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Peer-reviewed author version

Sentandreu-Mañó, Trinidad; Marques-Sule, Elena; Almenar-Bonet, Luis; Tomás, José; HANSEN, Dominique; Deka, Pallav; López-Vilella, Raquel; Klompstra, Leonie & VILACA CAVALLARI MACHADO, Felipe (2025) Predicting Sarcopenia and Frailty Risk in Patients Post Heart Transplantation. In: Clinical transplantation, 39 (1) (Art N° e70027).

DOI: 10.1111/ctr.70027
Handle: http://hdl.handle.net/1942/45012

Predicting sarcopenia and frailty risk in patients post heart transplantation

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ABSTRACT

Introduction. Currently there is scarce evidence on the prevalence and factors associated with sarcopenia risk or frailty risk in patients post heart transplantation (HTx). The objective of this study was to analyze the influence of sociodemographic, lifestyle, physical, and psychological factors on sarcopenia and frailty risk in patients post-HTx.

Methods. 133 patients post-HTx (59.4% men, mean age 56.5±12.7 years) participated in this cross-sectional study. The main outcomes were sarcopenia and frailty risk, and potential related predictors were comorbidities, time from transplantation, body mass index, sociodemographic factors, musculoskeletal pain, functional capacity, kinesiophobia, sleep problems, depression, physical activity, and diet quality. Multiple regression models were performed with all predictors, including polynomial regressions for predictors with a non-linear relationship.

Results. The predictor variables explained 73.93% of frailty's variance. Functional capacity (with non-linear relationship) and diet quality were significant predictors of frailty risk, whilst diabetes and physical activity were marginally significant. On the other hand, the predictors explained 73.52% of sarcopenia's variance. Diabetes, functional capacity (with non-linear relationship) and kinesiophobia were significant predictors of sarcopenia risk, whilst pain intensity and diet quality were marginally significant.

Conclusion. Multivariate analysis conducted on patients post-HTx revealed that functional capacity was associated with both sarcopenia and frailty risk. Additionally, diet quality was a predictive factor of frailty, while diabetes and kinesiophobia were predictors of sarcopenia. These findings emphasize the importance of proper management to prevent frailty and sarcopenia, which share common associated factors.

Key words: Sarcopenia; Frailty; Screening; Risk;

INTRODUCTION

Heart transplantation (HTx) is a Class 1 recommendation for patients with advanced heart failure (HF), refractory to medical/device therapy and who do not have absolute contraindications.[1] Remarkably, post-transplant survival rates have demonstrated significant improvement over time, with the median survival after adult HTx performed between 2002 and 2009 reaching 12.5 years.[2] The number of HTx appears to remain relatively stable in Europe, while steadily increasing in the United States and other regions across the globe, a trend observed from 2008 to 2016.[2] As a consequence, the number of individuals living with heart transplants is expected to rise in the coming years. These individuals are more prone to conditions such as frailty and sarcopenia, which are increasingly common with aging and cardiovascular diseases.[3–5] Screening for these conditions is crucial, as the management of these patients may require adaptations to exercise treatments and a more personalized approach to care.

Frailty and sarcopenia differ in nature, with frailty being a broader, age-related decline in various physiological systems affecting physical, cognitive, and social aspects, while sarcopenia is muscle disease characterized by low muscle strength and mass, which may contribute to frailty.[5–7] Nearly half of all HF patients are affected by frailty,[8,9] and patients with HF and frailty face a 1.5-fold increased risk of death or hospitalization compared to patients with HF without frailty.[9] Notably, frailty within 6 months before HTx is independently associated with increased mortality and prolonged hospitalization after transplantation.[10] Moreover, patients with a low psoas muscle area before HTx had a trend toward a three-fold increase in mortality risk (odds ratio, 3.03; 95% CI, 0.92–9.97).[11] Combining evidence from studies on sarcopenia and frailty in older adults, it becomes evident that both conditions, significantly elevate the risk of disability in activities of daily living (ADL).[12,13] While there is an overlap in the definitions of frailty and sarcopenia, it is essential to disentangle the shared and distinct factors associated with each condition. A more comprehensive understanding of their associate factors may lead to the development of targeted interventions to reduce sarcopenia and frailty risk in patients post-HTx.

