

## Recommendations for implementation of physical training guidelines for patients undergoing chronic hemodialysis

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### ABSTRACT

The exponential growth in the prevalence of chronic kidney disease (CKD) is currently one of the greatest public health challenges worldwide, with a high economic impact at the health level and on the quality of life of affected patients. In countries with a low organ donation rate, hemodialysis is the renal replacement treatment par excellence. Although hemodialysis improves patient survival, in the medium and long term it generates a series of consequences and pathophysiological adaptations that gradually cause a significant reduction in general physical function, affecting daily activities and quality of life. The evidence of the beneficial effects of exercise in patients with any stage of chronic kidney disease, including those on dialysis therapy, is well known. Different types of physical training programs have shown to significantly improve the physical function of patients. The positive impact on clinical aspects such as mental health, hemodialysis efficacy as well as associated healthcare costs is significant. In Latin American countries, these programs are still at a very incipient level of development. The present work is a review of recommendations that should be considered for the implementation of a physical training program for patients on chronic hemodialysis.

**Keywords:** Exercise therapy; Renal hemodialysis; Renal insufficiency, Chronic; Frailty; Quality of life.

#### Cite this article as:

Müller-Ortiz, H., Moscoso-Aguayo, P., Troncoso-Riquelme, J., Rain-Gajardo, M., Basaez-Fernandez, A., Opazo-Rios, L., Gonzalez-Burboa, A., Vera-Calzaretta, A., Zuñiga-San Martín, C., Pedreros-Rosales, C., Vasquez-Mendez, P., Orozco-Guillen, N., Delgado-Diaz, R., Muñoz-Aguilar, P., & Martinez-Soto, J.P. (2021). Recommendations for implementation of physical training guidelines for patients undergoing chronic hemodialysis. *Journal of Human Sport and Exercise*, 16(4proc), S1732-S1745. <https://doi.org/10.14198/jhse.2021.16.Proc4.20>



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Abstract submitted to: Spring Conferences of Sports Science. [Costa Blanca Sports Science Events](#), 21-22 June 2021. Alicante, Spain.

JOURNAL OF HUMAN SPORT & EXERCISE ISSN 1988-5202.

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doi:10.14198/jhse.2021.16.Proc4.20

## INTRODUCTION

Chronic Kidney Disease (CKD) is a pathology of multifactorial origin, of increasing prevalence in emerging economies and with a high socio-economic impact, both at a health, personal and family level (Davison et al., 2015).

The current renal replacement therapies proposed for advanced CKD are kidney transplantation and dialysis in its different modalities. Hemodialysis is a three-week intervention that requires an average effective time of 4 hours per session to achieve proper clinical results. However, this procedure negatively affects the quality of life of the patient both at a social, occupational, and recreational level. in the medium and long term (Zúñiga et al., 2009).

This pro-inflammatory state, characteristic of the pathophysiology of the disease and the continuous reduction of the basal metabolic rate of the patient, promotes dystrophic and degenerative mechanisms that directly affect the cardiovascular, respiratory, and musculoskeletal levels, among others (Andrade et al., 2019). Advanced CKD generates increased muscle protein catabolism by different mechanisms such as: the accumulation of uremic toxins, reduced protein and antioxidant intake, presence of anemia, hyperparathyroidism, recurrent infections, use of corticosteroids, and associated comorbidities. In turn, sedentary behaviour associated with comorbidities leads to a progressive deterioration of the patient's physical function and their ability to perform basic and instrumental activities of daily life, which determines physical deconditioning and an increase in morbidity and mortality (Hara et al., 2018; Howden et al., 2015; Raj et al., 2008; Stenvinkel et al., 2015; Tamura et al., 2009).

Recent studies have shown the important role of physical exercise in chronic hemodialysis patients (Heiwe & Jacobson, 2014; Howden et al., 2015; Müller-Ortiz et al., 2019; Rossi et al., 2014). This intervention generates a diversity of systemic adaptations at the muscular, bone, metabolic, respiratory and cardiovascular level, thus improving the clinical condition, quality of life and well-being of people in dialysis therapy (American College Sports Medicine, 2014; Ministerio de Salud, 2017; World Health Organization, 2010).

