Received: 30 April 2023 | Revised: 7 June 2023 | Accepted: 8 June 2023

DOI: 10.1002/ajhb.23945

ORIGINAL ARTICLE

American Journal of Human Biology WILEY

Fit-Fat Index is better associated with heart rate variability compared to fitness and fatness alone as indicators of cardiometabolic human health

Ginés Navarro-Lomas[1] | Abel Plaza-Florido[2,3] | Alejandro De-la-O[1] | Manuel J. Castillo[1] | Francisco J. Amaro-Gahete[1,2,4,5]

[1]EFFECTS-262 Research Group, Department of Physiology, Faculty of Medicine, University of Granada, Granada, Spain

[2]PROFITH "PROmoting FITness and Health Through Physical Activity" Research Group, Sport and Health University Research Institute (iMUDS), Department of Physical and Sports Education, Faculty of Sport Sciences, University of Granada, Granada, Spain

[3]Pediatric Exercise and Genomics Research Center, Department of Pediatrics, School of Medicine, University of California at Irvine, Irvine, California, USA

[4]CIBER de Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Granada, Spain

[5]Instituto de Investigación Biosanitaria, ibs.Granada, Granada, Spain

Correspondence

Ginés Navarro-Lomas and Francisco J. Amaro-Gahete, EFFECTS-262 Research Group, Department of Physiology, Faculty of Medicine, University of Granada, Avda. de la Investigación 11 18016 Granada, Spain.

Email: ginesnl1@gmail.com and amarof@ugr.es

Funding information

Ministerio de Educación y Formación Profesional, Grant/Award Numbers: FPU16/02760, FPU14/04172; National Institutes of Health, Grant/Award Number: U01 TR002004

Abstract

Objectives: Cardiorespiratory fitness and fatness indicators have been related to heart rate variability (HRV) parameters. The Fit-Fat Index (FFI) is a single index combining cardiorespiratory fitness and fatness indicators. To the best of our knowledge, no studies have previously analyzed whether FFI are related to cardiac autonomic nervous system activity assessed through HRV parameters. This study aimed (i) to examine the association of cardiorespiratory fitness, fatness indicators, and FFI with HRV parameters; and (ii) to report what of the different fatness indicators included in FFI is better associated with HRV parameters in sedentary adults.

Methods: One hundred and fifty healthy adults (74 women; 76 men), aged between 18 and 65 years old, participated in this cross-sectional study. We measured cardiorespiratory fitness (maximal oxygen consumption) and fatness indicators (waist-to-height ratio [WHR], fat mass percentage [FM%] and visceral adipose tissue [VAT]). Three FFIs were calculated as the quotient between cardiorespiratory fitness and one out of three possible fatness indicators: Fit-Fat Index calculated waist-to-height ratio (FFI_{WHR}), Fit-Fat Index calculated with FM% ($FFI_{FM\%}$), and Fit-Fat Index calculated with VAT (FFI_{VAT}). HRV parameters were measured in resting conditions using a Polar RS800CX.

Results: FFI_{WTHR}, $FFI_{FM\%}$ and FFI_{VAT} were related to different HRV parameters (β ranges between −0.507 and 0.529; R^2 ranges between 0.096 and 0.275; all $p < .001$) and the association was stronger with HRV parameters than the isolated fitness or fatness indicators (β ranges between −0.483 and 0.518; R^2 ranges between 0.071 and 0.263; all $p < .001$). FFI_{VAT} was the index more consistently associated with HRV parameters (β ranges between −0.507 and 0.529; R^2 ranges between 0.235 and 0.275; all $p < .001$).

Conclusion: Our study suggests that compound FFIs are better predictors of HRV parameters than either cardiorespiratory fitness or fatness indicators alone. The FFI_{VAT} was the best index in terms of its association to HRV.

1 | INTRODUCTION

Heart rate variability (HRV) refers to the time differences between successive R–R intervals (R peaks detected in ECG) during a given period of time (Navarro-Lomas et al., 2020; Task force of the European Society of Cardiology and the North American Society for Pacing and Electrophysiology, 1996). HRV is a non-invasive biomarker that reflects the status of the autonomic nervous system (Almeida-Santos et al., 2016; Navarro-Lomas et al., 2020; Wong & Figueroa, 2021). Increased vagal-related HRV parameters in resting conditions are indicators are associated to lower incidence of chronic cardiometabolic diseases, being therefore considered good indicators of general health and wellness (Navarro-Lomas et al., 2020; Tsuji et al., 1996).

Previously, well-recognized health-related biomarkers, such as cardiorespiratory fitness (Kokkinos et al., 2022, 2023; Laukkanen et al., 2022; Lavie et al., 2022) or body composition (Andreoli et al., 2016; Toomey et al., 2015; Wang et al., 1999), have been related to HRV parameters (Buchheit & Gindre, 2006; Plaza-Florido, Migueles, Mora-Gonzalez, et al., 2019; Teisala et al., 2014; Triggiani et al., 2019). Several biomarkers related to cardiorespiratory fitness (Melnikov et al., 2018; Weippert et al., 2018) affect the cardiac autonomic function (Buchheit & Gindre, 2006; Hagberg et al., 2001) and also generate intrinsic adaptations in the sinus node (Martinelli et al., 2005). On the other hand, high levels of adiposity favor pro-inflammatory processes (e.g., the release of Interleukin-6) (de Heredia et al., 2012), influencing the hypothalamic–pituitary–adrenal axis resulting in a poor vagal activity (Marsland et al., 2007; Sajadieh et al., 2004; Tian et al., 2015). Interestingly, fitter individuals are not always less fat, and conversely, fatter individuals are not always less fit (Ortega et al., 2018; Sloan et al., 2016). The Fit-Fat Index (FFI) has been proposed as an index able to unify in a single parameter degree of cardiorespiratory fitness and adiposity (Sloan et al., 2016).

Low FFIs are predictors of type 2 diabetes mellitus (Sloan et al., 2016, 2018), a condition frequently associated to a pro-inflammatory status (Loprinzi & Edwards, 2016), accelerated vascular aging (Heffernan & Loprinzi, 2021) and poor quality of life (Sloan et al., 2015). Moreover, FFIs have been proved to be a better predictor of cardiovascular risk than fitness or fatness separately (Sloan et al., 2016, 2018). To the best of our knowledge, no studies have previously analyzed whether FFIs are related to cardiac autonomic nervous system activity assessed through HRV parameters. The present study aimed (i) to examine the association of FFI calculated using different fatness indicators with HRV parameters; and (ii) to report what of the above-mentioned predictors is better associated with HRV parameters in sedentary adults. We hypothesize that (i) FFI will be better related to HRV parameters than fitness and fatness indicators separately; and (ii) FFI based on the direct measure of fatness (FM% and VAT) will have a more robust association with HRV parameters than FFI using waist-to-height ratio.