Therefore, this study aimed to: 1) explore the presence of sarcopenia risk, frailty risk, or both conditions in a sample of patients post-HTx; 2) comprehensively analyze the impact of sociodemographic, lifestyle, physical, and psychological factors on sarcopenia

and frailty risk in patients post-HTx. By addressing these objectives, this study seeks to provide valuable insights into the factors influencing frailty and sarcopenia risk among patients post-HTx, ultimately enhancing clinical recommendations and contributing to the long-term health and quality of life of these individuals.

METHODS

Design and participants

This study enrolled patients from an outpatient clinic in Spain during the period of June 2021 to June 2022 using a cross-sectional design. The criteria for inclusion were patients who had undergone HTx and had stable organ function, as well as the ability to walk independently. Patients who had recently experienced thoracic pain symptoms were not included in the study. The research followed the guidelines of the Declaration of Helsinki and informed consent from the participants was obtained prior to conducting the assessments. Approval for the study was granted by the Ethics Committee of the Institutional Board (IE1529273). Patients were requested to complete a set of questionnaires during a single visit with all assessments following the same order. The data collection session lasted approximately 45 to 60 minutes for each participant.

Measurements

All patients provided demographic and clinical data. A clinical interview was conducted to gather information from patients including gender, age, marital status, working status, education, months since transplantation, cardiovascular risk factors (diabetes, hypertension, dyslipidaemia, smoking), and body mass index (BMI).

Outcome variables

Frailty risk was assessed using the FRESH-screening tool, which comprised five indicators related to tiredness, falls, endurance, needing support while shopping and three or more visits to the emergency department in the past 12 months. Participants were

considered to be at risk of frailty if they responded affirmatively to two or more of these five indicators.[14] The internal consistency estimate in this sample was 0.72.

Sarcopenia risk was assessed with the SARC-F questionnaire. This instrument comprises five items: strength, assistance in walking, rising from a chair, climbing stairs, and experiencing falls. Each item is assigned a score ranging from 0 to 2, resulting in a total score ranging from 0 to 10. Higher scores indicate a greater risk of sarcopenia, and patients with a score of ≥4 points are considered symptomatic.[15] The internal consistency estimate in this sample was 0.87.

Predictor variables

Potential variables analyzed were musculoskeletal pain (pain problems, pain intensity, and pain frequency), functional capacity, kinesiophobia, sleep problems, depression, physical activity, and diet quality (healthy nutrition and adherence to Mediterranean diet).

Musculoskeletal pain was assessed using the following two questionnaires: the Musculoskeletal System Assessment Inventory (MSSAI)[16] and Cornell Musculoskeletal Discomfort Questionnaire (CMDQ)[17] measuring pain problems, pain intensity, and pain frequency. The MSSAI comprises two sections.[16] The first section consists of seven items that evaluate general information concerning musculoskeletal pain, using binary response choices (yes=1 or no=0). By summing the scores of all items, a variable named *pain problems* was obtained. Scores range from 0 to 7, with higher values indicating a greater presence of musculoskeletal pain issues. The internal consistency estimate for this sample was 0.87. The second section includes information on *pain intensity*. Participants indicated on a human body diagram the specific areas where they experienced musculoskeletal pain, designating zone 1 as the most painful location and zone 2 as the second most painful location. Using a five-point Likert scale ranging from 1 (mild pain) to 5 (unbearable pain), numeric values were assigned to represent the intensity of pain felt in zone 1 and zone 2. The assigned scores for each response were then summed to calculate a total score, which ranged from 2 to 10. A higher score on this variable, called as pain intensity, indicated a greater intensity of pain experienced. Internal consistency for this sample was 0.59. The Spanish version of CMDQ was employed to assess the musculoskeletal *pain frequency*. Patients indicated the frequency of pain experienced in zone 1 (most painful location) and zone 2 (second most painful location) using a five-

