal oxygen uptake (VO_{2max}) is an accepted measure for aerobic and cardiovascular fitness and is defined as the greatest amount of oxygen consumed during exercise (23). It is conveyed in milliliters of oxygen consumed per kilogram of body weight per minute. Patients with CKD tend to have a lower VO_{2max} when compared to the general population. Exercise capacity and tolerance are much lower in children with advanced stages of CKD and those getting renal replacement therapy, such as dialysis or kidney transplant (24,25). The reason for low exercise tolerance in CKD is multifold and includes anemia, cardiac function alterations, skeletal muscle changes and physical inactivity.

Anemia

CKD causes progressive loss of nephrons leading to decreased erythropoietin production and chronic anemia. Chronic anemia decreases oxygen carrying capacity of the blood and hence a lower $VO_{2max.}$ (26). The availability of recombinant erythropoietin has reduced the need for chronic blood transfusions for anemia in patients with CKD. The VO_{2max} in adolescents with CKD remain low when compared to healthy adolescents, even after correcting for anemia, suggesting there are multiple contributory factors to exercise intolerance in CKD (27).

Cardiac alterations in CKD

Cardiovascular disease contributes to majority of morbidity and mortality in CKD. Hypertension and coronary vascular disease contribute to the majority of cardiovascular changes. Definitive increase in left ventricular mass index (LVMI), an indicator of cardiovascular strain is noted in adolescents with CKD when compared to healthy population. This increase in LVMI was more prominent in children on dialysis than those on predialysis ESRD (28). The indices for diastolic dysfunction and left ventricular compliance were comparatively much worse in CKD patients than that of controls. The elevated ventricular mass and sympathetic activity contribute to the diastolic failure, both in children and in adults with CKD (29,30). The alterations in cardiac structure and function occur early in course of CKD and is associated with a declining exercise tolerance (31).

Alterations in skeletal muscles

Multiple studies have documented early stopping of exercise in CKD due to muscle fatigue (32-34). Skeletal muscle wasting in CKD occurs due to a multitude of factors including poor nutrition, increased catabolic state, loss of protein especially with peritoneal dialysis and physical inactivity. Patients with advanced stages of CKD are usually placed on protein restriction to prolong kidney life, but this leads to decreased muscle protein synthesis. In addition, the proinflammatory state of CKD along with the increased catabolic state and resistance to anabolic factors such as insulin and growth hormone, leads to muscle wasting (34-36).

Experimental studies of physical performance (six-minute walk distance and gait speed) have shown children on peritoneal dialysis to do poorly when compared to their healthy controls. Increased fat deposition in muscles and reduced quadriceps strength is documented in children with CKD when compared to their healthy peers (37). Chronic muscle wasting, decreased muscle protein synthesis and physical inactivity constitutes a vicious loop which contributes to further muscle atrophy and poor exercise tolerance in CKD.

Physical inactivity

Physical inactivity and restricted daily activities causes muscle atrophy and exercise intolerance. Physical inactivity and restriction even for a limited period of time for three weeks has shown to reduce VO_{2max} by 26% (38).

Adaptations with physical activity in CKD

Most studies that have looked at the effects of exercise in individuals with CKD predominantly include alteration of maximal oxygen uptake related to regular aerobic exercise. Studies have included different exercise programs. These include outpatient supervised aerobic exercises during non-dialysis days, and cycling during hemodialysis in outpatient non-supervised setting or inpatient setting (39-41). An increase in oxygen uptake between 20% and 40% following exercise training has been reported across studies. Studies in children and adolescents also have shown improvement in oxygen uptake and exercise performance following a regimen of 2 sessions per week of exercise during hemodialysis (42).

While there are more studies related to aerobic exercises, relatively few studies have looked at the effects of resistance training in patients with CKD, especially in children and adolescents (43,44). One randomized controlled trial of

26 adults with advanced CKD not on dialysis regimen reported improvement in strength and muscle mass following resistance training (45). The study showed that, following resistance training, there was a reduction in catabolic activity of muscle that is otherwise seen because of dietary protein restriction and increase protein loss in patients with CKD (45). Headley *et al.* looked at the effect of 12 weeks of resistance training in patients with CKD who were on hemodialysis (44). Their findings showed an improvement in muscle strength and endurance. Regular resistance exercises improve muscle strength, exercise tolerance and slow down muscle wasting in CKD.

