



REVIEW

Is High-Intensity Interval Training an Option for Post-Kidney Transplant Physical Rehabilitation Programmes? A Scoping Review

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Purpose: To systematically and broadly review the literature to show the available information on high-intensity interval training for kidney transplant recipients as an adjunct to physical rehabilitation.

Methods: A scoping review of high-intensity interval training for post-kidney transplant patients was conducted by searching the PubMed, EMBASE (Elsevier), Scopus (Elsevier), Web of Science, and PEDro databases. Full-text records on the subject were included. Articles not published in English were excluded. The selected articles went through careful production quality analysis using the PEDro scale.

Results: The search identified 26 articles, 3 of which met the inclusion criteria. The material demonstrated satisfaction, confidence, improvement in resting heart rate, and absence of adverse effects from high-intensity interval training for kidney transplant recipients. **Conclusion:** Based on this scoping review, high-intensity interval training for kidney transplant patients may be beneficial for physical and mental aspects and complement physical rehabilitation programmes, but there is a need for more studies with robust samples and long-term follow-up to confirm these benefits.

Plain Language Summary: Patients undergoing kidney transplantation are at increased risk of developing heart disease, which can result in a high risk of health complications and even death. Physical rehabilitation programmes, especially those that include exercise, have demonstrated physical capacity benefits for several populations, including organ transplant recipients. Researchers have recently explored high-intensity interval training as an option in rehabilitation programmes, but they still lack a clear understanding of its specific effects on kidney transplant patients. This study aimed to systematically review the available literature on high-intensity interval training for kidney transplant recipients, evaluating its potential in physical rehabilitation. The team reviewed several databases and, after analysis, identified three relevant articles. These articles showed that high-intensity interval-training can improve cardiac health, can enhance patient satisfaction and confidence, and does not cause any physical damage. In conclusion, high-intensity interval training appears to be beneficial for kidney transplant patients and can be included in rehabilitation programmes. However, additional studies with larger sample sizes and long-term follow-up are needed to confirm these results.

Keywords: cardiac rehabilitation, exercise, chronic renal insufficiency, organ transplantation, evidence-based practice

Introduction

Kidney transplantation is the gold standard treatment for end-stage kidney disease. Kidney transplant recipients have a significantly increased cardiovascular mortality rate compared with the general population, although lower than patients on maintenance dialysis. Nevertheless, short-term survival among kidney transplant recipients has improved considerably due to decreased mortality from infections and acute organ rejections.²

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Cardiovascular disease continues to be the leading cause of death among individuals with functioning grafts worldwide.^{3–5} The high prevalence of cardiovascular disease in kidney transplant recipients is partially linked to the presence of traditional cardiovascular risk factors, such as diabetes, dyslipidaemia, and hypertension.⁶ There are also post-transplant factors that contribute to cardiovascular risk, such as new-onset diabetes,⁷ the development of metabolic syndrome,⁸ and a sedentary lifestyle.⁹ Most kidney transplant recipients do not reach the levels of physical activity¹⁰ recommended by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines¹¹ and societies such as the National Kidney Foundation¹² and the Brazilian Association of Organ Transplantation¹³ in their usual routine. Hence, these individuals could benefit from personalised social and professional guidance and support to improve their daily physical activity.¹⁴

Exercise-based rehabilitation programmes are known to mitigate cardiovascular risk factors in the general population, ¹⁵ and they are also expected to have beneficial effects for kidney transplant recipients. Although the effects of such programmes have been extensively studied in heart and lung transplant recipients due to the direct influence of physical exercise on cardiac and pulmonary function, ^{16,17} uncertainties persist regarding their efficacy and safety for recipients of other solid organs. ^{16,18}

Among the various modalities of physical exercise investigated in contemporary studies, high-intensity interval training stands out. This regimen involves alternating sets comprising short or prolonged bursts (ranging from 30 seconds to 4 minutes) of high-intensity effort (> 85% maximum oxygen uptake [VO2max]), interspersed with brief or extended recovery periods (also ranging from 30 seconds to 4 minutes). High-intensity interval training has demonstrated utility, safety, and feasibility in heart transplant recipients and, more recently, in kidney transplant recipients. However, there is a dearth of evidence regarding the frequency, duration, benefits, and safety of high-intensity interval training specifically for kidney transplant recipients.