level scale: never (0 points), 1-2 times a week (1 point), 3-4 times a week (2 points), once a day (3 points), and many times a day (4 points).[17] The scores from each question were summed to generate a total score that ranged from 0 to 8 points, with higher scores indicating more frequent pain. The internal consistency estimate for this sample was 0.57.

Functional capacity was assessed using the Duke Activity Status Index (DASI), a questionnaire that correlates with peak oxygen uptake and metabolic equivalents. This tool comprises 12 activities related to personal care, ambulation, household tasks, sexual function and recreational activities. Each item answered positively is assigned an estimated weight, resulting in total scores ranging from 0 to 58.2. Higher scores indicate better functional capacity.[18] Internal consistency was 0.89 in this sample.

Kinesiophobia was assessed with the Tampa Scale for Kinesiophobia-11 (TSK-11). The TSK-11 comprises 11 components with a four-point Likert scale ranging from 1 (strongly disagree) to 4 (strongly agree). These values yield a total score ranging from 11 to 44, with higher scores indicating greater fear of movement.[19] Internal consistency was 0.84 in this sample.

Sleep problems were assessed using the Minimal Insomnia Symptom Scale (MISS), a brief questionnaire designed for screening insomnia.[20] The MISS comprises three items, and the responses are categorized in a five-point Likert scale ranging from 0 (none) to 4 (severe problems). Total score ranges from 0 to 12, with higher scores indicating higher sleeping difficulties. Internal consistency was 0.82 in this sample.

Depression was assessed using the 8-item Neuro-QOL Depression -Short Form.[21] Each item consists of five response options, ranging from 1 (never) to 5 (always). The total score ranges from 8 to 40, with higher scores indicating higher levels of depression. In this sample, internal consistency was 0.91.

Physical activity was assessed using the short-form International Physical Activity Questionnaire (IPAQ).[22] The short-form IPAQ includes items identifying the frequency and duration of four activity categories: vigorous activities, moderate activities, walking, and time spent sitting on a chair in the last week (sedentary time). The responses provided for each activity category were converted into time in minutes per week. To determine the overall volume of physical activity, the sum of vigorous, moderate, and walking

activities was calculated in terms of metabolic equivalent of task-minutes per week (METS·min·week).

Diet quality was assessed using two tools: the Index of Healthy Nutrition (IHN)[23] and the Mediterranean Diet Adherence Screener (MEDAS-14)[24]. Regarding the IHN, participants were asked about the frequency they consumed ten food groups. The overall IHN score was derived by summing up the individual scores obtained for each food group. A higher IHN score indicates a healthier dietary pattern.[23] Reliability in this sample was 0.74. The MEDAS-14 questionnaire consists of 14 questions, including 12 related to the frequency of food consumption and two concerning specific eating habits associated with the Mediterranean diet. Each participant's response was assigned a value of either 0 or 1. The resulting score ranges from 0 to 14, with higher scores indicating greater adherence to Mediterranean diet.[24] Reliability in this sample was 0.54.

