Clinical Kidney Journal, 2018, vol. 11, no. 6, 822–831

doi: 10.1093/ckj/sfy054
Advance Access Publication Date: 16 July 2018
CKJ Review

CKJ REVIEW

Chronic kidney disease: considerations for monitoring skeletal muscle health and prescribing resistance exercise

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ABSTRACT

Skeletal muscle wasting has gained interest as a primary consequence of chronic kidney disease (CKD) due to the relationship between skeletal muscle mass, mortality and major adverse cardiovascular events in this population. The combination of reductions in physical function, skeletal muscle performance and skeletal muscle mass places individuals with CKD at greater risk of sarcopenia. Therefore the monitoring of skeletal muscle composition and function may provide clinical insight into disease progression. Dual-energy X-ray absorptiometry and bioelectrical impedance analysis are frequently used to estimate body composition in people with CKD within clinical research environments, however, their translation into clinical practice has been limited. Proxy measures of skeletal muscle quality can be obtained using diagnostic ultrasound, providing a cost-effective and accessible imaging modality to aid further clinical research regarding changes in muscle composition. Clinicians and practitioners should evaluate the strengths and limitations of the available technology to determine which devices are most appropriate given their respective circumstances. Progressive resistance exercise has been shown to improve skeletal muscle hypertrophy of the lower extremities, muscular strength and health-related quality of life in end-stage renal disease, with limited evidence available in CKD predialysis. Fundamental principles (i.e. specificity, overload, variation, reversibility, individuality) can be used in the development of more advanced programs focused on improving specific neuromuscular and functional outcomes. Future research is needed to determine the applicability of skeletal muscle monitoring in clinical settings and the feasibility and efficacy of more advanced resistance exercise approaches in those with CKD predialysis.

Keywords: CKD, exercise, pre-dialysis, resistance training, ultrasonography

Received: 5.4.2018; Editorial decision: 26.5.2018

INTRODUCTION

Chronic kidney disease (CKD) is a major health concern highlighted by the reported increased risks of mortality and comorbidities [1, 2]. Worldwide it is estimated that 10–15% of the general population is affected by CKD [1]. Mounting evidence shows loss of skeletal muscle mass and decrements in skeletal muscle performance as primary consequences of CKD [3–6]. The implications of skeletal muscle atrophy associated with CKD include increased risk for adverse cardiovascular events [7], dysregulation of glucose homeostasis [8], decreased force-generating capacity [9] and reductions in physical function and balance [10]. Moreover, reductions in skeletal muscle mass are strongly associated with the progression of CKD [6]. Given this relationship, assessment of skeletal muscle morphology and performance may provide valuable clinical insights into the pathophysiology of CKD and the potential risk for CKD progression.

Resistance exercise has garnered interest as a potential countermeasure for skeletal muscle impairments in CKD [9, 11–13]. Positive effects on skeletal muscle strength have been observed following resistance exercise in CKD, with equivocal effects on skeletal muscle hypertrophy [12, 13]. Despite a greater proportion of individuals with CKD being predialysis, the majority of evidence comes from studies in patients with end-stage renal disease (ESRD). This has left a paucity of evidence regarding the effects of resistance exercise in those with CKD predialysis [14]. Due to the multiplicity of variables to consider, fundamental principles (i.e. specificity, progressive overload and variation) should be used to increase the likelihood that specified outcomes are achieved when prescribing resistance exercise for CKD [15]. The objectives of this brief review are to (i) describe skeletal muscle consequences associated with CKD, (ii) discuss the importance of monitoring changes in skeletal muscle health and (iii) briefly present principles of exercise physiology and programming strategies to inform the design of resistance exercise to address neuromuscular impairments in CKD predialysis.

SIGNIFICANCE OF CKD

CKD is defined most commonly by decreased kidney function for a duration of at least 3 months as measured by an estimated glomerular filtration rate (eGFR) $<60\,\mathrm{mL/min/1.73\,m^2}$ [2]. The chances of developing CKD are increased in those $\geq$50 years of age and are most common in those $\geq$70 years of age [16]. The most common risk factors for CKD include diabetes and high blood pressure followed by other factors such as cardiovascular disease, obesity, high cholesterol, lupus and family history [16]. The pathophysiology of CKD manifests in glomerulosclerosis, tubular atrophy and interstitial fibrosis, leading to reduced filtration capabilities of the kidneys [2]. This results in the accumulation and retention of uremic solutes thought to contribute to inflammation, immune dysfunction, vascular disease, platelet dysfunction and increased bleeding risk, reduced bone mineral density, altered drug metabolism, metabolic acidosis and skeletal muscle wasting [2, 4, 17].