Different types of physical training programs, such as aerobic, resistance or mixed, have been shown to significantly improve the aerobic capacity and muscle strength of patients significantly. Additionally, other clinical aspects such as blood pressure and heart rate (both maximum and resting) are positively impacted, resulting in less use of antihypertensive drugs and adequate blood pressure control (Intiso, 2014; Miller et al., 2002; Paglialonga et al., 2014; Pinho et al., 2012; Segura-Ortí, 2010). At the same time, these kind of programs have been effective in the management of conditions associated with mental health, reducing the incidence of anxiety-depressive disorders described in these patients (Allen et al., 2002; Rhee et al., 2019). Additionally, greater efficacy has been demonstrated in hemodialysis associated parameters, such as the urea clearance curve ( $Kt/V$ ), eventually reducing dialysis therapy exposure and associated economic costs (Parsons et al., 2006; Sheng et al., 2014).

Despite the explosive development of this type of interventions worldwide, in Latin America they still are in an early phase of implementation.

This work aims to provide evidence-based recommendations regarding the design and implementation of physical training guidelines as part of the comprehensive treatment of CKD patients on hemodialysis.

## GENERAL CONSIDERATIONS FOR THE IMPLEMENTATION OF THE INTRADIALYSIS EXERCISE

Intradialysis Physical Exercise (IPE) is related to the type of physical activity that is characterized by being planned, structured and repetitive, carried out with a specific objective, frequently associated with maintaining or improving one or more components of the person's physical condition in haemodialytic therapy, through a clear intention and systematicity (Caspersen et al., 1985; Garber et al., 2011).

IPE sessions mainly consist of a combination of aerobic, strength and/or resistance and flexibility exercises, which should be adapted to the seated position of the hemodialysis users (Heiwe & Jacobson, 2014; Intiso, 2014; Kim et al., 2019; Müller-Ortiz et al., 2019; Zúñiga et al., 2009). Due to the chronicity of dialysis therapy, the extracorporeal purification system is associated with a stretcher or armchair in order to keep the patient as comfortable as possible (Müller-Ortiz et al., 2019; Zúñiga et al., 2009). However, this resting position can be considered as a facilitator or barrier for free movement and displacement (Andrade et al., 2019; Hamm et al., 2011).

The invasion of the patient produced by the dialyzer connection, could generate unwanted effects during the procedure (removal of needles and/or blood lines, displacement of the arterio-venous fistula that facilitate bleeding and/or bruising, among others). Preliminary education is necessary, for the patient and the multidisciplinary team working on dialysis to obtain good results and avoid complications (Kurella et al., 2014; Narva et al., 2016). The concept of individuality in physical exercise overload takes on greater relevance in this group of patients. 80% of users are diabetic and/or chronic hypertensive, so their vital signs may undergo significant changes as the hemodialysis process progresses, a relevant problem when it comes to quantifying physical effort during the procedure (Howden et al., 2015; Intiso, 2014; Leehey et al., 2009; Umpierre et al., 2011). For this reason, it is recommended to establish the baseline state of the patient, start the IPE using prescription parameters according to the initial tolerance, and progress gradually depending on the clinical state, the functional capacity of the patient and the treatment goals (Andrade et al., 2019; Luyckx et al., 2018; Tuegel & Bansal, 2017).

Functional limitation, namely the degree to which physical function levels are reduced in hemodialysis patients, can be measured through tests such as the 6-minute walk test (6MWT) and the sit to stand test (STS), among others (Clarkson et al., 2017; Koufaki & Mercer, 2009; Segura-Ortí, 2010; Sheng et al., 2014; Simo et al., 2015; Yamagata et al., 2019). This functional assessment is not only relevant for the prescription of physical exercise, but also in some cases it has been shown to be a good predictor of mortality in CKD, as well as muscle strength (Isoyama et al., 2014; Raj et al., 2008; Stenvinkel et al., 2015; Wang & Mitch, 2014; Workeneh & Mitch, 2010; Yoo et al., 2017).

The resulting recommendation is to evaluate protein energy wasting to identify cachectic individuals with poor bone density or low body mass index ( $< 20 \text{ kg} / \text{m}^2$ ), and start strength exercises in them as soon as possible (Intiso, 2014; Segall et al., 2014; Stenvinkel et al., 2015; Yoo et al., 2017). Given the high prevalence of dependence in patients with end-stage renal disease, measuring the state of frailty and quality of life before and after performing an exercise program will help to evaluate the progression of training and the evolution of the disease, as well as, to guide on possible modifications in the exercise prescription (Kim et al., 2013; Matsuzawa et al., 2017; McAdams-Demarco et al., 2013; Walker et al., 2015).