Statistical analyses

All statistical analyses were performed in R.[25] These analyses included, descriptive statistics, smoothing (lowess) functions to associate quantitative predictors to frailty and sarcopenia, and multiple regressions to predict the outcomes (frailty and sarcopenia). Specifically, the multiple regression analyses employed the best subsets regression procedure (or the all-possible subsets regression procedure), which general idea was to select the subset of predictors (among all potential models) that do the best at meeting some well-defined objective criterion, in this case having the largest adjusted R-square.[26] The subsets regression was performed with the package leaps in R.[27] Regarding sample size calculations, the estimated a priori sample size in G*Power 3.1.9.7, with alpha of .05, power of .80, 13 predictors and a medium effect size for the coefficients (f-square= .15), was 131.[28]

RESULTS

A total of 133 patients (59.4% men) were included in the study. The mean age was 56.5 years (SD=12.7) ranging from 23 to 81 years. Descriptive statistics in terms of means, standard deviations and frequencies for all the variables under study are presented in Table 1. With regard to the cross-classification of frail and sarcopenic people, 15% of

the sample were both, 20.3% were frail but not sarcopenic, 0.8% sarcopenic but not frail, and the remaining 63.9% were neither classified as frail nor sarcopenic. Additionally, to these univariate descriptive statistics, all potential predictors of frailty and sarcopenia risk were associated bivariately with the two outcomes. These further analyses allow us to see which predictors were significantly associated in a bivariate way, either with frailty or with sarcopenia, and then proceed to further analysis.

Results from the bivariate associations between the predictors and outcomes (Table 2) show that there are a number of variables strongly associated to both frailty and sarcopenia. Among the statistically significant relations, kinesiophobia, sleep problems, diabetes, and depression were positively related to both sarcopenia and frailty. Regarding the significant and negative associations with sarcopenia and frailty, those were: functional capacity, physical activity, healthy nutrition, adherence to Mediterranean diet and education. Additionally, the three markers of pain (problems, intensity and frequency) were significant and positively related to sarcopenia risk.

Once linear associations were calculated between the outcomes (frailty and sarcopenia risk) and the quantitative predictors, we further analysed these relationships to try to find non-linearity. Accordingly, lowess functions were calculated for each relation between outcome and predictors. These smoothing functions show up that there were several potential non-linear relations with frailty and sarcopenia. Specifically, functional capacity, sleep problems and physical activity showed non-linear relations with both frailty and sarcopenia risk. Additionally, kinesiophobia had a non-linear relation with frailty while adherence to Mediterranean diet had a non-linear relation with sarcopenia. When we establish the multivariate models to predict the outcomes, those non-linear relations were also modelled as quadratic terms.

Results of the multiple regressions models estimated to predict risk of frailty and risk of sarcopenia are presented in Table 3. The best multiple regression to predict frailty included 13 predictors, of which functional capacity (quadratic effect) and healthy nutrition were statistically significant, and negative. Therefore, a healthier dietary pattern and functional capacity are associated to less likelihood of being frail. However, the relationship between frailty and functional capacity was non-linear. This relation is shown in Figure 1 (a). As observed, as functional capacity increases, frailty decreases, but only until one point in which the relation almost reaches a plateau. It is also worth noting that

two associations were marginally significant ($p < .1$), those of diabetes and physical activity. All in all, the predictors explained 73.93% of frailty risk's variance.

Regarding the multiple regression to predict sarcopenia, the model with highest explicative value included eight predictors, as seen in Table 3. The predictors significantly ($p < .05$) associated to sarcopenia were diabetes, functional capacity (quadratic effect), and kinesiophobia. Diabetes was positively associated to sarcopenia, as it was kinesiophobia. Therefore, kinesiophobia and diabetes seem risk factors for sarcopenia. On the other hand, functional capacity was negatively associated with sarcopenia, thus as functional capacity increases, the risk of being sarcopenic decreases. However, and as it was the case with frailty, the relationship between sarcopenia and functional capacity was non-linear. This relation is shown in Figure 1 (b). As observed, as functional capacity increases, sarcopenia decreases, but only until one point in which the relation almost reaches a plateau. It is also worth noting there was also marginally significant association ($p < .1$) with pain intensity which had a positive association with sarcopenia, and with adherence to Mediterranean diet with a negative association. Overall, the predictors explained 73.52% of sarcopenia risk's variance.

