

# Physical activity parameters as determinants of cardiovascular disease risk in kidney transplant recipients: an accelerometer-based study

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## Abstract

**Introduction:** Cardiovascular diseases are the leading cause of morbidity and mortality after kidney transplantation. Physical inactivity is an important factor for the development of cardiovascular disease (CVD) risk.

**Aim:** To evaluate CVD risk and its association with accelerometer-based physical activity (PA) parameters in kidney transplant recipients (KTRs).

**Material and methods:** This cross-sectional study included 43 KTRs. Number of steps, total energy expenditure, average sleep and lying times, average metabolic equivalent (MET), and PA duration were assessed with SenseWear Armband. CVD risk was predicted using a web-based interactive tool (HeartScore program).

**Results:** CVD risk was negatively correlated with number of steps, average MET and PA duration. Average MET and PA duration were significantly higher in KTRs with low CVD risk compared to KTRs with moderate CVD risk ( $p = 0.004$  and  $p = 0.007$ , respectively). Average MET, PA duration and number of steps were significantly higher in KTRs with low CVD risk compared to KTRs with high CVD risk ( $p < 0.001$ ,  $p < 0.001$  and  $p = 0.009$ , respectively). Number of steps was higher in KTRs with moderate CVD risk compared to KTRs with high CVD risk ( $p = 0.010$ ). The linear regression analysis revealed that average MET was a predictor of CVD risk, accounting for 15.9% of the variance.

**Conclusions:** CVD risk is associated with accelerometer-based PA parameters and average MET is a significant predictor of CVD risk after kidney transplantation in KTRs. Wearable technologies can be used to objectively measure PA parameters in order to determine CVD risk and to monitor the efficiency of PA interventions after kidney transplantation.

**Key words:** accelerometer, cardiovascular disease risk, kidney transplantation, physical activity.

## Summary

Cardiovascular disease risk is negatively correlated with number of steps, average metabolic equivalent and physical activity duration in kidney transplant recipients. Average metabolic equivalent is a significant predictor of cardiovascular disease risk after kidney transplantation. Using wearable technologies to measure physical activity parameters in kidney transplant recipients could help to identify the risk of cardiovascular diseases.

## Introduction

Kidney transplantation is the preferred treatment option for end-stage renal disease, providing significant survival and better quality of life compared to long-term dialysis [1]. In spite of better short-term outcomes, cardiovascular diseases are the leading cause of morbidity

and mortality after kidney transplantation [2]. The annual cardiovascular event rate was reported to be 3.5–5% among kidney transplant recipients (KTRs), while it was responsible for 40–50% of all-cause deaths [3].

Physical inactivity is a modifiable, but mostly neglected, risk factor for morbidity and mortality, while it is a strong predictor of cardiovascular and all-cause deaths

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in KTRs [4–6]. Although moderate-to-vigorous physical activity is associated with better long-term health outcomes among KTRs, most of the patients do not meet the requirements for regular physical activity demands [7, 8]. Even though KTRs are more active in daily life compared to hemodialysis patients according to accelerometer-based measurements, they still show high volumes of sedentary time and low volumes of health-enhancing physical activity [9, 10].

Similar to the general population, physical inactivity is associated with increased cardiovascular disease (CVD) risk and all-cause mortality among KTRs [6, 11]. The limited data indicating this relationship in kidney transplant literature included only questionnaire-based physical activity measurements [6, 7, 11]. However, self-administered questionnaires have disadvantages concerning over- and/or underestimation of physical activity level, whereas accelerometers provide objective measurements of several physical activity indicators such as energy expenditure, number of steps, average sleep time, etc. Although accelerometers have been used to determine physical activity level in KTRs in previous studies [9, 10], there has been no study investigating the relationship between accelerometer-based physical activity parameters and CVD risk in this group.

## Aim

The aim of the current study was to determine the relationship between physical activity parameters measured by a biaxial accelerometer and CVD risk and to investigate whether physical activity parameters are determinants of CVD risk in KTRs.

## Material and methods

### Subjects

This cross-sectional study included 43 KTRs recruited from the outpatient kidney transplant clinic in the Division of Nephrology, Department of Internal Medicine, Dokuz Eylul University between February 2022 and December 2023. Participants over 18 years of age who had undergone kidney transplant surgery at least 6 months prior to study initiation were included in the study. Pregnancy, multi-organ transplantation, severe visual impairment, presence of neurological diseases (e.g. Parkinsonism, stroke, epilepsy), history of lower extremity injury or surgery affecting participation in daily life, inability to walk independently and cognitive problems (Mini Mental State Examination test score < 24) were the exclusion criteria for the current study. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and the Institutional Non-invasive Research Ethics Board of Dokuz Eylul University (Protocol number: 6039-GOA, Approval number: 2022/4203). All subjects gave written consent to participate in the study after receiving appropriate verbal and written information.