## INTRADIALYSIS PHYSICAL EXERCISE PRESCRIPTION

### **Indications and contraindications**

In general, current evidence indicates that the IPE should be performed in the presence of qualified clinical staff (Luyckx et al., 2018; Müller-Ortiz et al., 2019; Tuegel & Bansal, 2017; Wang et al., 2016; Zúñiga et al., 2009).

All patients on chronic hemodialysis should participate in a physical training plan, except if there are contraindications. Contraindications must be differentiated into relative (subject to the experience of the professional and/or intervention team) or absolute (excluding). These recommendations are for guidance and should always have a dynamic character, taking into the current state of the patient (see Table 1).

Table 1. Contraindications to the prescription of exercise in patients exposed to hemodialysis.

<b>Absolute</b>	<b>Relative</b>
Recent AMI without surgical intervention	Patients < 3 months old from the start of hemodialysis
Unstable angina	Unstable hypertension (SBP > 200 y DBP > 110 mmHg)
Undiagnosed chest pain	Clinically manifest hypotension during exercise (SBP > 20 mmHg o DBP > 10 mmHg + STCH)
Significant change in resting EKG	Overt electrolyte disturbance
Uncontrolled arrhythmia (e.g.: AF, SVT)	Uncontrolled metabolic disease
Acute PE o DVT	Uncontrolled diabetes mellitus (> 300 mg/dL o < 70 mg/dL)
Inappropriate OAT titration	Changes in hypoglycaemic scheme
Acute systemic infectious process	Active liver disease (e.g.: Hepatitis)

*Abbreviations: AMI: Acute myocardial infarction; EKG: Electrocardiogram; AF: Atrial Fibrillation; SVT: supraventricular tachycardia; OAT: Oral anticoagulant treatment; SBP Systolic blood pressure; DBP: diastolic blood pressure; STCH: Signs of transient cerebral hypoperfusion; PE: Pulmonary embolism; DVT: Deep venous thrombosis.*

The generation of adverse events during the prescription of physical exercise in patients exposed to hemodialysis is very rare, as long as there is a risk categorization or stratification prior to entering the program (Aucella et al., 2014; Aucella et al., 2014; Gould et al., 2014; Ikizler, 2019; Johansen & Painter, 2012; Manfredini et al., 2017; Matsuzawa et al., 2017; Rhee et al., 2019).

The most commonly described events in the literature are those of cardiovascular origin, such as acute myocardial infarction, refractory arterial hypertension and arterial hypotension with the presence of symptoms/signs of transient cerebral hypoperfusion (decrease > 20 mmHg in systolic blood pressure + dizziness, nausea, blurred vision, paleness and/or syncope) (Greenwood et al., 2014; Intiso, 2014; Johansen & Painter, 2012; Rhee et al., 2019; Van Craenenbroeck et al., 2015). This symptomatology may be initially silent and only evident during the prescription of physical exercise, given the low basal metabolic rate, cachectic state, polypharmacy, concomitant diseases such as diabetes mellitus, arterial hypertension and dysautonomies, among others (Andrade et al., 2019; Capitanini et al., 2014; Hamm et al., 2011). For this reason, although the prescription of the submaximal stress test remains controversial for stratification of cardiovascular risk in these patients, there is consensus on the need for periodic assessment of hemodynamic variables (pulse rate and blood pressure values) and the gradual increase in intensity,

frequency, time and type of intervention (American College Sports Medicine, 2014; Andrade et al., 2019; Garber et al., 2011; Manfredini et al., 2017).

### **Security considerations for conducting the IPE**

In order to reduce adverse events that could put the patient and/or dialysis therapy at risk, it is necessary to take into account certain precautions before, during and after the prescription of physical exercise (Olvera-Soto et al., 2016; Segura-Ortí, 2010; Simo et al., 2015).

Constant measurement of vital signs and the screening of symptoms is highly recommended, with focus on signs such as pain, dyspnoea, nausea, blurred vision, dizziness, fatigue, cramps, among others, in order to eventually interrupt the exercise and manage them properly. The high prevalence of diabetic patients requires the measurement of capillary glycemia in those with recurrent hypoglycemia, bad metabolic control, changes in the insulin scheme and/or oral hypoglycemic agents (Carney, 2015; Colberg et al., 2010; Ishikawa et al., 2012; Leehey et al., 2009; Sigal et al., 2006; Smith et al., 2012). In the event of hypoglycemia prior to or during the intervention, a supportive diet or parenteral glucose intake should be considered, depending on the situation.