DISCUSSION

Our findings underscore the intricate interplay between a range of potential predictors and frailty or sarcopenia risk in patients post-HTx. Notably, we observed significant bivariate associations between several predictors and both frailty and sarcopenia risk, suggesting potential avenues for intervention and prevention strategies. Moreover, our investigation revealed non-linear relationships between functional capacity and the risk of developing frailty or sarcopenia. These insights contribute to a deeper understanding of the underlying mechanisms driving frailty and sarcopenia, offering valuable implications for clinical practice and future research.

Functional capacity emerged as a significant predictor of both sarcopenia and frailty risk, exhibiting a non-linear association pattern. A previous study aimed at comparing preoperative subjective assessment, cardiopulmonary exercise testing, DASI, and N-terminal pro-B-type natriuretic peptide for predicting death or complications after major elective non-cardiac surgery revealed that lower DASI scores were predictive of 30-day death or myocardial infarction, as well as 30-day death or myocardial injury.[29]

Notably, the Spearman correlation coefficient between DASI scores and peak oxygen consumption was 0.41 ($p<0.0001$), indicating a relationship that appears to be more linear in nature.[29] A possible explanation for the non-linear association pattern is the limited range of total scores in our questionnaires (ranging from 0 to 5 for frailty risk and 0 to 10 for sarcopenia risk), which may exhibit a characteristic floor effect. This characteristic could imply that patients above a certain threshold level of functional capacity, as measured by the DASI questionnaire, would likely score close to zero on the scales, potentially resulting in a flattening or plateau in the association between functional capacity and sarcopenia/frailty risk. In patients with pulmonary hypertension a DASI score ≥26 was the optimal cut-off value to discriminate patients with better and worse long-term prognosis,[30] this is approximately the score when the association between functional capacity and sarcopenia/frailty risk start to flatten in this study (Figure 1).

Nutrition plays a crucial role in the multidimensional intervention in cardiac rehabilitation, particularly in frail or sarcopenic patients, where poor nutritional status is often a key pathophysiological mechanism for these conditions.[7,31,32] Our study found an association between a healthier dietary pattern and lower frailty risk, consistent with previous research.[33,34] For instance, León-Muñoz et al.[33] examined the association between dietary patterns empirically derived from food consumption and the risk of frailty in older adults. Their study revealed that a 'prudent' pattern showed a protective association with frailty, while a 'Westernized' pattern was associated with an increased risk of two frailty components: slow walking speed and weight loss.[33] Furthermore, a study investigated if protein-energy supplementation could prevent functional decline in frail older adults of low socioeconomic status.[34] Results indicated that protein-energy supplementation reduced the progression of functional decline in this group.[34] Hence, drawing from research conducted on elderly individuals without cardiovascular diseases, specific nutritional interventions—such as nutritional counselling and/or protein supplementation combined with exercise training—may hold promise for mitigating frailty among at-risk patients with cardiovascular disease.[31]

Our study revealed significant associations between diabetes and kinesiophobia as predictors of sarcopenia among patients post-HTx. The presence of diabetes poses a notable risk for sarcopenia, potentially due to insulin resistance in skeletal muscle. Notably, skeletal muscle in individuals with diabetes may exhibit both insulin resistance and anabolic resistance, intricate physiological and molecular mechanisms contributing

to muscle atrophy and sarcopenia.[35] Additionally, research exploring the mediational effect of ADL and kinesiophobia between cardiac function and health status in patients with chronic heart failure found that cardiac function not only directly, but also indirectly influenced health status through kinesiophobia and ADL.[36] These indirect effects accounted for 43% of the total effect.[36] Moreover, another study found that in patients hospitalized for cardiovascular disease, kinesiophobia is associated with cardiac anxiety, social complexity, educational level, and self-efficacy.[37] Furthermore, kinesiophobia decreased the likelihood of cardiac rehabilitation initiation by 8% per point.[37]