### Study protocol

Demographic (age, gender, body mass index) and clinical variables (time since diagnosis, time of transplantation, donor type, immunosuppression regimen, etc.) were recorded.

### Physical activity

We used the SenseWear Armband (BodyMedia, Inc., Pittsburgh, PA, USA) is a biaxial activity monitor that measures physical activity level through sensors for heat flow, skin temperature, and galvanic skin responses. The monitor was attached with the elastic strap around the non-dominant arm (over the triceps muscle) and used to quantify a 7-day physical activity profile. The device measures number of steps, total energy expenditure (calories), average sleep time during the day and night (minutes), average lying time during the day and night (minutes), average metabolic equivalent (MET), active energy expenditure (calories) consumed during moderate intensity (3 MET) physical activity and physical activity duration (minutes, 3 MET) [12].

### Cardiovascular disease risk

The HeartScore program, a web-based interactive tool, was used to predict the risk of CVD ([https://www.heartscore.org/tr\\_TR/access-heartscore](https://www.heartscore.org/tr_TR/access-heartscore)). The program is based on SCORE (Systematic Coronary Risk Evaluation) risk charts derived from 12 prospective studies from 11 European countries [13]. The program calculates the 10-year disease risk after entering factors such as gender, age, total cholesterol, systolic blood pressure, and smoking status. Subjects are classified as follows according to their HeartScore score: low risk: < 1%, moderate risk: ≥ 1% to < 5%, high risk: ≥ 5% to < 10% and very high risk: ≥ 10%.

### Statistical analysis

SPSS Version 29.0 for Windows (IBM Corp.) was used for data analysis. Descriptive statistics (i.e., means, standard deviations, and frequencies) were used to summarize the participants' demographic and clinical characteristics. The Shapiro-Wilk test, histogram and probability graphs were used to assess the normality of data distribution. Based on these results, the variables in comparisons of physical activity according to CVD risk factors were not normally distributed. Non-parametric tests were used for this statistical analysis. However, the other variables were normally distributed, and parametric tests were used for correlation and regression analysis.

Pearson's correlation coefficient was used to determine the quantitative correlations between accelerometer-based physical activity parameters and CVD risk. The strength of correlations was classified as very weak ( $r = 0-0.19$ ), weak ( $r = 0.2-0.39$ ), moderate ( $r = 0.40-0.59$ ), strong ( $r = 0.6-0.79$ ), and very strong ( $r = 0.8-1$ ).

Significantly correlated variables were examined by linear regression analysis to determine the predictors of CVD risk in KTRs. The enter method of the SPSS program was used for regression analysis.

Physical activity parameters were compared between the groups of KTRs classified according to their HeartScore score with the Kruskal-Wallis test. Significant results were analyzed by post-hoc tests using the Mann-Whitney U test with Bonferroni correction for pairwise comparisons. The level of significance was set at 0.05, except for post-hoc analysis, in which the significance level was set at 0.016 (0.05/3) after Bonferroni correction.

**Table I.** Demographic and clinical characteristics, physical activity parameters and cardiovascular disease risk scores of kidney transplant recipients

Parameter	Mean ± SD or n (%)
Age [years]	44.24 ±13.91
Gender:	
Female	19 (44.2)
Male	24 (55.8)
Body mass index [kg/m <sup>2</sup> ]	26.42 ±4.60
Pre-transplant dialysis duration [months]	45.73 ±80.65
Pre-transplant dialysis type:	
Hemodialysis	22 (51.2)
Peritoneal dialysis	9 (20.9)
Hemodialysis and peritoneal dialysis	2 (4.7)
Donor type:	
Live	24 (55.8)
Cadaveric	19 (44.2)
Time passed after kidney transplantation:	
< 5 years	11 (25.6)
5–15 years	18 (41.9)
> 15 years	14 (32.6)
Education:	
< Senior high school	10 (23.3)
≥ Senior high school	33 (76.7)
Employment status:	
Employed/student	27 (62.8)
Unemployed	8 (18.6)
Retired	8 (18.6)
Physical activity parameters:	
Total energy expenditure [joules]	74447.07 ±18778.89
Active energy expenditure (3.0 METs) [joules]	18069.37 ±12786.80
Physical activity time (3.0 METs) [min]	1054.51 ±702.21
Average metabolic equivalent [MET]	1.54 ±0.27
Lying time [min]	3519.49 ±559.53
Sleep time [min]	2759.42 ±444.40
Steps per day	7163.75 ±3213.50
HeartScore (%)	3.84 ±3.11

MET – metabolic equivalent. Values are expressed as mean ± standard deviations or number of individuals (%).