Blood pressure should be monitored regularly during physical exercise, especially in hypertensive patients. If the values rise (according to current guidelines and/or clinical criteria), it is indicated to suspend resistance exercises, decrease their intensity or introduce pauses in order to avoid greater cardiovascular and renal stress (American College Sports Medicine, 2014; Clarkson et al., 2017; Garber et al., 2011; Miller et al., 2002; Unger et al., 2020).

In those patients who have an arteriovenous fistula (AVF) for hemodialysis, blood pressure should always be measured in the opposite arm, avoiding as far as possible exercising that arm during hemodialysis (Müller-Ortiz et al., 2019; Zúñiga et al., 2009).

To avoid a hypotensive response during IPE, the effective workload must be prioritized during the first half of hemodialysis and never after it (Miller et al., 2002; Yamagata et al., 2019). Certifying the reestablishment of hemodynamic variables close to baseline values is a sign of high security in prescribing IPE, considering a period of at least 20 minutes after cessation of exercise, in order to avoid hypotensive events (Groussard et al., 2015; Intiso, 2014; Pinho et al., 2012; Segura-Ortí, 2010). Finally, to check the impact of exercise on the effectiveness of dialysis, it is recommended to calculate urea clearance (spKt / V), before starting an exercise program and then, if possible, every 4 weeks (Parsons et al., 2006).

### **Basic principles for the correct prescription of the IPE**

The following principles should be included in the exercise prescription, according to the objectives of both the multidisciplinary team and the user (see Table 2).

#### *Frequency*

It refers to the number of days per week in which the IPE is carried out. In the case of hemodialysis patients, the recommended frequency is associated with the days of extracorporeal clearance (Capitanini et al., 2014; Gomes et al., 2018; Johansen & Painter, 2012; Luyckx et al., 2018; World Health Organization, 2010).

#### *Intensity*

It refers to the level or magnitude of effort that the individual must perform to carry out an activity or exercise. During aerobic exercise, it is essential to use an effort perception scale to guide the intensity of the exercise,

since the heart rate can be directly influenced by the hemodynamic changes typical of hemodialysis and/or the use of beta-blocking drugs, for this, we suggest the modified Borg scale (Jorquera & Cancino, 2012; Morishita et al., 2018) (see Figure 1), as this is better understood by users, since the effort assessment is expressed on a scale from 0 to 10, compared to the original scale that is expressed from 6 to 20.

Table 2. Prescription principles and recommendations for intradialysis physical exercise (IPE).

<b>How to correctly prescribe the IPE session?</b>			
	<b>Aerobic</b>	<b>Strength</b>	<b>Flexibility</b>
Frequency	3 days/week	2-3 days/week	2-3 days/week
Intensity	<u>Mild</u> HRR: 40% -59% HR <sub>Max</sub> : 50-75% Borg: 12-13 / 4-5 or according to tolerance. 60-65% PPO	<u>Mild</u> 50-70% 1-MR RPE: 15-17	Static: Stretch to the point of tension or slight discomfort. PNF: 20% -75% of the maximum voluntary contraction.
Repetitions	12-15 reps		
Sets	≤ 2 sets are effective to the development of muscular endurance		
Time	Start with 10 - 15 min, or according to tolerance. Progress to 30 - 45 min of continuous activity; increase from 3-5 min / wk.	Recovery times of 2-3 min between sets. Rest > 48 hrs. for each muscle group.	Static: 60 sec. by joint; (10-30 s hold per stretch); PNF: 3-6 sec. contraction; 10-30 sec. assisted stretching.
Duration	> 6 months		
Type	Cycle ergometer or arm ergometer	Free weights or resistance bands	Static stretching or PNF.
Temporality	During the first 2 hours of Hemodialysis		
<b>What to monitor in an IPE session and when?</b>			
	<b>Before</b>	<b>During</b>	<b>At the end</b>
Vital Signs: HR, ABP, SpO <sub>2</sub> , BF, T°	Always	Mainly ABP and HR	Always
ABP (in case of HT)	Always	Keep values < 220/110 mmHg	Values close to baseline
Borg Scale	Always	Regularly (especially in beta- blocked patients)	Close to baseline values
Signs y Symptoms (pain, fatigue, dizziness, cramps, etc.)	Always	Always	Always
BGT (in case of being diabetic)	Assess contraindications	-	Always

Abbreviations: HRR: Heart Reserve Rate; HR<sub>Max</sub>: Maximum Heart Rate; Borg: Perceived Exertion Scale; PPO: Peak power output; 1-MR: 1-Maximum Repetition; RPE: Rating of perceived exertion; PNF: Proprioceptive neuromuscular facilitation. ABP: Arterial Blood Pressure; SpO<sub>2</sub>: Oxygen Saturation; BF: Breathing Frequency; T°: Temperature; BGT: Blood Glucose Test; HT: Hypertension.