Based on this knowledge gap, the aim of this scoping review was to identify studies elucidating the potential use of high-intensity interval training for kidney transplant patients within physical rehabilitation programmes. A scoping review enables a comprehensive examination of the existing literature and facilitates the exploration of knowledge gaps. Therefore, this review serves as an initial step in data collection, providing a foundation for future research endeavours.

Materials and Methods

Protocol and Logging

We conducted a scoping review to identify and delineate the existing evidence base, adhering to the guidelines outlined in the JBI Reviewer's Manual on Scoping Reviews.²² The reporting of this review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRIMAS-ScR), as outlined by Tricco et al.²³ To ensure reproducibility and transparency, we outlined the methodology employed in this study in a protocol that is freely accessible on the Open Science Framework (OSF).²⁴ Because our research did not involve the use of human data, submission to the Human Research Ethics Committee was unnecessary.

Eligibility Criteria

We established the eligibility criteria following the Population, Concept, and Context (PCC) framework outlined in the JBI Manual.²² The study population comprised adult kidney transplant recipients. To address the concept, we included articles employing high-intensity interval training, and we designated the context as rehabilitation centred on physical exercise. We included the following study designs: clinical trials, cross-sectional analyses, and case-control studies.

This scoping review was limited to articles published between 2018 and 2023 and written in English to increase the feasibility and quality. The exclusion criteria were: (1) articles published before 2018, (2) articles published in any language other than English, (3) articles that did not relate to adult kidney transplant recipients, and (4) articles that did not address high-intensity training as an approach to exercise-based rehabilitation.

Sources of Information and Search Strategy

To identify potentially relevant documents, we initially searched PubMed (National Library of Medicine) using the following Medical Subject Headings (MeSH) associated with the Boolean operators OR and AND, "trans plantation recipients", "kidney", "high-intensity interval training", and "rehabilitation exercise". Then, we searched EMBASE (Elsevier), Scopus (Elsevier), Web of Science, and PEDro. We conducted the literature search in September 2023 and updated it in April 2024. <u>Table S1</u> contains the complete search strategy.

Article Selection

Two authors selected the titles and abstracts of the documents independently. VL performed the data mapping process and BSS reviewed it. Disagreements between the reviewers were dealt with by consensus and, if there was no agreement, a final decision was made by a third reviewer (VRSFM).

The following data were extracted: title, authors, year of publication, country of data collection, study design, sample details (eg, sample size, biological sex, age, and kidney disease–related information), the primary and secondary endpoints (where applicable), protocol details, and the results.

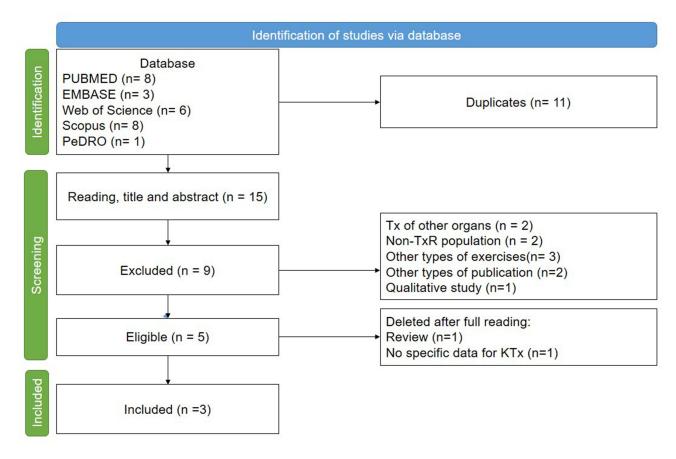
We did not evaluate the quality of the evidence of the included articles, because a scoping review does not aim to critically assess the risk of bias. However, we did assess the methodological quality of the articles by using the PEDro scale. This assessment tool allowed us to evaluate the methodological construction and the results presented by the authors based on the characteristics of randomised clinical trials. The PEDro scale includes 11 criteria, 10 of which be scored: 25