The economic costs associated with CKD are significant, especially in patients with ESRD [18]. It is estimated that the socioeconomic burden is likely to continue to increase as a result of the aging population, prolonged survival among people with chronic diseases and the rising prevalence of frailty among other factors [19]. However, high economic costs have been reported as a result of CKD alone. Baumeister *et al.* [20] found that the high economic costs related to CKD were mainly due to excess inpatient care and drug costs and were independent of important comorbidities. Dialysis treatment is a major factor contributing to the high financial costs of CKD treatment. The average annual direct costs of dialysis treatment in Stage 5 CKD per patient has been reported to range between $30 000 and $60 000, with significantly higher costs associated with early dialysis initiation ($10–14\,\mathrm{mL/min/1.73\,m^2}$ versus $5–7\,\mathrm{mL/min/1.73\,m^2}$) [21]. Thus, in addition to potential health and quality of life benefits, treatments capable of maintaining kidney function or delaying the onset of dialysis treatment would provide substantial socioeconomic benefit.

SKELETAL MUSCLE WASTING AND DYSFUNCTION IN CKD

Skeletal muscle wasting has gained interest as a primary consequence of CKD due to the relationship between skeletal muscle mass, mortality and major adverse cardiovascular events [3–5, 7, 22–26]. Carrero *et al.* [24] reported a 30% incident rate of muscle atrophy in patients starting dialysis with a hazard ratio of death of 2.62. Significant associations between loss of lean mass and kidney disease severity and physical function have also been reported [6, 27]. Maintenance of lean mass is dependent on the relationship between protein synthesis and protein degradation. In CKD, this relationship is altered favoring protein degradation and thus accelerating the rate at which skeletal muscle mass is lost [3, 4, 22]. The upregulation of the ubiquitin–proteasome system (UPS) is suggested to contribute to this process given its role in regulating protein degradation [3, 4, 22]. Other potential mechanisms include metabolic acidosis, insulin/insulin-like growth factor 1 (IGF-1), inflammation, appetite regulation and microRNA expression [4]. For example, decrements in microRNA 29a (miR-29a) and miR-29b levels, which are suggested to contribute to decreased muscle myogenesis and CKD-induced muscle atrophy through an upregulation of Yin Yang 1 (YY1), were observed in a CKD rodent model [28].

Decrements in physical function are also commonly observed in individuals with CKD concomitant to losses in skeletal muscle mass [10, 29–32]. For example, patients with CKD predialysis were shown to experience reductions in strength, balance and gait speed, suggesting compromised physical function early in the disease process [31]. Further, physical function of patients with CKD not treated with dialysis is shown to be a stronger predictor of 3-year mortality than kidney function or commonly measured serum biomarkers [33]. Upon the initiation of dialysis, rapid and sustained declines in physical function are known to occur [29, 34]. For example, younger individuals on dialysis experienced poorer physical function compared with older individuals not on dialysis [29]. The reductions in physical function in the younger individuals with CKD on dialysis occurred independent of skeletal muscle mass loss [29]. Determining which factors contribute to declines in physical function will inform future treatment options to be introduced prior to or following dialysis initiation.

Individuals with CKD (both predialysis and ESRD) may be at greater risk of sarcopenia given the combined reductions in physical function, skeletal muscle performance and skeletal muscle mass [5, 6, 35–39]. While several definitions of sarcopenia exist, sarcopenia has been most recently defined as a syndrome classified by reductions in skeletal muscle mass plus a loss of physical function and/or skeletal muscle strength [40, 41]. Foley *et al.* [42] reported that the prevalence of sarcopenia, defined as the proportion of muscle mass to total body mass, increased with decreasing kidney function. Using the European Working Group on Sarcopenia in Old People (EWGSOP) criteria, elderly patients with ESRD demonstrated a high prevalence of sarcopenia (37% in men and 29.3% in women) [42, 43]. Similarly, Souza *et al.* [37] reported the prevalence of sarcopenia ranging between 11.9% and 28.7% using the EWGSOP and the Foundation for the National Institutes of Health Sarcopenia Project criteria in patients with CKD predialysis. The increased risk for sarcopenia further highlights the need for valid and reliable screening methods across the CKD spectrum. Additionally, the effects of exercise on sarcopenia in CKD are currently unknown.