Cardiac adaptation with exercise training in CKD

Aerobic exercise positively affects the structural and functional alterations in left ventricle (46). In one study, a regimen of aerobic exercise training of 3 times per week in an outpatient supervised setting for 6 months the investigators reported improvement in cardiac systolic function. The improvement in cardiac systolic function was indicated by an increase in the ejection fraction, stroke volume and cardiac output (46). An improvement in myocardial contractility was indicated by echocardiographic findings of an increase in left ventricular end diastolic dimension and a decrease in end diastolic volume. In addition, there was an increase in left ventricular posterior wall and interventricular septum thickness. In a different aerobic exercise regimen of 30 minutes per day, 3 days per week, for 3 months, an improvement in left ventricular ejection fraction and a decline in pulmonary artery and systemic vascular resistance were reported (43).

Skeletal muscle adaptation with exercise training in CKD

Regular resistance training by patients with CKD has been shown to improve muscle strength, endurance and exercise tolerance. In one study, a 6-month of resistance training by CKD patients on hemodialysis reported improvement in skeletal muscle function and structure (47). Skeletal muscle function improvement was assessed based on muscle biopsy, that showed an increase in muscle fiber cross sectional area, new muscle fiber formations, and regeneration of previously degenerated muscle fibers (47). Study also showed that resistance training contributed to an increase in maximal oxygen carrying capacity and exercise tolerance in patients with CKD (48).

Effects of exercise on quality of life

Health related quality of life (HRQoL) is a commonly used instrument to measure various parameters of quality of life. These parameters include physical functioning (self-care, daily activities, employment), emotional health (anxiety, depression, hostility), and social functioning. Patients with CKD have reported severe limitations of daily activities as well as emotional difficulties including depression, anxiety, irrational fear, getting easily irritable, and mood swings (49). Studies in adults with CKD have shown positive effects of exercise on physical and emotional aspects of quality of life, and ability to continue to work and pursue academics (50-52).

Physical activity recommendations in CKD

Prior to initiating an exercise program, a thorough medical examination and response to exercise training should be assessed. Exercise programs should include both aerobic and resistance training and should individualized based on personal goals, circumstances, and needs.

General principles of exercise, such as proper warm-up and cool down should be followed. The exercise program should progress gradually from low to high intensity and from short to longer durations. Persons who are on continuous ambulatory peritoneal dialysis should exercise with fluid in the abdomen, unless the person is not able to tolerate exercising with fluid in the abdomen (17,23). Persons who are on hemodialysis can engage in exercise while on dialysis or on non-dialysis days (23). To avoid a fall in systemic blood pressure, exercise during the first half of a dialysis session is preferred (23). The individual can exercise the arm with the vascular access, as long as the weight is not directly borne on the access site itself (17). Because the heart rate response to exercise is not a reliable indicator for exercise intensity in persons on hemodialysis, the Rate of Perceived Exertion is a preferred measure (23). Persons who have a transplanted kidney should reduce intensity of exercise during a period of rejection (23).

The exercise prescription for persons with CKD is based on the same principles as health children and adults. The parameters included in the prescription are frequency, intensity, duration and type of physical activity. According to the American College of Sports Medicine guidelines, aerobic exercise should be done 3-days per week, at a moderate intensity (23). The moderate intensity is defined as an activity done at 40% to 59% of individual's oxygen uptake reserve or a rate of perceived exertion of 11–13 on a scale of 6–20 (23). Each exercise session should be a continuous exercise for 20–60 minutes' duration; however, shorter periods of exercise can be cumulated for a total of 20–60 minutes.