Prior to the study, power analysis was performed using the G Power 3.0.10 program based on the results of the study of Carvalho *et al.* and 39 subjects were found adequate considering the 95% (5% type I error level) confidence interval and 80% power [9].

## Results

Forty-three KTRs were enrolled in the study. Table I shows demographic and clinical variables, physical activity parameters and CVD risk score of the subjects. Table II shows correlations between physical activity parameters and CVD risk score. Physical activity time, average MET and step counts were negatively correlated with CVD risk score ( $p < 0.05$ ) (Table II).

Table III shows the comparisons of physical activity parameters between KTRs with different CVD risk. Physical activity time, average MET and number of steps were significantly different between KTRs with low, moderate and high CVD risks ( $p < 0.001$ ,  $p < 0.001$  and  $p = 0.012$ , respectively) (Table III). Post hoc analysis showed longer physical activity time in KTRs with low CVD risk than KTRs with moderate and high CVD risks ( $p = 0.007$  and  $p < 0.001$ , respectively) (Table III). The average MET was significantly higher in KTRs with low CVD risk than KTRs with moderate and high CVD risks ( $p = 0.004$  and  $p < 0.001$ , respectively) (Table III). The step count was significantly lower in KTRs with high CVD risk than low and moderate CVD risks ( $p = 0.009$  and  $p = 0.010$ , respectively) (Table III).

Linear regression analysis was performed to determine the predictors of CVD risk in KTRs. The regression analysis revealed that average MET was a significant and independent predictor of CVD risk in KTRs, explaining 15.9% of the variance in the HeartScore. The regression model was accepted as adequate as the  $F$  value was significant ( $F = 7.764$ ,  $p = 0.008$ ) (Table IV). The regression equation for prediction of the CVD risk score was calculated using the explanatory variable (average MET) and coefficients in KTRs (Table IV). The regression equation for KTRs is: CVD risk score = 11.034 + (−4.656 × average MET).

**Table II.** Correlations between physical activity parameters and cardiovascular disease risk score in kidney transplant recipients

Parameter	HeartScore	
	$r$	$P$ -value
Total energy expenditure [joules]	−0.276	0.073
Active energy expenditure (3.0 METs) [joules]	−0.285	0.064
Physical activity time (3.0 METs) [min]	−0.361	0.017*
Average metabolic equivalent [MET]	−0.399	0.008**
Lying time [min]	0.134	0.391
Sleep time [min]	0.031	0.845
Steps per day	−0.315	0.039*

MET – metabolic equivalent, \* $p < 0.05$ , \*\* $p < 0.01$ , Pearson correlation coefficient.

**Table III.** Comparisons of physical activity parameters between kidney transplant recipients with different cardiovascular disease risks

Parameter	HeartScore/low risk (n = 15)	HeartScore/moderate risk (n = 14)	HeartScore/high risk (n = 12)	P-value
Total energy expenditure	69818.00 (57721.00–100199.00)	74161.00 (68583.00–88429.50)	66730.00 (60399.75–72081.50)	0.435
Active energy expenditure	19664.00 (13406.00–36212.00)	16989.00 (7033.00–23323.50)	9761.50 (8181.50–15945.00)	0.056
Physical activity time	1299.00 (1145.00–1612.00)	939.50 (435.25–1272.75)	577.00 (440.25–930.55)	< 0.001** Post hoc: 1 > 2 <sup>§</sup> , 1 > 3 <sup>§</sup>
Average metabolic equivalent	1.70 (1.60–1.90)	1.50 (1.38–1.63)	1.40 (1.30–1.50)	< 0.001** Post hoc: 1 > 2 <sup>§</sup> , 1 > 3 <sup>§</sup>
Lying time	3305.00 (3207.00–3662.00)	3317.00 (2961.50–3920.00)	3742.00 (3341.00–4030.00)	0.161
Sleep time	2656.00 (2566.00–2849.00)	2733.00 (2164.50–3045.00)	2808.00 (2539.00–3112.25)	0.631
Steps per day	7571.00 (5712.00–10567.00)	8017.29 (5517.86–11387.75)	4500.57 (2984.64–7055.07)	0.012* Post hoc: 1 > 3, 2 > 3

\**p* < 0.05, \*\**p* < 0.001, Kruskal-Wallis test; <sup>§</sup>*p* < 0.016, Bonferroni correction. Values expressed as median and interquartile ranges (25<sup>th</sup>–75<sup>th</sup>).