CLINICALLY VIABLE APPROACHES TO ASSESSING CHANGES IN SKELETAL MUSCLE IN CKD

Monitoring skeletal muscle composition and function may provide clinical value given the concerns of skeletal muscle wasting and neuromuscular dysfunction in CKD and its relationship with mortality [23]. Dual-energy X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI) and bioelectrical impedance analysis (BIA) are frequently used to estimate skeletal muscle morphology and body composition in people with CKD within clinical research environments. However, the translation of these imaging modalities into clinical practice for the purpose of body or tissue composition analysis has been limited [44, 45].

CT and MRI both allow for the assessment of skeletal muscle volume and cross-sectional area (CSA) [44, 45]. CT imaging allows for the differentiation of tissues *in vivo* based on attenuation characteristics, whereas MRI allows for tissue segmentation via water and fat proton resonance frequencies and relaxation times [44–46]. Advantages to these methods include their high-resolution, three-dimensional construction, regional and CSA assessments and the ability to provide measures of muscle quality [44, 45]. Previous studies using both CT and MRI have documented changes in skeletal muscle in patients with CKD [47–49]. For example, in a natural history study examining changes in skeletal muscle and fat CT imaging showed a greater loss of skeletal muscle CSA in predialysis CKD as compared with those receiving hemodialysis or peritoneal dialysis [47]. Similarly, MRI of the lower leg has been used to detect significant skeletal muscle atrophy in patients on hemodialysis [48]. Despite the valuable information obtained from CT and MRI, the high equipment cost, subject size restrictions and radiation exposure (i.e. CT) associated with these devices pose a challenge to their clinical application [44]. Moreover, the inherent difficulty of obtaining whole body estimates of skeletal muscle mass with CT and MRI confers distinct clinical advantages to DXA and BIA for body composition analysis.

DXA has been identified by sarcopenia consensus groups as the reference standard for whole body and regional estimates of fat mass and fat-free mass (FFM) [50, 51]. Renal disease, age, sex and nutritional status may alter states of hydration, imposing differing degrees of influence on DXA body composition estimate values of FFM [52]. Hydration status may exert a nominal effect on DXA FFM estimates in overweight and obese people [53] but result in significant differences in repeated measures involving lean individuals [54]. The analysis of body composition in community clinical settings often relies on BIA due its affordability, relatively safe usage and general portability. Electrical impedance generated via BIA provides the means to estimate body cell mass through the reactance (Xc) and total body water through the resistance (R) [55, 56]. Importantly, the calculation of FFM using BIA requires the use of validated equations that account for age, health status and racial/ethnic background [52, 55, 57]. Given that BIA is dependent on tissue-specific conductivity, altered states of hydration and chronic fluid imbalances adversely affect the accuracy and reliability of the body composition estimates [55, 58]. Therefore limitations to using BIA to assess post-exercise adaptations in people with CKD may be associated with peripheral edema, changes in diuretic use and the timing of hemodialysis procedures in those with ESRD. Promising alternate approaches to standard BIA include using the derived Xc and R for vector analysis or phase angle (ϕ) measurement. BIA phase angle has some prognostic utility for people with CKD and may reflect diminished muscle composition or lower body cell mass as a function of age or pathology [45, 59].