Resistance training should be done 2 days per week. There should be an interval of 48 hours between sessions for resistance training for the same muscle groups (23). In a given session, 8–10 different major muscle groups should be included (23). The modality, either free weights or machine, will depend on individual preference. The intensity for resistance training should be at 60–75% of one repetition maximum for the individual (23). Generally, one set of 10 to 15 repetitions is preferred depending up on persons exercise tolerance.

The usual adverse events associated with exercise in an unconditioned individual are injuries to the musculoskeletal and cardiovascular system. Most data on risks associated with exercise have been derived from studies done in healthy adults who are engaged in regular high intensity exercise (53,54). Bone and metabolic disorder is a known complication of CKD manifested by decrease in bone density, vitamin D deficiency and secondary hyperparathyroidism. The bone disorder of CKD places these children at risk for fracturing bones and for a prolonged recovery phase after a skeletal injury.

The risk of adverse events from exercise is relatively higher in adults with other chronic diseases. Adults with CKD are most likely to also have diabetes mellitus, hypertension and obesity that increase their risk for exercise-related adverse events (55,56). This requires a careful screening and evaluation prior to structuring an exercise program of adults with CKD and associated other chronic diseases. Studies show that once appropriate level of physical conditioning is attained, progressively increased exercise intensity tend to pose relatively less risk (55,56).

Renal trauma directly resulting from sport participation is infrequent. Most such injuries have been reported in contact or collision sports. Though there has been a lot of debate and concerns over the participation in contact sports by children and adolescents with a solitary kidney, the current recommendations favor allowing participation after a thorough patient and family education about potential risks to the solitary kidney (57-60). This recommendation also extends for those with CKD, and those receiving dialysis therapy (60). In case of a transplanted kidney, the kidney is placed in the extra peritoneal space in the abdomen and thereby is at a relatively higher risk for injury when compared to native solitary kidney. In these cased contact or collision sports are not recommended. Most cased of severe kidney trauma related to sport participation that require surgical removal of the injured kidney have been reported in sledding, skiing and rollerblading (61). Although, participation in American football has been associated with a relatively higher rate of renal trauma, most such injuries are of low grade. On the other hand, most sever renal trauma has been reported from motor vehicle crashes and bicycle accidents. Bicycle riding is a common cause of blunt renal trauma (62).

Contact or collision sports should be avoided by persons with ectopic location of the solitary kidney (pelvic or iliac) or in the presence of multicystic dysplastic kidneys, moderate to severe hydronephrosis or other ureteropelvic junction abnormalities (57,59). Though renal transplant patients have successfully enrolled and excelled in many national and international sport events including track and field, swimming, table tennis, tennis, badminton, bowling, volleyball, golf, bicycling, and road races, the current recommendation suggest to avoid collision sports. Though risk for peritoneal dialysis catheter exit site contamination in children and adolescents who participate in swimming is a valid concern, the risk is found to be minimal with proper dressing and caring for the catheter (63). Likewise, with proper protection of the vascular access site and arterio-venous fistula in hemodialysis patient will reduce risk for contamination and inadvertent injury with sports (64).

Conclusions

Patients with CKD are at risk for poor exercise tolerance secondary to a multitude of factors including anemia, changes in cardio vascular morphology and function, alterations in skeletal muscle and physical inactivity. The poor exercise tolerance leads to a vicious cycle of more physical inactivity, which on its own contributes to deconditioning, muscle atrophy causing difficulty in engaging day to day activities and affecting the overall quality of life. A thorough medical examination and response to stress testing are suggested before initiating any exercise regimen. Exercise regimens should include a combination of aerobic and resistance training for maximal benefit. Aerobic exercises such as cycling, jogging, running or walking at moderate intensity for three to five days a week to begin with is recommended. Resistance training using free weights, resistance bands or machines are recommended for two to three days a week with initiation at low to moderate intensity with gradual stepwise increase in intensity to allow for physiological body conditioning. Although the risks of high grade renal injury in contact or collision sports remain minimal for individuals with single kidney, there remains no consensus recommendation. Individuals with solitary kidney should be given a qualified approval to participate in contact sports after proper explanation of all the potential risks involved including the need for renal replacement therapy if severe injury occurs to the functioning single kidney.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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