2 | METHODS

2.1 | Participants

A total of 150 adults (74 women) aged between 18 and 65 years old participated in this study. Participants were healthy, sedentary (i.e., <20 min of physical activity on <3 days/week during the last 3 months) and recruited from the province of Granada (Spain). Participants were enrolled in two different randomized controlled trials which aimed to investigate the effects of different exercise training modalities on health-related parameters: (i) the FIT-AGING study (clinicaltrial.gov: ID: CT03334357) (Amaro-Gahete et al., 2018)—$n = 70$ middle-aged adults—and (ii) the BEER-HIIT study (ClinicalTrials.gov ID: NCT03660579)—$n = 80$ young adults. The inclusion criteria were: (i) to have a stable body weight over the previous 3 months (i.e., changes <5 kg); and (ii) do not have any health problem (e.g., cancer or chronic metabolic disease) that could be aggravated by physical activity. Both studies followed the principles of the Declaration of Helsinki (7th revision of October 2013) and were approved by the Human Research Ethics Committee of the "Junta de Andalucía" (0838-N-2017) and the University of Granada (321/CEIH/2017), respectively. All participants provided written informed consent in both projects.

2.2 | Study design

To test our hypothesis, we used a cross-sectional design. Participants came to our laboratory between 8.00 and

10.00, avoiding any physical activity since they woke up. The specific study pre-conditions were: (i) not to show altered sleep pattern the night before; (ii) to be abstained from alcohol intake and drugs or stimulant consumption 24 h before; and (iii) to avoid moderate-intensity physical activity (24 h) and vigorous-intensity physical activity (48 h) before the test. The environmental conditions were standardized (temperature ranges between 22 and 23°C).

2.3 | Fitness measurement

Maximal oxygen consumption (VO_2max) was determined through a maximum treadmill (H/P/Cosmos Pulsar treadmill, H/P/Cosmos Sport & Medical GMBH, Germany) exercise test (i.e., the modified Balke protocol (Balke & Ware, 1959)). Before the test, we conducted a warm-up (i.e., walking at 3.5 km/h for 1 min and 4 km/h for 2 min). Then, an incremental protocol started at 5.3 km/h (0% grade) for 1 min. Subsequently, the grade was increased by 1% every minute until reaching the volitional extenuation of the participants. We measured O_2 consumption and CO_2 production with an indirect calorimeter using an oronasal mask (model 7400, Hans Rudolph Inc., Kansas City, MO, United States) equipped with a prevent TM metabolic flow sensor (Medgraphics Corp., MN, United States). Before each test, we performed a flow calibration with a 3-L calibration syringe and we calibrated the gas analyzer with two standard gas concentrations. The Breeze Suite software (version 8.1.0.54 SP7, MGC Diagnostic®) was used to average O_2 consumption and CO_2 production every 5 s. The 6–20 Borg scale (Borg, 1982) was used to measure the rated perceived exertion (RPE) at each stage and exhaustion (during the last 15 s). Previously, we performed a familiarization process with the RPE scale. Moreover, we recorded heart rate values every 5 s using a Polar RS800 (Kempele, Finland). VO_2max achieving criteria were: (i) to reach a respiratory exchange ratio ≥1.1, (ii) a plateau in VO_2 (change of <100 mL/min in the last 30 s), and (iii) a heart rate between 10 beats/min of the age-predicted maximal heart rate (209–0.73 × age) (Tanaka et al., 2001). The peak oxygen uptake value during the exercise test was considered if these criteria were not met (Midgley et al., 2007).

2.4 | Fatness measurement

Height and weight were measured using an electronic scale (model 799, Electronic Column Scale, Hamburg, Germany). To assess waist circumference, we followed the standard procedures of the International Society for the Advancement of Kinanthropometry (ISAK) (Norton et al., 1996). Waist circumference was measured, at the end of a normal expiration, at the mid-point between the iliac crest and the bottom of the rib cage. We repeated the measure three times and rated the mean of them. The waist-to-height ratio was calculated as waist circumference (cm)/height (cm). Fat mass, FM% and VAT were measured by conducting a Dual Energy X-Ray Absorptiometry (DXA; HOLOGIC, Wi) scan.

2.5 | Fit-Fat Index

FFI represents the quotient between fitness (i.e., relative to body weight VO_2max) and fatness (Sloan et al., 2016). We calculated three different FFI, using three indicators of fatness as divisors: waist-to-height ratio (FFI_{WTHR}), FM% ($FFI_{FM\%}$) and VAT (FFI_{VAT}).

2.6 | Heart rate variability

Participants were lying in a supine position on a stretcher while the R–R signal was assessed for 15 min (after 10 min of acclimation) using the Polar RS800CX (Williams et al., 2016) (Polar Electro, Kempele, Finland). Participants were instructed to meet the following instructions: (i) not to talk or move; and (ii) to relax as much as possible but to be simultaneously awake. We downloaded the R-R recordings using the Polar Pro Trainer 5® software (Polar Electro, Finland), and a trained researcher (Plaza-Florido et al., 2020) analyzed them with the Kubios HRV Standard®, version 2.2 software (University of Eastern Finland, Kuopio, Finland) (Tarvainen et al., 2014). We followed the methodology described in previous studies (Plaza-Florido et al., 2021) using: (i) a Lambda value of 500; (ii) a cubic interpolation at the default rate of 4 Hz.; and (ii) the medium filter provided by the Kubios HRV software (Alcántara et al., 2020).