It is important to acknowledge several limitations of our study. Firstly, we did not employ recommended tools for frailty evaluation in cardiac rehabilitation, such as the Edmonton Frailty Scale or Clinical Frailty Scale from the CSHA study.[7] Another potential option is the recently proposed HFA Frailty Score, which was developed during a workshop convened by the Heart Failure Association.[5] This scoring system considers four main domains – clinical, functional, psycho-cognitive, and social – as determinants of frailty in HF patients. It's worth noting, however, that frailty has been shown to correlate with medical outcomes in the elderly, independent of the specific measurement tool used.[7] Moreover, while we employed the SARC-F questionnaire for assessing sarcopenia risk, it's important to note that modified versions of the SARC-F questionnaire, incorporating measurements such as calf or arm circumference, have demonstrated superior diagnostic performance compared to the original questionnaire. Additionally, our measures were self-reported, and utilizing physical activity monitors for measuring physical activity, exercise tests for functional capacity assessment, and handgrip strength, bioelectrical impedance analysis, or dual-energy X-ray absorptiometry for assessing muscle strength and mass would have provided more reliable data. On the other hand, two variables (pain intensity and pain frequency) present a low reliability. This may be due to the low number of indicators these variables have, or to the fact that these measures could have a “formative” nature. A formative measure happens when the indicators are considered to be the cause of the overall measure, and they may not covary at all, which in turn would made a low alpha by definition. That is, the overall measure is a function of the accumulation of indicators. Finally, although our models explain a substantial amount of variance for sarcopenia or frailty risk, it's essential to recognize that the sample size is relatively small, leading to certain predictors exhibiting associations that were marginally significant. Despite their marginal significance, it is noteworthy that in larger

sample sizes, these relationships may achieve statistical significance. Consequently, predictors such as diabetes and physical activity in frailty, as well as pain intensity and diet quality in sarcopenia, merit further investigation in larger samples. Such investigations could offer a more comprehensive understanding of their impact on the conditions under study.

CONCLUSION

In conclusion, although frailty and sarcopenia risk have common associated factors, proper management is crucial for preventing these conditions. When all these relevant biopsychosocial variables are explored by multilevel analysis in patients post-HTx, the findings show that healthier dietary pattern emerges as a predictive factor for frailty risk, while diabetes and kinesiophobia appear to be predictors of sarcopenia risk. Additionally, functional capacity exerts an impact on both conditions. Therefore, a comprehensive approach that addresses these modifiable risk factors is essential for effectively preventing and managing frailty and sarcopenia risk in patients post-HTx. Special attention should be given to patients post-HTx with diabetes and poor diet quality, as they may have a higher likelihood of experiencing both frailty and sarcopenia risk, an issue deserving further investigation. Finally, it seems important to address the kinesiophobia that patients may present and emphasize educating individuals on overcoming fear of movement, empowering them to feel safe and confident in their physical activity.

Funding statement
This work was supported by project PID2021-124418OB-I00 funded by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe".

Contribution statement
T.S-M. participated in study concept and design, acquisition of data, analysis and interpretation of data, drafting of the article, and statistical analysis. E.M-S. participated in study concept and design, acquisition of data, analysis and interpretation of data, drafting of the article, and statistical analysis. T. S-M and E. M-S are the co-first authors of this work. L.A-B, J.M.T, D.H, P.D, R.L-V and L.K. participated in study concept and design, analysis and interpretation of data, critical revision of the article for important intellectual content. F.V.C.M. participated in study concept and design, drafting of the article, analysis and interpretation of data, critical revision of the article for important intellectual content, and study supervision.

Conflict of interest
The authors declare no conflicts of interest.