A wide range of methods are used to estimate postexercise changes in skeletal muscle. The selected assessment method is governed by cost, accessibility, testing burden and measurement capabilities, as well as test analytics such as accuracy, reliability and responsiveness. Skeletal muscle adaptations in people with CKD have been characterized using DXA following low-intensity strengthening exercises featuring calisthenics and ankle weights [60], measuring total body potassium upon completion of a progressive resistance exercise (PRE) regimen during a period of restricted protein intake [61] and estimating muscle mass using CT scanning after a high-intensity PRE regimen [9]. Methods of body composition and muscle tissue analysis beyond DXA and BIA confer some advantages concerning the assessment of muscle morphology and morphemetry [62]. Changes in muscle morphology attributable to high levels of intramuscular adipose tissue have been associated with impaired lower extremity muscle performance and declines in functional performance [63, 64]. Estimates of intramuscular adipose tissue measured via CT scanning may be a responsive measure of skeletal muscle adaptations to strengthening exercise in people with CKD—even in the absence of muscle hypertrophy [9]. However, this observation is equivocal and requires additional study to better understand the usefulness of postintervention CT attenuation values regarding PRE program efficacy in those with kidney disorders [65].

Diagnostic ultrasound has been utilized to obtain proxy measures of skeletal muscle quality providing a cost-effective and accessible imaging modality to aid further clinical research regarding postexercise changes in muscle composition [66–70]. Skeletal muscle quality via computer-aided gray-scale analysis of echogenicity is shown to be independently associated with muscle strength [69, 70]. In addition, echogenicity has demonstrated the potential for a greater magnitude of associations with scaled peak force when compared with age [69]. Figure 1 depicts diagnostic ultrasound images of the mobile wad compartment acquired over the surface of the brachioradialis in a patient with CKD Stage 3 predialysis (Figure 1A) and CKD Stage 4 predialysis (Figure 1B). Gray-scale histogram analysis of the axial view scans was calculated using ImageJ (version 1.48; National Institutes of Health, Bethesda, MD, USA). The histogram in Figure 1A is shifted to the left and the gray-scale values are lower compared with Figure 1B. These ultrasound features suggest that the muscle tissue of the brachioradialis in the patient with CKD Stage 3 may have a better composition profile compared with the muscle tissue of the patient with CKD Stage 4. These examples demonstrate the potential clinical application of diagnostic ultrasound for assessing muscle quality with CKD progression. Further investigations are needed to confirm the validity and reliability of such measures.