Following the HRV Kubios software standard procedures (Tarvainen et al., 2014), HRV parameters in time-domain (i.e., standard deviation of RR intervals [SDNN], square root of the mean squared differences between successive RR intervals [RMSSD]), Frequency-domain (i.e., High Frequency [0.15–0.40 Hz]) and Poincare Plot were derived. SDNN is considered an indicator of global autonomic modulation linked with vagal activity in short-term recordings (Shaffer & Ginsberg, 2017). RMSSD and High Frequency are related to vagal modulation (Shaffer & Ginsberg, 2017). Poincare Plot analysis is considered an indicator of heart rate complexity (Tayel & AlSaba, 2015). From Poincare Plot, we obtained SD1 (standard deviation of Poincare plot orthogonal to the line-of-identity) and SD2 (standard deviation of Poincare plot along the line-of-identity), and we calculated an index of sympathetic activity (i.e., Stress Score) and an indicator of autonomic balance (i.e., Sympathetic/Parasympathetic Ratio [S/PS Ratio]), according to a previous study (Naranjo-Orellana et al., 2015).

We also calculated corrected HRV parameters to remove the HRV dependence on heart rate (Plaza-Florido et al., 2021; Plaza-Florido, Migueles, Sacha, & Ortega, 2019), based on two assumptions: (i) if HRV parameters were negatively correlated with heart rate, the correction procedure consisted in calculating ratios between HRV parameters and different powers of the mean R–R interval; (ii) if HRV parameters were positively correlated with heart rate, the correction procedure was performed by multiplying HRV parameters by the adequate powers of the mean R–R interval. The calculations were as follows: Corrected SDNN = SDNN/MeanRR^1, RMSSD = RMSSD/meanRR$^{1.3}$, corrected high frequency = high frequency/meanRR$^{1.2}$, corrected stress score = stress score × MeanRR^1, and corrected S/PS ratio = S/PS ratio × mean RR^1.

2.7 | Statistical analysis

The distribution of all variables was analyzed with the Shapiro–Wilk test, *Q*–*Q* plots and visual check of histograms. Descriptive parameters were reported as mean (standard deviation). Non-normal variables, including HRV parameters (i.e., SDNN, RMSSD, High Frequency, Stress Score and S/PS ratio) and VAT were presented as median and interquartile range. Non-normal variables were transformed using Napierian logarithms. To analyze the association between cardiorespiratory fitness, fatness indicators (i.e., Waist-to-height ratio, FM%, and VAT) and FFI (i.e., FFI_{WTHR}, $FFI_{FM\%}$, FFI_{VAT}) with HRV parameters corrected by heart rate we performed multiple linear regression analyses (model 0). These calculations were also performed adjusting by sex and age (model 1) as basic confounders. β (standardized regression coefficient), R^2 (adjusted determination coefficient) and *p* (level of significance) were obtained from these linear regression analyses. *p* values of less than .05 were accepted to indicate statistical significance. All analyses were performed using the Statistical Package for Social Sciences (SPSS, v.24.0, IBM SPSS Statistics, IBM Corporation). The figures were created using GraphPad Prism 7 (GraphPad Software, San Diego, CA, USA).

3 | RESULTS

The baseline characteristics of all participants are shown in Table 1. A total of 150 participants (49.3% women) were presented in the analysis, including young (80 participants) and middle-aged adults (70 participants).

Table 2 show the linear regression models of fitness and fatness with corrected HRV parameters (i.e., SDNN, RMSSD, High Frequency, Stress Score and S/PS Ratio). Cardiorespiratory fitness was positively associated with corrected SDNN, RMSSD and High Frequency (model 0; β ranges between 0.348 and 0.444; R^2 ranges between 0.115 and 0.191; all $p < .001$), while was inversely related to Stress Score (model 0; $\beta = -0.399$, $R^2 = 0.154$, $p < .001$) and S/PS ratio (model 0; $\beta = -0.407$, $R^2 = 0.160$, $p < .001$). The waist-to-height ratio was negatively related to SDNN, RMSSD and High Frequency (model 0; β ranges between -0.399 and -0.441; R^2 ranges between 0.153 and 0.189; $p < .001$), while positive relationships were observed with Stress Score (model 0; $\beta = 0.372$, $R^2 = 0.133$ $p < 0.001$) and S/PS Ratio (model 0; $\beta = 0.398$, $R^2 = 0.153$, $p < .001$). Furthermore, negative associations were noted of FM% with SDNN, RMSSD and High Frequency (model 0; β ranges between -0.277 and -0.395; R^2 ranges between 0.071 and 0.150; all $p< .001$) while positive linear regression models were established between FM% with Stress Score (model 0; $\beta = 0.360$; $R^2 = 0.123$, $p < .001$) and S/PS ratio (model 0; $\beta = 0.372$; $R^2 = 0.132$, $p < .001$). Moreover, VAT was positively associated with Stress Score (model 0; $\beta = 0.464$; $R^2 = 0.210$, $p < .001$) and S/PS Ratio (model 0; $\beta = 0.483$; $R^2 = 0.228$, $p < .001$). VAT was negatively related to SDNN, RMSSD and High Frequency (model 0; β ranges between -0.486 and -0.518; R^2 ranges between 0.231 and 0.263; all $p < .001$). When these relationships were adjusted by sex and age (model 1; β ranges between -0.234 and 0.269; R^2 ranges between 0.276 and 0.372; all $p < .001$), these significant associations between fitness / fatness indicators with HRV parameters were maintained.

The relationships between the FFI_{WHR} and corrected HRV parameters are presented in Figure 1. FFI_{WTHR} was positively associated with SDNN, RMSSD and High Frequency (β ranges between 0.427 and 0.484; R^2 ranges between 0.177 and 0.229; all $p < .001$). Furthermore, a negative association was noted of FFI_{WTHR} with Stress Score ($\beta = -0.444$; $R^2 = 0.192$, $p < .001$) and S/PS ratio ($\beta = -0.460$; $R^2 = 0.207$, $p < .001$). After including sex and age (model 1; β ranges between -0.200 and 0.179; R^2 ranges between 0.290 and 0.369; all $p < .001$), the associations were similar than those obtained in model 0 (unadjusted analysis).

Table 3 shows associations between $FFI_{FM\%}$ and FFI_{VAT} with HRV parameters. $FFI_{FM\%}$ had a positive

TABLE 1 Descriptive characteristics of the participants.