- 1. the eligibility criteria were specified;
- 2. the subjects were randomly distributed into groups (in a crossover study, the subjects were randomly placed in groups according to the treatment received);
- 3. the subject allocation was concealed;
- 4. the groups were similar regarding the most important prognostic indicators;
- 5. all subjects participated blindly in the study;
- 6. all therapists who administered the therapy did so blindly;
- 7. all evaluators who measured at least one key result did so blindly;
- 8. the measurements of at least one key result were obtained in more than 85% of the subjects initially distributed among the groups;
- 9. all subjects from whom outcome measurements were presented received the treatment or control condition according to allocation or, when this was not the case, at least one of the outcomes was analysed based on "intention to treat";
- 10. the results of inter-group statistical comparisons were described for at least one key outcome; and
- 11. the study presented both precision measures and variability measures for at least one key outcome.

The author with the greatest expertise in methodological evaluation tools performed this evaluation; in case of divergence, a second author was consulted for quality analysis.

Results

A search of the PubMed, Embase, Web of Science, Scopus, and PEDro databases returned 26 records. Following the removal of duplicates, we reviewed the titles and abstracts of 15 articles. Of these, we excluded nine articles that addressed solid organ transplantation without specifying the transplanted organ; excluded kidney transplant patients; did not use high-intensity interval training as an exercise therapy; or referred to other types of publications, such as recommendations. Finally, we evaluated five full texts for eligibility. As shown in the PRISMA flow diagram¹⁸ (Figure 1), we included three articles that met the inclusion criteria.



 $\textbf{Figure I} \ \ \textbf{PRISMA} \ \ \textbf{flow} \ \ \textbf{diagram} \ \ \textbf{illustrating} \ \ \textbf{the} \ \ \textbf{process} \ \ \textbf{of} \ \ \textbf{study} \ \ \textbf{selection}.$

Notes: Adapted from PRISMA Flow Diagram. Adapted from Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.²³

The three articles were published between 2021 and 2022. In terms of study design, one article utilised a convenience sample, while two employed randomisation. Geographically, two of the articles originated from the United Kingdom and the other was from Belgium. In one article, the sample included recipients of various organs such as the heart, lungs, liver, and kidneys. The data extracted from the included articles are summarised in Table 1 and Table 2 presents the evaluation of the articles based on the PEDro scale.

Table I Summary of the Literature Included

Author/Year	Local	Study Design	Transplanted Organ
Cappelle M et al 2021 ²¹	Belgium	Single-arm intervention	Heart, lung, liver, and kidneys
Billany RE et al 2022 ²⁶	United Kingdom	Randomized	Renal only
Hutchinson GM et al 2022 ²⁷	United Kingdom	Randomized	Renal only

Table 2 Assessment of Methodological Quality Using the PEDRO Scale

Autor	Crit. I	Crit. 2	Crit. 3	Crit. 4	Crit. 5	Crit. 6	Crit. 7	Crit. 8	Crit. 9	Crit. 10	Crit. 11
Cappelle M et al, 2021 ²¹	YES	NO	YES	YES	YES						
Billany RE et al, 2022 ²⁶	YES	YES	NO	YES	NO	NO	NO	NO	NO	YES	YES
Hutchinson GM et al 2022 ²⁷	YES	YES	NO	NO	NO	NO	NO	YES	YES	YES	YES

Abbreviation: Crit, Criterion. **Source**: Own preparation, 2024.

Table 3 Describes the Objectives and Protocols of High-Intensity Interval Training Applied by the Studies, as Well as the Primary and Secondary Outcomes

Author/Year	Cappelle M et al 2021 ²¹	Billany RE et al 2022 ²⁶	Hutchinson GM et al 2022 ²⁷		
Goal	To investigate the effects of a HIIT program on physical performance in solid organ recipients	Determine the feasibility and acceptability of HIIT in RxT	To explore the physiology and immunological impact of eight weeks of HIIT on RxT recipients		
Equipment	Ergonomics for lower limbs	Ergonomics for lower limbs	Ergonomics for lower limbs		
Intensity	80–95% of HRmax	80% of peak VO ₂	> 90% peak VO ₂		
HIIT Protocol	3 times a week, high-intensity intervals of up to 2 minutes at 80–95% of maximum HR, training lasting 30 minutes for 6 months	Warm-up 5 minutes and cool-down 10 minutes; 2 hIIT protocols: HIIT (16 minutes with intervals of 4.2 and 1-minute duration at 80% of peak VO ₂ for 24 sessions (8 weeks) total session time 30 minutes; HIIT B (4x4 minutes interval training 80% VO ₂ peak, separated by 3-minute active rest at 60% of peak VO ₂) Total session time 30 minutes	HIIT A (4, 2 and I min intervals; 80–90% VO2peak), HIIT B (4 × 4 min intervals; 80–90% VO ₂ peak) for 24 supervised stationary bike sessions (approx. 3x/week for 8 ± 2 weeks)		
Primary outcome	Increase in VO ₂ max and decrease in resting HR	HIIT has been shown to be safe and viable in RxT, with no adverse effects.	There was no impairment in immunity in the short or long-term		
Secondary outcome	HIIT is safe and may result in a beneficial effect on the physical performance of stable RxT.	HIIT was well accepted and tolerated by RxT.	HIIT did not cause immunological changes		