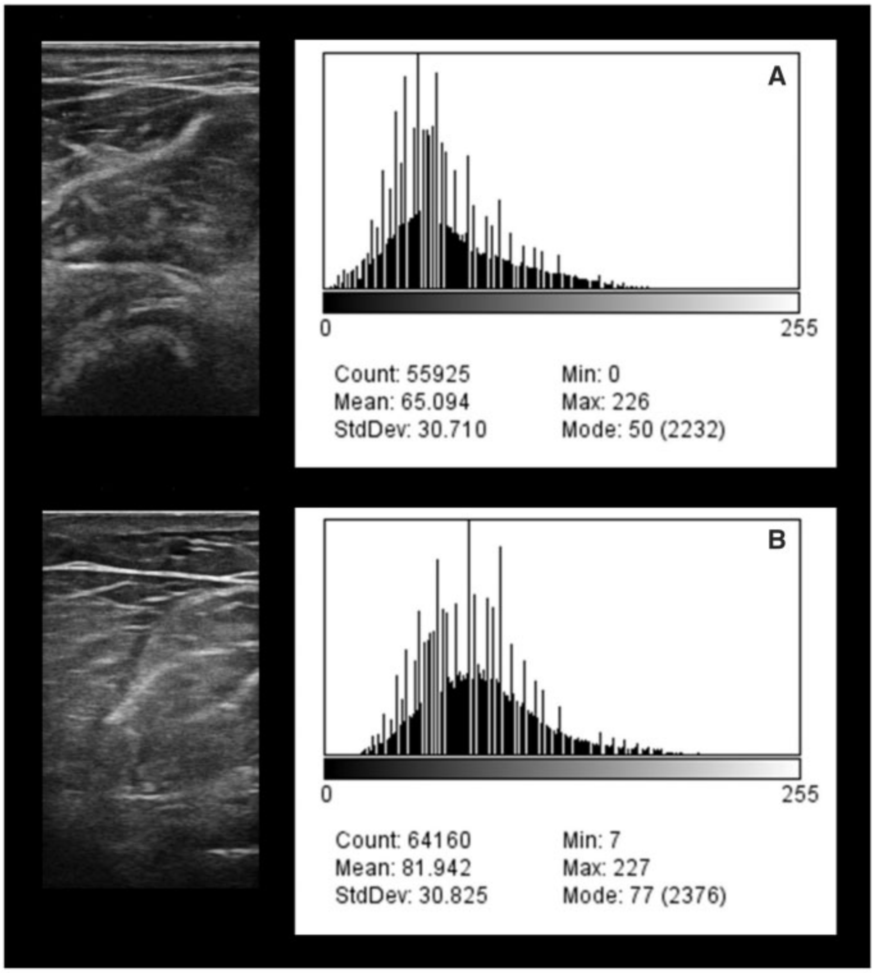

FIGURE 1: Exemplar musculoskeletal ultrasound images and gray-scale histograms of the proximal forearm in men with CKD. (**A**) The ultrasound scan and gray-scale histogram of a 65-year-old man with Stage 3 CKD with a grip strength value of 0.53 (scaled to body weight) and a Short Physical Performance Battery score of 11. (**B**) The ultrasound measures of a 71-year-old man with Stage 4 CKD with a grip strength value of 0.15 and a Short Physical Performance Battery score of 7.

Postexercise changes in muscle morphology may differ based on exercise program elements such as mode of muscle action, movement velocity, relative workload, exercise volume and program duration [71]. Diagnostic ultrasound allows for the analysis of postexercise changes in muscle thickness and area, fascicle length and pennation angle [72]. Additionally, specialized diagnostic ultrasound modes such as Doppler may characterize focal muscle blood flow, and quantitative image acquisition and analysis techniques allow for muscle volume estimates [73–77]. Imaging modalities also allow for the assessment of nonuniform adaptations involving skeletal muscle architecture that vary based on the dominant mode of muscle action used during a PRE regimen [71, 72]. Clinicians and practitioners alike should evaluate the strengths and limitations of the available technology to determine which devices are most appropriate.

RESISTANCE EXERCISE IN CKD

Aerobic and resistance exercise, both alone and in combination, have shown beneficial outcomes on health and function in those with CKD [78]. Specifically, regular exercise is seen to improve physical fitness, walking capacity, cardiovascular outcomes, some nutritional parameters and health-related quality of life (HRQoL) [78]. According to the findings from a systematic review and meta-analysis, PRE significantly improved skeletal muscle hypertrophy of the lower extremities, muscular strength and HRQoL [12]. These findings were corroborated in a systematic review of patients with ESRD that reported skeletal muscle hypertrophy, increased lower-body strength and improved aspects of HRQoL in response to resistance exercise [13]. However, to date, limited evidence exists on the effects of resistance exercise in patients with CKD predialysis [11, 79]. The available evidence in this subpopulation of CKD posits the potential for PRE to increase skeletal muscle hypertrophy [80, 81] and strength [61, 81] with no indication of exacerbated inflammatory responses [82].

Despite promising findings of the effects of resistance exercise on neuromuscular health and function in CKD, large variations exist among the protocols investigated. Differences in exercise program design and exercise mode make it difficult to decipher which elements of the exercise regime are most essential. For example, the type of external load applied has included free-weight dumbbells [9], weight machines [80, 81], ankle cuffs/weights [9, 60, 83], elastic bands [9, 84] and pneumatic equipment [85]. The duration of interventions has ranged from 8 weeks to 6 months. Regarding workload assignment, exercise intensity has been defined and monitored according to ratings of perceived exertion and relative exercise intensity (i.e.