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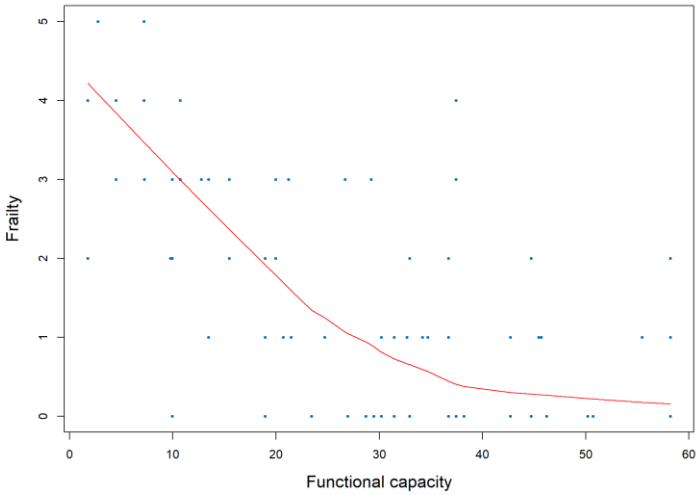
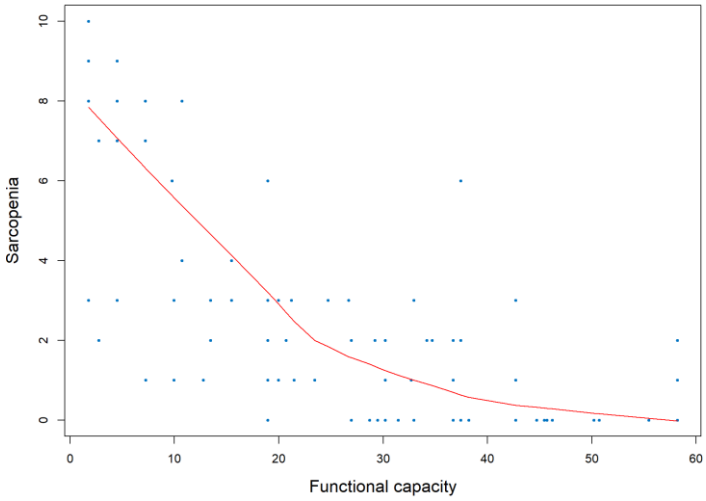
Figure 1. Non-linear relations of functional capacity with frailty (a) and sarcopenia risk (b).



(a)



(b)

Table 1. Descriptive statistics for the variables under study are shown as means and standard deviations or as absolute and relative frequencies.

Variable	Participants (n=133)
Male, n (%)	79 (59.4)
Age (years)	56.5±12.7
Marital status, n (%)	
Married/partner	104 (78.2)
Single	17 (12.8)
Widow	6 (4.5)
Divorced	6 (4.5)
Working status, n (%)	
Working	10 (7.5)
Unemployed	13 (9.8)
Retired	110 (82.7)
Education, n (%)	
No education	10 (7.5)
Primary	31 (23.3)
Secondary	59 (44.4)
University	33 (24.8)
Time since transplantation	55±41.9
Cardiovascular risk factors, n (%)	
Hypertension	43 (32.3)
Diabetes	35 (26.3)
Dyslipidaemia	31 (23.3)
Smoking, n (%)	
Smoker	1 (0.8)
Former	81 (60.9)
Never	51 (38.3)
BMI (kg/m^2)	24.5±4.1
FRESH total score	1.3±1.48
SARC-F total score	1.9±2.67
MSSAI pain problems	2.8±2.4
MSSAI pain intensity	2.4±2.2
CMDQ pain frequency	1.5±1.7
DASI	31.8±18.1
TSK-11	25.8±6.8
MISS	4.7±3.2
NeuroQOL depression	14.1±6.5
IPAQ (MET min week)	1574.7±1579.9
IHN	73.8±12.3
MEDAS-14	9.9±2

Data are described as mean values, standard deviations (SD), or absolute and relative frequencies. BMI: body mass index; MSSAI: Musculoskeletal System Assessment Inventory; CMDQ: Cornell Musculoskeletal Discomfort Questionnaire; DASI: Duke Activity Status Index; TSK-11: Tampa Scale for Kinesiophobia-11; MISS: Minimal Insomnia Symptom Scale; IPAQ: International Physical Activity Questionnaire; IHN: Index of Healthy Nutrition; MEDAS-14: Mediterranean Diet Adherence Screener.