The modified Borg Scale can also be complemented with a facial scale for better understanding (Jorquera & Cancino, 2012; Morishita et al., 2018). Performing moderate intensity exercise (increased heart rate, sweat generation and/or Borg = 5-6 or 12-13) is recommended and progress according to the patient's tolerance. Likewise, exercise should be preceded by warm-up activities and end with cool-down activities, both with a working heart rate close to 50% (American College Sports Medicine, 2014; Andrade et al., 2019; Garber et al., 2011; Gomes et al., 2018; Manfredini et al., 2017; Matsuzawa et al., 2017; Müller-Ortiz et al., 2019; Yamagata et al., 2019).







Original Scale		Modified Scale		Facial Scale
6	Without effort	0	Null	 <b>0</b>
7	Extremely light	0,5	Barely noticeable	
8		1	Very light	
9	Very light	2	Light	 <b>2</b>
10		3	Moderate	
11	Light	4	Something heavy	 <b>4</b>
12		5	Heavy (hard)	
13	Something hard	6		 <b>6</b>
14		7	Very hard	
15	Hard (heavy)	8		 <b>8</b>
16		9		
17	Very heavy	10	Extremely hard	 <b>10</b>
18		*Maximum		
19	Extremely hard			
20	Maximum exercise			

Figure 1. Original versus modified Perceived Exertion Scale or Borg scale, associated with facial scale. Any of these modalities is shown to the patient, where the physiotherapist must ask to the user how intense his/her effort was after the performed exercise. The numbers that present a description in white reflect a slight increase in the previous named category (E.g.: the number 6 in the modified scale shows "heavy-hard" work, which is closer to "very hard" work and is associated with number 13 of the original scale that mentions

work as “*somewhat hard*”; both numbers correspond to moderate intensity work, which is also reflected in the facial scale). Adapted from literature (Jorquera & Cancino, 2012; Morishita et al., 2018).

#### *Time (duration)*

It refers to the amount of physical exercise that the person should perform in a period. It is recommended that patients achieve 30 to 60 min of continuous exercise within the first two hours of hemodialysis. In addition, IPE programs should last no less than 6 months in order to optimize the effectiveness and impact on general physical function (American College Sports Medicine, 2014; Aucella et al., 2014; Garber et al., 2011; Matsuzawa et al., 2017; Peña-Amaro et al., 2009; Rhee et al., 2019; Sheng et al., 2014; Walker et al., 2015; Yamagata et al., 2019).

#### *Type*

It refers to the type of physical activity or exercise to be performed. In general, most studies use aerobic exercise as the main training (Garber et al., 2011; Heiwe & Jacobson, 2014; Leehey et al., 2009; Zelle et al., 2017). However, the combination of aerobic exercise with resistance exercise has shown significant improvements in maximal oxygen consumption, which is closely correlated with an improvement in cardiorespiratory fitness (Cheema et al., 2014; Isoyama et al., 2014; Matsuzawa et al., 2017; Simo et al., 2015; Yoo et al., 2017). The cycle ergometer, pedal board or arm ergometer adapted to the dialysis chair are the most used in aerobic exercise, while in resistance exercise, elastic bands and free weights are described (Cho et al., 2018; Gomes Neto et al., 2018; Kim et al., 2013; Paglialonga et al., 2014; Sheng et al., 2014; Smith et al., 2012; Yamagata et al., 2019). Finally, an inspiratory threshold valve can be used to improve not only respiratory muscle function but also aerobic capacity (Da Silva et al., 2011; Moscoso et al., 2020).



**Flexibility Exercise**

**Aerobic Exercise**

**Resistance Exercise**

**Inspiratory Muscle Training**

*Source: Physical training program in hemodialysis patients at Hospital Base Valdivia and Hospital de Ancud, Chile.*

Figure 2. Illustration of types of intradialysis exercises.