Table 1. Resistance exercise recommendations for older adults

	Neuromuscular target				
	Hypertrophy		Strength		Power
Modality	Free weights; machines	Machine-based	Free weights; machines	Machine-based	Free weights; machines
Frequency	2–3 days/week on nonconsecutive days	3 days/week on nonconsecutive days	2–3 days/week on nonconsecutive days	2 days/week on nonconsecutive days	2–3 days/week on nonconsecutive days
Intensity	60–80% 1-RM	51–69% 1-RM	60–80% 1-RM	70–79% 1-RM	30–60% 1-RM
Training volume	1–3 sets/exercise; 8–12 repetitions/set	2–3 sets/exercise; 7–9 repetitions/set	1–3 sets/exercise; 8–12 repetitions/set	2–3 sets/exercise; 7–9 repetitions/set	1–3 sets/exercise; 6–10 repetitions/set
Contraction velocity	Slow to moderate	N/A	Slow to moderate	N/A	High
Rest intervals	1–3 min between sets	120 ss between sets	1–3 min between sets	60 ss between sets	1–3 min between sets
Duration	N/A	50–53 weeks	N/A	50–53 weeks	N/A
Additional comments	Multiple- and single-joint exercises	6 s time under tension per repetition; 2.5 s rest between repetitions	Multiple- and single-joint exercises	6 s time under tension per repetition; 4 s rest between repetitions	Should be conducted in combination with training to improve strength; multiple- and single-joint exercises

Resistance exercise recommendations for enhancing muscular hypertrophy, strength, and power for older adults as proposed by the American College of Sports Medicine (ACSM) [90] and a systematic review and meta-analysis performed by Borde et al. [92].
1-RM, 1 repetition maximum; min, minute; N/A, data not available.

percentage repetition maximum), while training volume has typically been prescribed at 3 sets of 8–15 repetitions [13]. The lack of standardization across studies complicates data interpretation, limiting the understanding of the potential benefit of resistance exercise for those with CKD.

PRACTICAL CONSIDERATIONS FOR THE DESIGN OF RESISTANCE EXERCISE

Recommendations for maintaining or enhancing skeletal muscle fitness

The American College of Sports Medicine (ACSM) recommends that resistance exercise be performed using 1–4 sets of 8–12 repetitions (2–3 days/week), at loads between 60% and 80% of an individual's 1-repetition maximum (1-RM), for improving general or overall muscular fitness (Table 1) [86–88]. The current recommendations for resistance exercise specific to CKD are in accordance with the ACSM guidelines [89–92]. These guidelines propose the use of 8–10 multijoint exercises per session performed two times per week. Exercise intensity is encouraged to range between 60% and 70% of a person's 1-RM or 5-RM with a minimum of 1 set of 10–15 repetitions completed. A gradual increase in volume (i.e. progressing to 2–4 sets per exercise) is also encouraged with 2–3 min of rest between sets and at least 48 h rest between exercise sessions (Table 2). While such recommendations seem to be sufficient for enhancing overall muscular fitness, the inclusion of advanced exercise program designs may be necessary when attempting to target specific neuromuscular characteristics. Such programs may also allow for individualization of exercise programs based on personal factors and CKD severity.

Guiding principles for resistance exercise prescription

Fundamental principles can be used to guide resistance exercise prescription. These principles include specificity, progressive overload, variation, reversibility and individuality [15]. Specificity refers to the similarities between the training stimulus being applied and the physiological adaptation of interest. This includes (i) muscle actions involved, (ii) speed of the muscle contraction, (iii) range of motion, (iv) muscle groups emphasized, (v) bioenergetic requirements and (vi) training load (i.e. intensity and volume) [15]. Progressive overload describes gradual, planned increases in training stimuli to promote continued gains in health and performance. Variation describes the systematic manipulation of one or more training variables at specified times throughout the training process [15]. Variation differs from traditional progressive overload in that certain training variables may be reduced or removed within a given period of the training cycle. Reversibility describes the loss of exercise-induced adaptations following the secession of exercise and individuality refers to the unique individual responses to a given exercise stimulus. By using such principles, informed decisions can be made during the planning and design of exercise interventions to ensure the safety of the participant while maximizing health and functional benefits.

Considerations for targeting specific neuromuscular outcomes

The prescription of workload assignment is dictated by the neuromuscular or functional outcomes of interest. For example, a resistance exercise regime may aim to improve skeletal muscle hypertrophy, strength or power, as well as functional outcomes such as gait speed or walking distance. Due to the lack of information on resistance exercise programming in CKD, evidence concerning older adults is often used to guide the exercise prescription for this patient population [58, 89–91]. For enhancing muscular strength and hypertrophy it is recommended that 1–3 sets per exercise be performed using a slow to moderate lifting velocity with loads corresponding to 60–80% 1-RM for 8–12 repetitions with rest periods of 1–3 min [86]. Further, dose–response relationships have been identified for training period, intensity, time under tension (i.e. the duration of each repetition) and rest between sets, highlighting the importance of these variables for promoting muscular strength and morphological (i.e. CSA, volume, thickness) adaptations in older adults [87, 93–95]. For