	All ($n = 150$; 76 men/74 women)			Young adults ($n = 80$; 42 men/38 women)			Middle-aged adults ($n = 70$; 34 men/36 women)		
	All	**Men**	**Women**	**All**	**Men**	**Women**	**All**	**Men**	**Women**
Age (years)	37.7 (15.7)	37.9 (15.8)	37.6 (15.7)	24.0 (5.8)	24.8 (6.5)	23.1 (4.9)	53.5 (4.9)	54.2 (5.2)	52.89 (4.6)
Heart rate variability									
Heart Rate (bpm)	66.7 (9.9)	65.0 (9.3)	68.4 (10.2)	69.4 (10.2)	66.9 (8.8)	72.1 (11.1)	63.6 (8.5)	62.7 (9.5)	64.5 (7.5)
SDNN (ms)	35.9 (26.7)	37.6 (30.5)	34.0 (22.3)	46.5 (32.5)	50.2 (37.1)	40.8 (27.7)	27.3 (17.9)	28.7 (22.7)	26.6 (13.3)
RMSSD (ms)	33.6 (30.6)	35.0 (31.8)	33.2 (29.7)	46.6 (43.9)	49.3 (46.8)	42.8 (40.8)	25.6 (21.2)	26.1 (26.0)	25.6 (19.6)
High frequency (ms^2)	477.4 (985.5)	394.7 (990.0)	503.3 (1025.4)	1000.0 (1220.5)	976. (1268.8)	1018.1 (1188.5)	247.5 (405.2)	167.1 (391.4)	268.4 (397.7)
Stress score	27.2 (15.1)	27.2 (17.3)	27.3 (12.5)	34.7 (15.8)	36.9 (18.9)	32.7 (12.0)	20.7 (10.8)	19.3 (10.8)	22.2 (10.8)
S/PS ratio	0.958 (1.628)	0.901 (1.653)	0.988 (1.582)	0.551 (0.835)	0.445 (0.971)	0.642 (0.723)	1.54 (2.63)	1.43 (5.22)	1.77 (1.92)
Cardiorespiratory fitness									
VO_2max (ml kg^{-1})	2475.0 (628.9)	2960.5 (439.5)	1976.4 (333.8)	2596.1 (576.0)	2997.0 (488.0)	2153.1 (245.8)	2336.5 (661.6)	2915.4 (373.2)	1789.9 (314.3)
VO_2max (ml kg^{-1} min^{-1})	34.6 (7.0)	36.9 (6.7)	32.3 (6.7)	38.2 (6.1)	39.9 (6.7)	36.4 (4.9)	30.5 (5.6)	33.3 (4.5)	27.9 (5.3)
Anthropometry and body composition									
Weight (kg)	72.1 (14.6)	81.5 (12.8)	62.4 (8.9)	68.5 (13.3)	76.1 (12.4)	60.0 (8.3)	76.2 (15.0)	88.2 (9.9)	64.9 (9.0)
Height (cm)	168.6 (9.1)	174.9 (7.4)	162.1 (5.6)	168.9 (8.6)	173.9 (8.2)	163.5 (5.0)	168.2 (9.8)	176.2 (6.2)	160.7 (5.8)
Body mass index (kg/m^2)	25.2 (4.0)	26.6 (3.9)	23.8 (3.5)	23.9 (3.7)	25.2 (3.6)	22.5 (3.2)	26.8 (3.8)	28.5 (3.5)	25.2 (3.4)
Waist circumference (cm)	87.5 (13.8)	93.8 (13.0)	81.1 (11.6)	80.8 (11.7)	86.2 (10.9)	74.8 (9.4)	95.3 (12.0)	103.2 (8.4)	87.8 (9.7)
Waist-to-height ratio	0.519 (0.078)	0.537 (0.076)	0.501 (0.076)	0.478 (0.067)	0.496 (0.067)	0.458 (0.061)	0.566 (0.062)	0.587 (0.055)	0.547 (0.063)
Fat mass (kg)	24.7 (9.0)	25.1 (10.1)	24.4 (7.9)	20.0 (6.7)	20.0 (7.5)	20.1 (5.9)	30.1 (8.4)	31.4 (9.4)	28.9 (7.2)
FM% (%)	34.4 (9.6)	30.3 (8.8)	38.7 (8.5)	29.8 (7.7)	26.5 (7.5)	33.6 (6.0)	39.7 (8.8)	35.0 (7.9)	44.0 (7.3)
VAT (cm^3)	430.8 (533.0)	555.8 (609.8)	298.0 (405.4)	260.3 (209.3)	330.2 (259.1)	221.2 (117.1)	794.7 (524.0)	950.6 (537.4)	629.0 (437.0)

Note: Data are shown as means (standard deviation). Median (IQR: interquartile range) are presented for HRV parameters (i.e., SDNN, RMSSD, high frequency and S/PS ratio) and VAT because these variables showed a non-normal distribution.

Abbreviations: bpm, beats per minute; cm, centimeters; kg, kilograms; min, minute; ml, milliliters; ms, milliseconds; ms^2, milliseconds squared; RMSSD, square root of the mean squared differences between successive RR intervals; SDNN, standard deviation of RR intervals.

TABLE 2 Linear regression analysis of fitness and fatness indicators with corrected HRV parameters.

	Fitness			Fatness								
	VO_2max (ml kg min^{-1})			Waist-to-height ratio			FM% (%)			Ln VAT		
	β	R^2	p	β	R^2	p	β	R^2	p	β	R^2	p
Corrected HRV parameters												
Model 0												
Ln corrected SDNN	0.444	0.191	<.001	−0.399	0.153	<.001	−0.395	0.150	<.001	−0.494	0.239	<.001
Ln corrected RMSSD	0.376	0.135	<.001	−0.441	0.189	<.001	−0.330	0.103	<.001	−0.518	0.263	<.001
Ln corrected high frequency	0.348	0.115	<.001	−0.407	0.160	<.001	−0.277	0.071	<.001	−0.486	0.231	<.001
Ln corrected stress score	−0.399	0.154	<.001	0.372	0.133	<.001	0.360	0.123	<.001	0.464	0.210	<.001
Ln corrected S/PS ratio	−0.407	0.160	<.001	0.398	0.153	<.001	0.372	0.132	<.001	0.483	0.228	<.001
Model 1												
Ln corrected SDNN	0.172	0.372	<.001	−0.103	0.361	<.001	−0.124	0.362	<.001	−0.201	0.370	<.001
Ln corrected RMSSD	0.151	0.330	<.001	−0.162	0.333	<.001	−0.127	0.325	<.001	−0.234	0.339	<.001
Ln Corrected high frequency	0.166	0.287	<.001	−0.137	0.283	<.001	−0.103	0.276	<.001	−0.208	0.288	<.001
Ln corrected stress score	−0.104	0.348	<.001	0.070	0.345	<.001	0.067	0.344	<.001	0.147	0.350	<.001
Ln corrected S/PS ratio	−0.188	0.296	<.001	0.152	0.289	<.001	0.168	0.290	<.001	0.269	0.304	<.001