**Table IV.** Linear regression model of cardiovascular disease risk in kidney transplant recipients

Model	B	SE	β	t	P-value	95% CI
Constant	11.034	2.618		4.215	< 0.001**	5.748 to 16.321
Average metabolic equivalent	-4.656	1.671	0.399	-2.786	0.008*	-8.031 to -1.281

*R* = 0.399, *R*<sup>2</sup> = 0.159, adjusted *R*<sup>2</sup> = 0.139 (*F* = 7.764, *p* = 0.008\*), SE – standard error, β – standardized regression coefficient, CI – confidence interval, \**p* < 0.05, \*\**p* < 0.001.

## Discussion

In our study, in which we investigated the relationship between physical activity parameters measured by a 7-day worn accelerometer and CVD risk in KTRs, we found negative correlations between CVD risk and number of steps, average MET and physical activity duration. Moreover, average MET was a significant predictor of CVD risk in KTRs. Average MET and physical activity duration were significantly higher in KTRs with low CVD risk compared to KTRs with moderate CVD risk. Average MET, physical activity duration and number of steps were significantly higher in KTRs with low CVD risk compared to KTRs with high CVD risk. Number of steps was higher in KTRs with moderate CVD risk compared to KTRs with high CVD risk.

There is an increasing interest in using accelerometers to measure physical activity parameters accurately in various populations. However, studies using accelerometer to measure physical activity in KTRs are limited. Carvalho *et al.* compared physical activity in daily life between KTRs and hemodialysis patients. KTRs engaged in more active time per day than hemodialysis patients, with longer walking and standing durations. Moreover, 65% of KTRs were classified as active compared with only 20% of the hemodialysis group [9]. In that study, time since transplantation was a significant predictor for daily physical activity. Contrary to these findings, in another accelerometer-based study by Vallance *et al.*,

KTRs showed high volumes of sedentary time and low volumes of health-enhancing physical activity [10].

Similar to the general population, sedentary life style is associated with cardiovascular events, which are major causes of morbidity and mortality after kidney transplantation [4–7]. However, there are limited data indicating a direct relationship between physical activity and CVD risk in KTRs. Only four original articles investigating this relationship have been published [5–7, 14]. Kang *et al.* investigated cardiovascular risk factors among 4030 KTRs and found higher risk in KTRs who were the least physically active [5]. In Zelle *et al.*'s study, physical activity was negatively associated with metabolic syndrome, history of CVD, fasting insulin, and triglyceride concentration [6]. Parallel to all these findings, higher moderate-to-vigorous physical activity level was found to be associated with less post-transplant diabetes mellitus and cardiovascular and all-cause mortality independently of age, sex, and kidney function [7]. Totti *et al.* divided 42 KTRs into two groups as active and sedentary KTRs, according to World Health Organization recommendations (< 150 or > 150 min/week, respectively) and observed cardiovascular risks over a 3-year period [14]. They found an increase in the cardiovascular risk profile in sedentary KTRs and a decrease in the active group [14]. Similar to our findings, these results support the preventive effects of being physically active on potential cardiovascular risk factors in KTRs.

In all these studies investigating the relationship between physical activity and CVD risk, physical activity was measured using a self-reporting, questionnaire-based survey method at a single point in time. To the best of our knowledge, this is the first study investigating the relationship between physical activity and CVD risk in KTRs using a 7-day worn accelerometer. Parallel to the previous findings, our results indicated a negative relationship between CVD risk and number of steps, average MET and physical activity duration in KTRs. Moreover, according to the regression analysis, average MET was a significant predictor of CVD risk.

We also divided our KTRs into three groups, having low, moderate and high CVD risk. Physical activity parameters including average MET, physical activity duration and number of steps also differed between these groups. According to our findings, CVD risk worsens as the physical activity parameters decrease.

The relatively small sample size is the main limitation of our study while the strength is the use of an accelerometer to measure physical activity level. This is the first study investigating the relationship between CVD risk and physical activity in KTRs, in which wearable technology is used to determine accurate physical activity parameters. Moreover, by applying a regression analysis, we could identify a predictor of CVD risk among physical activity parameters after kidney transplantation.

## Conclusions

CVD risk was negatively correlated with the number of steps, average MET and physical activity duration in KTRs. Moreover, average MET was found to be a significant predictor of CVD risk. CVD risk worsens as the measurable physical activity parameters decrease after kidney transplantation. Using wearable technologies to assess daily physical activity parameters during a certain period of time (7 days) rather than using questionnaire-based surveys at a single time point provides more accurate results and reveals the direct relationship between physical activity and CVD risk among KTRs.

## Funding

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## Ethical approval

The study was conducted in accordance with the ethical standards the Institutional Non-invasive Research Ethics Board of Dokuz Eylul University (Protocol number: 6039-GOA, Approval number: 2022/4203).

## Conflict of interest

The authors declare no conflict of interest.

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