Table 2. Resistance exercise recommendations for Chronic Kidney Disease

	Neuromuscular target		
	Muscular fitness		
Modality	Weight-bearing activity, thera-bands, machines and free weights	N/A	N/A
Frequency	2 days/week on nonconsecutive days	≥ 2 days/week on nonconsecutive days	2 days/week
Intensity	60–70% 1-RM	N/A	60–70% 1-RM or 5-RM
Training volume	1 set/exercise; 8–12 exercises; 10–15 repetitions/set	8–10 exercises involving major muscle groups; 10–15 repetitions/exercise	Minimum of 1 set of 10–15 repetitions; gradually increase to 2–4 sets; choose 8–10 different exercises to work major muscle groups
Contraction velocity	N/A	N/A	N/A
Rest intervals	N/A	N/A	2–3 minutes between sets; ≥ 48 hours between sessions
Duration	N/A	N/A	N/A
Additional comments	Flexibility exercise can be performed 5–7 days/week for a duration of 10 min/session	N/A	Multijoint exercises affecting more than one muscle group and targeting agonist and antagonist muscle

Resistance exercise recommendations for Chronic Kidney Disease (CKD) as proposed by Johansen & Painter [87], Smart *et al.* [88], and Roshanravan *et al.* [89].
1-RM, 1 repetition maximum; min, minute; N/A, data not available.

enhancing lean body mass, programs consisting of higher volume were associated with the greatest increases, [93] while maximal strength favors training at higher intensities (i.e. 60–80% 1-RM) [87, 94, 95].

Power training (i.e. resistance exercise using low loads performed at high contraction velocities) has been appealing to rehabilitation and exercise professionals given the strong relationship between muscular power and functional outcomes in older adults [96]. To improve muscular power, it is recommended that training include 1–3 sets per exercise performed using high lifting velocities with loads corresponding to 30–60% 1-RM for 6–10 repetitions with rest periods of 1–3 min [86]. However, no consensus regarding optimal loading for the maximization of muscular power in older adults currently exists [95, 97]. In mobility-limited elderly adults, high-velocity resistance training using light loads (i.e. 40% 1-RM) on pneumatic devices resulted in similar improvements in power output and physical performance compared with power training using heavy resistance (i.e. 70% 1-RM) [97]. Therefore, training both the force and velocity components of the force–velocity curve seems beneficial for improving muscular power in older adults as proposed by the ACSM [86]. Contraction velocity and volume were found to be critical factors for increasing muscular power [98]. High-velocity contractions were superior to slow and moderate velocities while lower training volume was associated with greater improvements in muscular power [98]. Currently the available evidence on the effects of resistance exercise for improving muscular power in CKD is scarce. Therefore studies investigating power training interventions in those with CKD are warranted.

A major challenge working with clinical populations is the safety and tolerability of increasing workloads. As seen in Table 2 [89–91], exercise intensities between 50% and 80% of 1-RM are most effective for eliciting gains in muscle hypertrophy and strength [88]. Depending on disease severity, comorbidities, age, fitness level, genetics, and social and psychological factors, such intensities may not be feasible for those with CKD when initiating a resistance exercise program. Sequencing exercise intensity in a manner that focuses on the development of neuromuscular capacity may overcome this challenge. The application of periodized exercise has been used in clinical and rehabilitation settings as a way to manage exercise intensity [99, 100]. Periodization models provide a conceptual basis describing the systematic manipulations of exercise stimuli in an attempt to account for the accumulation of fatigue and stagnation in training adaptations [15, 101]. Resistance exercise intervention design informed by a block periodization model is presented in Table 3. Training parameters are prescribed in accordance with the neuromuscular outcome of interest and assumes translation of adaptations from one training block to the next (i.e. phase potentiation) [101]. The concept of block periodization aims to develop muscular work capacity, strength and power during different periods of training in a sequential manner (Figure 2). While this provides one example of the organization of workload based on specified outcomes, future research is required to determine the feasibility, efficacy and effectiveness of such approaches in this subpopulation of CKD.