Abbreviations: Model 0, unadjusted; Model 1, adjusted by sex and agel; VO_2max, maximal oxygen consumption; Ln, Napierian logarithm; SDNN, standard deviation of RR intervals; RMSSD, square root of the mean squared differences between successive RR intervals; S/PS, sympathetic/parasympathetic ratio; ml, milliliters; kg, kilograms; min, minutes; m^2, meter squared; ms, milliseconds; ms^2, milliseconds squared; %, percentage; β, standardized regression coefficient; R^2, adjusted determination coefficient; p, level of significance.

association with SDNN, RMSSD and High Frequency (β ranges between 0.320 and 0.434; R^2 ranges between 0.096 and 0.183; all p< .001); and negative relationships with stress score ($\beta = -0.441$; $R^2 = 0.189$, $p < .001$); and S/PS ratio ($\beta = -0.391$; $R^2 = 0.147$, $p < .001$). Similarly, FFI_{VAT} was positively related to SDNN, RMSSD and High Frequency (β ranges between 0.494 and 0.529; R^2 ranges between 0.239 and 0.275; all $p < .001$), but negatively associated with stress score ($\beta = -0.490$; $R^2 = 0.235$, $p < .001$) and S/PS Ratio ($\beta = -0.507$; $R^2 = 0.252$, $p < .001$). After including sex and age (model 1; β ranges between −0.269 and 0.228; R^2 ranges between 0.282 and 0.374; all $p < .001$) in the analysis, the reported significant relationships were maintained.

4 | DISCUSSION

The present study shows that higher FFI values (i.e., higher fitness, lower fatness) are associated with increased vagal-related and reduced sympathetic-related HRV parameters in healthy adults. Importantly, FFI_{WHR}, $FFI_{FM\%}$ and FFI_{VAT} were better related to HRV parameters than either fitness or fatness indicators, alone. Moreover, we prove that a FFI based on the VAT predicts HRV parameters more accurately than FFI based on the waist-to-height ratio or FM%. These findings are highly relevant since we prove, for the first time, that FFI is positively associated with vagal-related HRV parameters and inversely related to sympathetic activity in healthy adults.

It has been well documented that fitness and fatness indicators are related to several cardiovascular risk factors in adults (e.g., high fasting glucose levels, hypercholesteremia, hypertension or inflammatory biomarkers) (Ashwell & Gibson, 2009; de Heredia et al., 2012; Erez et al., 2015; Kaminsky et al., 2019; Park et al., 2017). In this line, reduced fitness (Ferreira et al., 2018; Martinelli et al., 2005) and increased fatness (Koenig et al., 2015) are able to induce a reduction of vagal-related HRV

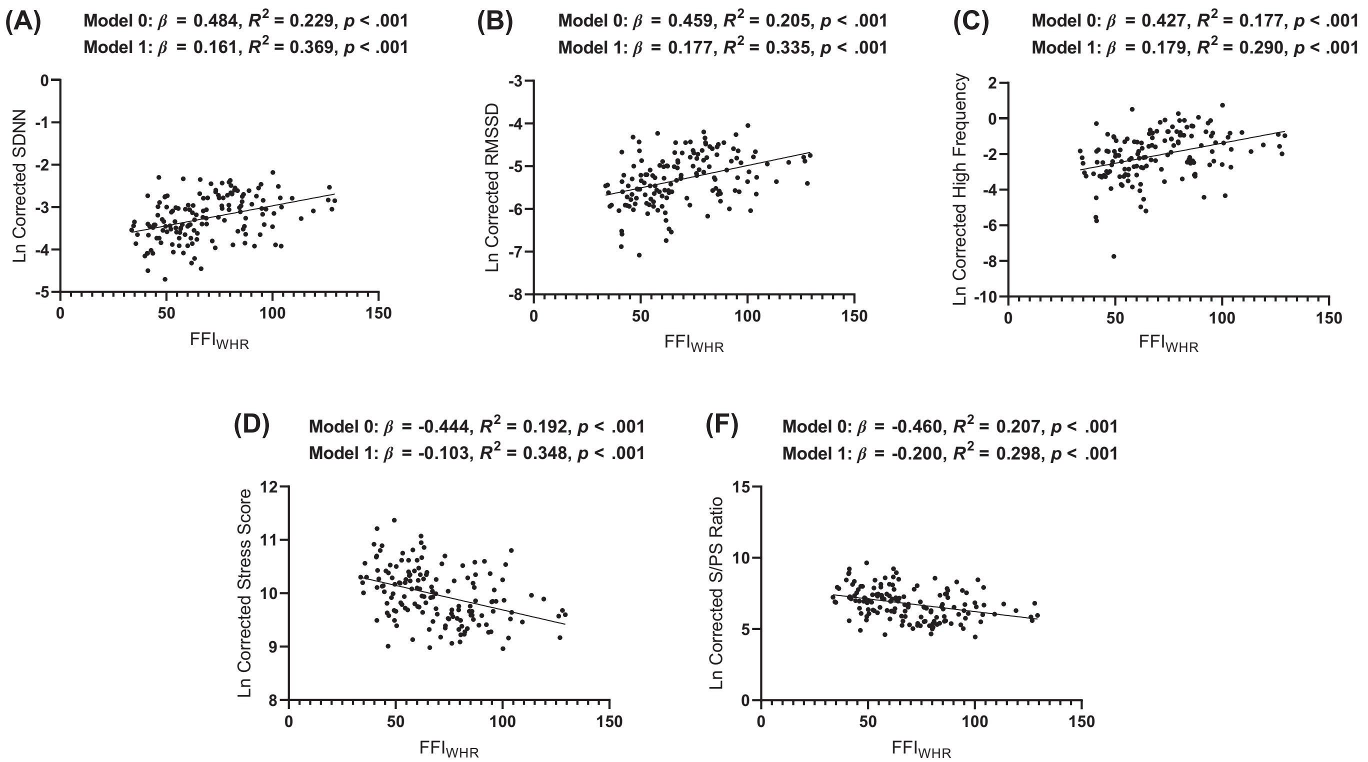

FIGURE 1 Linear regression analysis of FFI_{WHR} with corrected heart rate variability parameters. Model 0, unadjusted analysis; Model 1, adjusted by sex and age; FFI_{WHR}, Fit-Fat Index calculated waist-to-height ratio as fatness indicator; Ln, Napierian logarithm; SDNN, standard deviation of RR intervals; RMSSD, square root of the mean squared differences between successive RR intervals; S/PS, sympathetic/parasympathetic ratio; β, standardized regression coefficient; R^2, adjusted determination coefficient; *p*, level of significance.