Table 2. Bivariate associations between the predictors and outcomes (frailty risk and sarcopenia risk).

	Frailty risk		*Sarcopenia risk*	
Predictor	*r/t/F*	*p-value*	*r/t/F*	*p*
Gender	0.11	>.05	1.15	>.05
Marital status	0.91	>.05	0.74	>.05
Working status	-0.19	>.05	0.84	>.05
Education	5.41	<.01	3.28	<.05
Diabetes	-3.28	<.01	-2.68	<.01
Hypertension	-0.52	>.05	-0.31	>.05
Dyslipidaemia	-0.44	>.05	-0.35	>.05
Smoking	0.58	>.05	0.88	>.05
Age	.00	>.05	-.07	>.05
Time since transplantation	-.01	>.05	-.06	>.05
BMI	-.17	<.10	-.22	<.05
Pain problems	.24	<.10	.32	<.01
Pain intensity	.17	<.10	.28	<.01
Pain frequency	.14	>.05	.21	<.01
Functional capacity	-.75	<.01	-.73	<.01
Kinesiophobia	.63	<.01	.58	<.01
Sleep problems	.33	<.01	.28	<.01
Frailty risk	--	--	.81	<.01
Sarcopenia risk	.81	<.01	--	--
Depression	.33	<.01	.36	<.01
Physical activity	-.51	<.01	-.48	<.01
Healthy nutrition	-.36	<.01	-.39	<.01
Adherence to Mediterranean diet	-.36	<.01	-.46	<.01

Note: r= Pearson correlation coefficient; t= t-test; F=F-statistic (ANOVA); correlations, t-tests or ANOVAs were applied depending on the nature of the variables.

Table 3. Multiple linear regressions to predict frailty and sarcopenia risk.

	Frailty risk				*Sarcopenia risk*		
Predictor	*Estimate*	*t-value*	*p*	*Predictor*	*Estimate*	*t-value*	*p*
Intercept	4.89	4.35	<.01	Intercept	11.32	5.13	<.01
Age	0.12	-1.33	.183	Age	-0.01	-1.27	.206
Gender (male)	0.12	0.85	.395	Diabetes	0.62	2.08	.038
Marital status				BMI	-0.04	-1.36	.173
Single	0.07	0.26	.796				
Widow	0.43	-1.21	.227				
Divorced	0.38	1.08	.280				
Working (retired)	0.28	1.91	.236	Pain intensity	0.12	1.94	.054
Education				Functional capacity			
Primary	0.33	1.07	.286	Linear	-0.26	-9.35	<.01
Secondary	0.41	1.30	.195	Quadratic	0.002	6.75	<.01
University	0.09	0.27	.781				
Diabetes	0.30	1.82	.070	Kinesiophobia	0.05	1.98	.049
Time since transplantation	0.01	1.59	.113	Sleep problems			
				Linear	0.13	0.93	.353
				Quadratic	-0.02	-1.27	.207
BMI	-0.02	-0.87	.325	Mediterranean diet adherence			
				Linear	-0.74	-1.85	.066
				Quadratic	0.02	1.15	.298
Pain frequency	-0.05	-1.21	.226				
Functional capacity							
Linear	-0.11	-6.43	<.01				
Quadratic	0.01	3.96	<.01				
Kinesiophobia							
Linear	-0.02	-0.29	.766				
Quadratic	0.01	0.81	.418				
Physical activity							
Linear	0.00	-1.67	.090				
Quadratic	0.00	1.62	.101				
Healthy diet	0.01	-2.34	.020				

Note: Estimates are unstandardized regression slopes; BMI: body mass index.