## FINAL COMMENTS

The current epidemiological panorama globally associates an increasingly aging population with an increasingly high burden of disease. Obesity, dyslipidemia, arterial hypertension and type 2 diabetes mellitus are diagnosed at an earlier age, yielding more obese adults with the presence of micro and macrovascular complications, high cardiovascular morbidity and mortality, and CKD.



At the same time, CKD patients have a low quality of life compared to the general population and frequently present alterations in their physical function, increasing the risk of morbidity and mortality, especially in frail patients. There is enough evidence to support the safety and benefits of exercise in these patients, so ideally there should be exercise programs in all dialysis units. These effects have scientific support at the cellular and molecular level that directly affects clinical outcomes.

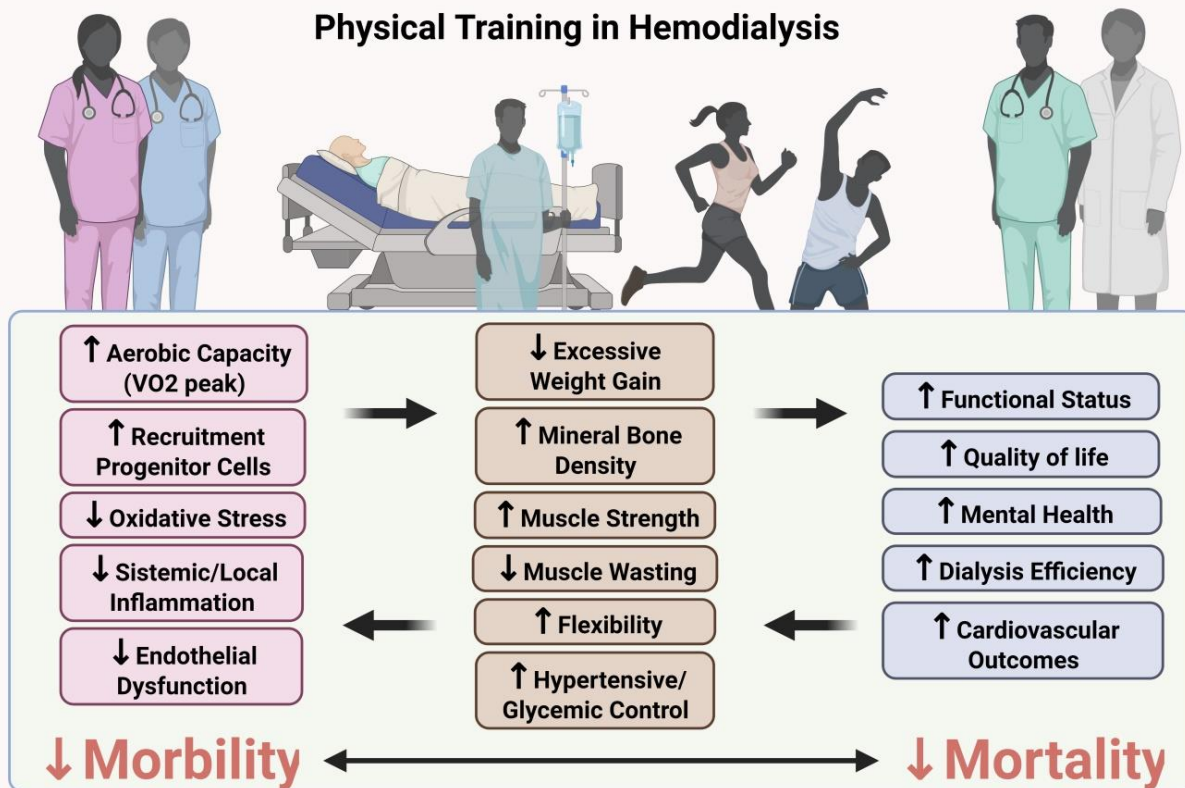


Figure 3. Schematic view of the main beneficial effects observed with the prescription of physical training in hemodialysis patients. The supervision of the clinical staff is of great importance to avoid adverse effects.

The implementation of an intradialytic exercise program requires, together with the incorporation of physiotherapists in the renal health teams, education and dissemination of the benefits that regular exercise entails, especially the improvement in the functionality, psychological state and quality of life of patients (Greenwood et al., 2014).

Considering the reported clinical benefits and the improvement in quality of life associated with physical exercise in hemodialysis patients, it is imperative to promote its early incorporation as part of regular therapy in dialysis units across Latin America, supervised by trained physiotherapists. In addition, a new line of work and clinical research of wide projection is thus opened for the benefit of patients with CKD.

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