TABLE 3 Linear regression analysis of $FFI_{FM\%}$ and FFI_{VAT} with corrected HRV parameters.

	Ln $FFI_{FM\%}$			Ln FFI_{VAT}		
	β	R^2	*p*	*β*	R^2	*p*
Model 0						
Ln corrected SDNN	0.434	0.183	<.001	0.528	0.274	<.001
Ln corrected RMSSD	0.361	0.125	<.001	0.529	0.275	<.001
Ln corrected high frequency	0.320	0.096	<.001	0.494	0.239	<.001
Ln corrected stress score	−0.391	0.147	<.001	−0.490	0.235	<.001
Ln corrected S/PS ratio	−0.404	0.158	<.001	−0.507	0.252	<.001
Model 1						
Ln corrected SDNN	0.162	0.367	<.001	0.216	0.374	<.001
Ln corrected RMSSD	0.150	0.328	<.001	0.228	0.339	<.001
Ln corrected High frequency	0.149	0.282	<.001	0.212	0.290	<.001
Ln corrected stress score	−0.086	0.345	<.001	−0.146	0.351	<.001
Ln corrected S/PS ratio	−0.202	0.295	<.001	−0.269	0.306	<.001

Abbreviations: Model 0, unadjusted; Model 1, adjusted by sex and age; $FFI_{FM\%}$, Fit-Fat Index calculated with FM% as a fatness indicator; FFI_{VAT}, Fit-Fat Index calculated with VAT as a fatness indicator; Ln, Napierian logarithm; SDNN, standard deviation of RR intervals; RMSSD, square root of the mean squared differences between successive RR intervals; S/PS, sympathetic/parasympathetic ratio; *β*, standardized regression coefficient; R^2, adjusted determination coefficient; *p*, level of significance.

parameters, which are also associated with a higher incidence of several chronic cardiometabolic diseases (e.g., type 2 diabetes mellitus or obesity) (Navarro-Lomas et al., 2020; Tsuji et al., 1996). Our results hold up these findings, supporting the well-known associations between increased fitness (i.e., VO_2max) and reduced fatness indicators (i.e., waist-to-height ratio, FM% and VAT) with increased vagal activity and a reduced sympathetic influence on the autonomic nervous system, according to HRV parameters dynamics.

The FFI_{WHR} has emerged as a simple and useful tool to predict several cardiovascular issues (e.g., type 2 diabetes mellitus development, inflammatory status, or measures of vascular aging) more precisely than fitness and fatness features separately (Heffernan & Loprinzi, 2021; Loprinzi & Edwards, 2016; Sloan et al., 2015, 2016, 2018). Our results suggest that FFI_{WHR} is positively associated with well-known vagal-related HRV parameters (i.e., SDNN, RMSSD and high frequency), and negatively related to Stress Score (i.e., a sympathetic activity measure [Navarro-Lomas et al., 2020]) and S/PS ratio (i.e., an indicator of autonomic balance [Navarro-Lomas et al., 2020]). Physiological mechanisms that justify this association could be related to the combined influence of factors that determine VO_2max (Buchheit & Gindre, 2006; Hagberg et al., 2001). In addition, the release of pro-inflammatory cytokines by adipose tissue has a negative impact on vagal-related HRV parameters (Tian et al., 2015). Hence, a higher FFI_{WHR} would be associated with a reduced pro-inflammatory status, increasing the vagal tone in the cardiac autonomic function (Ernst, 2017). Therefore, according to our results, and independently of the participants' sex and age, an increased FFI_{WHR} seems to be related both to a higher vagal modulation and to a reduced sympathetic influence in the cardiac activity, potentially reducing cardiovascular risk.

In our study, FFI_{WHR} showed stronger relationships (higher β and R^2) with HRV parameters than cardiorespiratory fitness and waist-to-height ratio alone. These results highlight the fact that fitness and fatness are not always directly associated (Ortega et al., 2018; Sloan et al., 2016). Interestingly, when sex and age were considered as a covariate in the analysis, FFI_{WHR} showed a similar relation with HRV parameters compared to cardiorespiratory fitness and waist-to-height ratio separately. This result could be explained by the heterogeneous age range of the two groups involved in this study (i.e., young adults [18–40 years old] and middle-aged adults [45–65 years old]). Age is a non-modifiable factor that affects HRV parameters (Thayer et al., 2009) through a decrease in the influence of vagal tone in the HRV parameters (Antelmi et al., 2004). Hence, FFI_{WHR} could be an adequate tool to analyze HRV, providing additional information about the autonomic nervous system, according to HRV dynamics, compared to VO_2max and waist-to-height ratio separately. However, taking into account the sex and age, we can conclude that FFI_{WHR} looks to provide similar information to VO_2max and waist-to-height ratio alone.

Importantly, we calculated two FFI based on fatness indicators obtained by DXA analyses (i.e., $FFI_{FM\%}$ and FFI_{VAT}). Both indices offer additional information about HRV parameters compared with those obtained by VO_2max, FM% and VAT alone, respectively. Nevertheless, FFI_{VAT} was the best predictor of HRV compared with FFI_{WHR} and $FFI_{FM\%}$. VAT—obtained by DXA—refers to visceral adiposity within the abdominal region (Ibrahim, 2010), whereas the FM% is a measure of total body fat—also obtained by DXA (Swainson et al., 2017)—being the waist-to-height ratio an indirect measure of central fat distribution (Swainson et al., 2017). Interestingly, previous studies have suggested that VAT is better related than general body fat to further impairments of the autonomic nervous system activity (Triggiani et al., 2019). This assumption is based on a bigger production of pro-inflammatory cytokines (e.g., interleukin-6 [IL-6] or tumor necrosis factor-alpha [TNFα]) by VAT (You & Nicklas, 2006), which has a negative influence on vagal activity (Tian et al., 2015). These are important reasons to conclude that VAT could be the most valuable fatness indicator in this context.