Abbreviations: HIIT, high intensity interval training; HRmax, maximum heart rate; VO2, oxygen volume; RxT, kidney transplant; HR, heart rate.

As shown in Table 3, all three articles used lower limb ergometry. In one article, ²¹ the authors determined the exercise intensity based on the maximum heart rate (HRmax), while the authors of the other two articles^{26,27} used peak VO₂. The interventions occurred three times a week and each session lasted 30 minutes for 6 months²¹ or at least 6 weeks and at most 10 weeks.^{26,27}

The summary of the anthropometric and clinical characteristics of all the included articles is shown in Table 4. The clinical presentation of the samples was heterogeneous: two articles provided biochemical data, ^{26,27} while only one provided information on immunosuppressive drugs. ²¹

Table 4 Anthropometric and Clinical Characteristics of the Study Samples

Characteristics / Study	Cappelle ²¹	Billany ²⁶		Hutchinson ²⁷	
Single Groups		HIIT A	HIIT B	HIIT A	HIIT B
Sample, n; Man/Woman	15 (11/4)	8 (3/5)	8 (6/2)	8 (3/5)	8 (6/2)
Age, years	40.7±14.8	41±14	51±11	41±14	51±11
Body mass, kg	72.0±13.1	68.5±15.6	84.1±24	68.5±15.6	84.1±24
BMI, kg/m²	23.9±3.4	25.9±5.4	28.5±7.1	25.9±5.4	28.5±7.1
Serum creatinine, mmol/L	N/A	104±27	133±60	104±27	133±60
GFR, mL/min/1.73 m2	N/A	62 ± 18	57 ± 22	62 ± 18	57 ± 22
Transplant time, months	43,2 (24 -111,6)	12±20	44±86	12±20	44±86

(Continued)

Table 4 (Continued).

Characteristics / Study	Cappelle ²¹	Cappelle ²¹ Billany ²⁶			Hutchinson ²⁷		
Single Groups		HIIT A	ніт в	HIIT A	ніт в		
Medication, n (%)							
Azathioprine	2 (13)	N/A	N/A	N/A	N/A		
Mycophenolate mofetil	12 (80)	N/A	N/A	N/A	N/A		
Cyclosporine	I (7)	N/A	N/A	N/A	N/A		
Tacrolimus	12 (80)	N/A	N/A	N/A	N/A		
Steroids	8 (53)	6 (75)	2 (25)	6 (75)	2 (25)		
всс	N/A	8 (100)	8 (100)	8 (100)	8 (100)		
Antihypertensive	N/A	7 (88)	7 (88)	7 (88)	7 (88)		
Anti-diabetes	N/A	1(13)	3 (38)	1(13)	3 (38)		
Statin	N/A	4 (50)	5 (63)	4 (50)	5 (63)		

Notes: Data presented as mean and standard deviation.

Abbreviations: BMI, body mass index;GFR, glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure, mmHg; millimeters of mercury; N/A, not informed; BCC, calcium channel blockers.

One of the articles acknowledged heterogeneity in the sample concerning the type of transplant, a factor that could potentially influence physical performance.²⁶ This is attributed to variations in immunosuppressive drug indications and dosages, which adhere to the standard treatment protocol for each specific type of transplanted organ. It is widely recognised that steroids exert a direct catabolic effect on skeletal muscle, thereby detrimentally affecting muscle strength and exercise capacity.