SAFETY CONSIDERATIONS FOR RESISTANCE EXERCISE

It is recommended that exercise prescription for clinical populations should involve a multidisciplinary approach to ensure the safety of the participant while maximizing potential benefits [58]. This may include a team of medical experts, rehabilitation professionals and exercise specialists. Due to the high risk of cardiovascular disease associated with CKD, patients should consult with their physician prior to engaging in exercise. For a complete list of absolute and relative contraindications to resistance exercise and testing see Smart *et al.* [90] and the ACSM's *Guidelines for Exercise Testing and Prescription* [92]. All resistance exercise programs should be individually tailored for each person by a multidisciplinary team. Lower training intensities and volumes and longer exposure to given workloads may be required at the initiation of training. Furthermore, training should

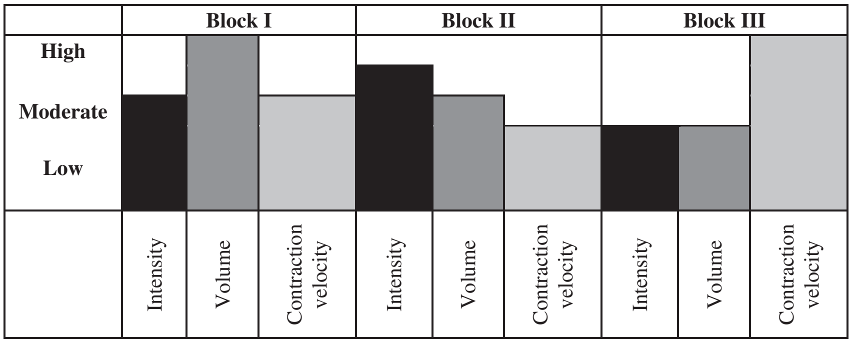

FIGURE 2: Block periodization model depicting intensity, volume and contraction velocity across the training period.

Table 3. Theoretical example of a block periodization model for resistance exercise adapted for individuals with CKD predialysis

Block	I (Weeks 1–4)	II (Weeks 5–8)	III (Weeks 9–12)
Emphasis	Work capacity	Maximal strength	Muscular power
Intensity	70% 1-RM	75% 1-RM	40% 1-RM
Volume	3 × 12	3 × 10	3 × 6
Contraction velocity	Slow to moderate	Slow to moderate	High

be progressed cautiously and informed by individualized responses [92]. The principles outlined above provide additional guidance to ensure patient safety through appropriate exercise progression while still promoting specific adaptations to meet the desired goals.

CONCLUSIONS

CKD is a complex condition that poses a severe threat to skeletal muscle health and function. Monitoring changes in skeletal muscle health might provide critical information regarding the overall health status of patients with CKD regardless of stage. Several options for monitoring skeletal muscle in clinical settings are currently available. Most notably, BIA and diagnostic ultrasound offer promising approaches due to the mobility and minimal space requirements for such technology. Inclusion of skeletal muscle assessments during routine appointments may aid in the understanding of disease progression following the diagnosis of CKD.

Currently, limited information is available regarding the application of resistance exercise in CKD predialysis. While resistance exercise has been shown to be beneficial for combating decrements in skeletal muscle health and function, questions remain concerning the responsiveness of skeletal muscle to various loading stimuli and the feasibility of such schemes in this patient population. Periodization models may offer a useful framework for the planning exercise regimes based on CKD stage and functional abilities to ensure patient safety through appropriate progression while still working towards achieving patient goals. Future research should seek to better understand the impact of resistance exercise to improve muscular power and the relationship between long-term resistance exercise and disease progression.

FUNDING

This publication was supported by the Veterans Affairs (VA) Center for Innovation (AM-251 12-11-2015), Georgetown–Howard Universities Center for Clinical and Translational Science Consortium (NIH/NCATS; UL1TR000101), VA Office of Academic Affiliations (38 U.S.C 7406) and the Rehabilitation Research & Development Service at the VA Office of Research and Development (IK2RX001854-01).

CONFLICT OF INTEREST STATEMENT

None declared.

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