Although our promising results, some limitations arise in our study. Firstly, no causal relationships can be established as our study is observational. In addition, although we do not use a gold standard method in the HRV measurement, the Polar RS800CX has been proved as valid and reliable to assess HRV in adults (Williams et al., 2017). Moreover, our study was based on individuals aged 18–65. Although we included the analysis of age as a possible confounder, our findings should not be extrapolated to other populations (e.g., children, adolescents, or older adults). Finally, we have a relatively small sample size. Future studies using bigger cohorts are needed to corroborate or contrast our findings. In contrast, the principal strength of this study is the quality of the measures, since we assess cardiorespiratory fitness through a maximal exercise test with gas analysis and maximal O_2 consumption (i.e., gold-standard method), and fatness indicators were obtained by an objective and direct method using DXA.

5 | CONCLUSIONS

In conclusion, the results of our study suggest (i) that FFI is better associated with HRV parameters than fitness and fatness indicators alone; (ii) that an increased FFI is related to higher vagal and reduced sympathetic influences on cardiac autonomic function according to HRV dynamics; and (iii) that a FFI based on VAT is better associated with HRV parameters than other FFI based on the waist-to-height ratio or FM%. Future studies should confirm, contrast and expand our findings in populations with different clinical conditions such as type 2 diabetes mellitus or obesity.

AUTHOR CONTRIBUTIONS

Manuel J. Castillo and Francisco J. Amaro-Gahete conceived and designed the study; Ginés Navarro-Lomas, Alejandro De-la-O, and Francisco J. Amaro-Gahete collected the data; Ginés Navarro-Lomas conducted the statistical analysis; Ginés Navarro-Lomas drafted the manuscript; and Alejandro De-la-O, Abel Plaza-Florido, Manuel J. Castillo, and Francisco J. Amaro-Gahete revised it. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

ACKNOWLEDGMENTS

The authors would like to thank the participants for their involvement in this research. Abel Plaza-Florido and Francisco J. Amaro-Gahete are supported by the Spanish Ministry of Education (FPU16/02760, and FPU14/04172). Abel Plaza-Florido contribution was funded in part by NIH grant #: U01 TR002004 (REACH project).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Ginés Navarro-Lomas https://orcid.org/0000-0002-9995-3455

Abel Plaza-Florido https://orcid.org/0000-0002-5374-3129

Alejandro De-la-O https://orcid.org/0000-0002-0614-4545

Manuel J. Castillo https://orcid.org/0000-0002-1196-9488

Francisco J. Amaro-Gahete https://orcid.org/0000-0002-7207-9016

REFERENCES

Alcántara, J., Plaza-Florido, A., Amaro-Gahete, F., Acosta, F., Migueles, J., Molina-Garcia, P., Sacha, J., Sanchez-Delgado, G., & Martinez-Tellez, B. (2020). Impact of using different levels of threshold-based artefact correction on the quantification of heart rate variability in three independent human cohorts. *Journal of Clinical Medicine*, *9*(2), 325. https://doi.org/10.3390/JCM9020325

Almeida-Santos, M. A., Barreto-Filho, J. A., Oliveira, J. L. M., Reis, F. P., da Cunha Oliveira, C. C., & Sousa, A. C. S. (2016). Aging, heart rate variability and patterns of autonomic regulation of the heart. *Archives of Gerontology and Geriatrics*, *63*, 1–8. https://doi.org/10.1016/j.archger.2015.11.011

Amaro-Gahete, F. J., De-la-O, A., Jurado-Fasoli, L., Espuch-Oliver, A., Robles-Gonzalez, L., Navarro-Lomas, G., de Haro, T., Femia, P., Castillo, M. J., & Gutierrez, A. (2018). Exercise training as S-klotho protein stimulator in sedentary healthy adults: Rationale, design, and methodology. *Contemporary Clinical Trials Communications*, *11*, 10–19. https://doi.org/10.1016/j.conctc.2018.05.013

Andreoli, A., Garaci, F., Cafarelli, F. P., & Guglielmi, G. (2016). Body composition in clinical practice. *European Journal of Radiology*, *85*(8), 1461–1468. https://doi.org/10.1016/J.EJRAD.2016.02.005

Antelmi, I., Silva DePaula, R., Mansur, A. J., & José Grupi, C. (2004). Influence of age, gender, body mass index, and functional capacity on heart rate variability in a cohort of subjects without heart disease. *The American Journal of Cardiology*, *93*, 381–385. https://doi.org/10.1016/j.amjcard.2003.09.06

Ashwell, M., & Gibson, S. (2009). Waist to height ratio is a simple and effective obesity screening tool for cardiovascular risk factors: Analysis of data from the British National Diet and nutrition survey of adults aged 19–64 years. *Obesity Facts*, *2*(2), 97–103. https://doi.org/10.1159/000203363

Balke, B., & Ware, R. W. (1959). An experimental study of physical fitness of air force personnel. *United States Armed Forces Medical Journal*, *10*(6), 675–688.

Borg, G. A. V. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise*, *14*(5), 377–381. https://doi.org/10.1249/00005768-198205000-00012

Buchheit, M., & Gindre, C. (2006). Cardiac parasympathetic regulation: Respective associations with cardiorespiratory fitness and training load. *American Journal of Physiology: Heart and Circulatory Physiology*, *291*(1), 451–458. https://doi.org/10.1152/AJPHEART.00008.2006/ASSET/IMAGES/LARGE/ZH40070667660002.JPEG

de Heredia, F. P., Gómez-Martínez, S., & Marcos, A. (2012). Obesity, inflammation and the immune system. *Proceedings of the Nutrition Society*, *71*(2), 332–338. https://doi.org/10.1017/S0029665112000092

Erez, A., Kivity, S., Berkovitch, A., Milwidsky, A., Klempfner, R., Segev, S., Goldenberg, I., Sidi, Y., & Maor, E. (2015). The association between cardiorespiratory fitness and cardiovascular risk may be modulated by known cardiovascular risk factors. *American Heart Journal*, *169*(6), 916–923. https://doi.org/10.1016/J.AHJ.2015.02.023

Ernst, G. (2017). Heart-rate variability—More than heart beats? *Frontiers in Public Health*, *5*, 240. https://doi.org/10.3389/fpubh.2017.00240