Effects of High-Intensity Interval Training on Hemodynamic Variables

The pre- and post-intervention hemodynamic variables, systolic and diastolic pressures, and heart rate were measured in two articles and are presented in Table 5. For one article, in kidney transplant recipients, resting heart rate decreased after 6 months of high-intensity interval training compared with pre-training (baseline 83.9 ± 17.3 bpm, post-training 79.5 ± 14.3 bpm, p = 0.04). However, there were no changes in resting SBP or DBP.²¹ Billany et al²⁶ reported that there were no hemodynamic changes after high-intensity interval training. Overall, only 40% of the participants achieved the required intensity during the intervention, and it took just over half the duration of the intervention to achieve this. The data suggest that a familiarisation period and a longer intervention may be beneficial. In addition, constant absences for health

Table 5 Hemodynamic Variables of the Samples From the Pre- and Post-Intervention Studies

Study	Capelle ²¹		Billany ²⁶				
Group	Unique		HIIT A		НІІТ В		
	Pre	Post	Pre	Post	Pre	Post	
SBP mmHg	130.9 ± 37.7	138.8 ± 18.5	122 ± 12	122 ± 11	131 ± 17	122 ± 13	
DBP mmHg	82.9 ± 13.8	81.3 ± 15.7	84 ± 6	80 ± 4	79 ± 6	75 ± 6	
HR rest	83.9 ± 17.3	79.5 ± 14.3	77 ± 4	76 ± 8	76 ± 4	67 ± 4	

Notes: Data presented as mean and standard deviation.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; mmHg, millimeters of mercury.

reasons (colds, justified by the continuous administration of immunosuppressants) may have influenced the fact that the participants did not reach the intensity and frequency of the target exercise. Finally, the authors of the third included article did not describe hemodynamic variables because they aimed to investigate changes in circulating immune and inflammatory cells during the 8-week intervention.²⁷ The authors concluded that high-intensity interval training exercises do not adversely affect the immunity of kidney transplant recipients.

Effects of High-Intensity Interval Training on Anthropometric Variables

Two articles^{21,26} reported that there were no changes in body mass and the body mass index before and after the intervention with high-intensity interval training.

Discussion

In this scoping review, we identified that there are scarce data regarding high-intensity interval training as an option for physical exercise—based rehabilitation programmes for kidney transplant recipients. Nevertheless, this modality is recommended for the healthy population.²⁸ Moreover, studies have demonstrated its benefit and feasibility for some clinical populations such as heart transplant patients²⁹ and lung transplant recipients.³⁰ The guidelines indicate that kidney transplant patients should practice regular physical exercise³¹ but do not describe the ideal time to start after transplantation, as well as the frequency, intensity, and duration. However, a unanimous view for healthy and clinical populations is the continuous and regular performance of physical exercise with a focus on better quality of life and exercise capacity and, consequently, a reduction of the cardiovascular risk.^{28,32}

The physiological profile of kidney transplant recipients is well known: they have experienced the burden of chronic kidney disease, such as heart failure, systemic arterial hypertension, and sarcopenia before transplantation. After kidney transplantation, there is a need to make lifestyle changes to minimise acute or chronic rejection. These changes include medication adherence, body mass control, adequate diet, and regular physical exercise, whether supervised or at home. There has been limited on high-intensity interval training as a viable option within exercise-based rehabilitation programmes. This scarcity has arisen partly due to the exclusion of kidney transplant recipients from studies or their grouping with recipients of other organ types, thus impeding precise data extraction.

Conclusion

Exercise therapy, particularly high-intensity interval training, demonstrates well-known benefits for healthy individuals and has recently emerged as a approach for kidney transplant patients. Chronic kidney disease and the post-transplant process directly influence the body's physiology, but high-intensity interval training shows potential despite these challenges. Although studies remain limited, researchers have not identified significant events that would render this option unfeasible in rehabilitation programmes based on physical exercise. Qualified rehabilitation professionals closely monitor transplant patients during and after high-intensity interval training to minimise the risk of complications. As a result, high-intensity interval training can serve as a tool in specific cases for kidney transplant patients, promoting engagement and adherence to rehabilitation programmes.

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Disclosure

The authors report no conflicts of interest in this work.

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