Ferreira, R. B., Peçanha, T., Nadal, J., Materko, W., Bartels, R., Perrout De Lima, J. R., Roncally, A., & Carvalho, S. (2018). Maximum oxygen uptake prediction model based on heart rate variability parameters for young healthy adult males at rest. *Open Access Biostatistics & Bioinformatics*, *2*, 1–7. https://doi.org/10.31031/OABB.2018.02.000536

Hagberg, J. M., Moore, G. E., & Ferrell, R. E. (2001). Specific genetic markers of endurance performance and VO_{2max}. *Exercise and Sport Sciences Reviews*, *29*(1), 15–19. https://doi.org/10.1097/00003677-200101000-00004

Heffernan, K., & Loprinzi, P. (2021). The fitness fatness index is inversely associated with measures of vascular aging derived from blood pressure in a representative sample of adults in the United States. *The Korean Journal of Sports Medicine*, *39*(3), 95–101. https://doi.org/10.5763/KJSM.2021.39.3.95

Ibrahim, M. M. (2010). Subcutaneous and visceral adipose tissue: Structural and functional differences. *Obesity Reviews*, *11*(1), 11–18. https://doi.org/10.1111/J.1467-789X.2009.00623.X

Kaminsky, L. A., Arena, R., Ellingsen, Ø., Harber, M. P., Myers, J., Ozemek, C., & Ross, R. (2019). Cardiorespiratory fitness and cardiovascular disease—The past, present, and future. *Progress in Cardiovascular Diseases*, *62*(2), 86–93. https://doi.org/10.1016/J.PCAD.2019.01.002

Koenig, J., Windham, B. G., Ferrucci, L., Sonntag, D., Fischer, J. E., Thayer, J. F., & Jarczok, M. N. (2015). Association strength of three adiposity measures with autonomic nervous system function IN APPARENTLY healthy employees. *The Journal of Nutrition, Health & Aging*, *19*(9), 879–882. https://doi.org/10.1007/S12603-015-0508-X

Kokkinos, P., Faselis, C., Samuel, I. B. H., Lavie, C. J., Zhang, J., Vargas, J. D., Pittaras, A., Doumas, M., Karasik, P., Moore, H., Heimal, M., & Myers, J. (2023). Changes in cardiorespiratory fitness and survival in patients with or without cardiovascular disease. *Journal of the American College of Cardiology*, *81*(12), 1137–1147. https://doi.org/10.1016/J.JACC.2023.01.027

Kokkinos, P., Faselis, C., Samuel, I. B. H., Pittaras, A., Doumas, M., Murphy, R., Heimall, M. S., Sui, X., Zhang, J., & Myers, J. (2022). Cardiorespiratory fitness and mortality risk across the spectra of age, race, and sex. *Journal of the American College of Cardiology*, *80*(6), 598–609. https://doi.org/10.1016/J.JACC.2022.05.031

Laukkanen, J. A., Isiozor, N. M., & Kunutsor, S. K. (2022). Objectively assessed cardiorespiratory fitness and all-cause mortality risk: An updated meta-analysis of 37 cohort studies involving 2,258,029 participants. *Mayo Clinic Proceedings*, *97*(6), 1054–1073. https://doi.org/10.1016/J.MAYOCP.2022.02.029

Lavie, C. J., Sanchis-Gomar, F., & Ozemek, C. (2022). Fit is it for longevity across populations. *Journal of the American College of Cardiology*, *80*(6), 610–612. https://doi.org/10.1016/J.JACC.2022.05.030

Loprinzi, P. D., & Edwards, M. K. (2016). CVD-related fit-fat index on inflammatory-based CVD biomarkers. *International Journal of Cardiology*, *223*, 284–285. https://doi.org/10.1016/J.IJCARD.2016.08.194

Marsland, A. L., Gianaros, P. J., Prather, A. A., Jennings, J. R., Neumann, S. A., & Manuck, S. B. (2007). Stimulated production of proinflammatory cytokines covaries inversely with heart rate variability. *Psychosomatic Medicine*, *69*(8), 709–716. https://doi.org/10.1097/PSY.0B013E3181576118

Martinelli, F. S., Chacon-Mikahil, M. P. T., Martins, L. E. B., Lima-Filho, E. C., Golfetti, R., Paschoal, M. A., & Gallo-Junior, L. (2005). Heart rate variability in athletes and nonathletes at rest and during head-up tilt. *Brazilian Journal of Medical and Biological Research*, *38*(4), 639–647. https://doi.org/10.1590/S0100-879X2005000400019

Melnikov, A. A., Bobylev, A. S., & Kylosov, A. A. (2018). Associations of Alu I/D polymorphism of the angiotensin converting enzyme gene and 4b/a polymorphism of the nitric oxide synthase gene with heart rate variability and cardiovascular hemodynamics in rowers. *Human Physiology*, *44*(5), 605–607. https://doi.org/10.1134/S0362119718050080

Midgley, A. W., McNaughton, L. R., Polman, R., & Marchant, D. (2007). Criteria for determination of maximal oxygen uptake: A brief critique and recommendations for future research. *Sports Medicine*, *37*(12), 1019–1028. https://doi.org/10.2165/00007256-200737120-00002

Naranjo-Orellana, J., de La Cruz Torres, B., Cachadiña, E. S., de Hoyo, M., & Domínguez Cobo, S. (2015). Two new indexes for the assessment of autonomic balance in elite soccer players. *International Journal of Sports Physiology and Performance*, *10*(4), 452–457. https://doi.org/10.1123/ijspp.2014-0235

Navarro-Lomas, G., Alejandro, D.-L.-O., Jurado-Fasoli, L., Castillo, M. J., Femia, P., & Amaro-Gahete, F. J. (2020). Assessment of autonomous nerve system through non-linear heart rate variability outcomes in sedentary healthy adults. *PeerJ*, *8*, e10178. https://doi.org/10.7717/peerj.10178

Norton, K., Whittingham, N., Carter, L., Kerr, D., Gore, C., & Marfell-Jones, M. (1996). Measurement techniques in anthropometry. In K. Norton & T. Olds (Eds.), *Anthropometrica*. University of New South Wales Press.

Ortega, F. B., Ruiz, J. R., Labayen, I., Lavie, C. J., & Blair, S. N. (2018). The fat but fit paradox: What we know and don't know about it. *British Journal of Sports Medicine*, *52*(3), 151–153. https://doi.org/10.1136/BJSPORTS-2016-097400

Park, E., Meininger, J. C., Kang, D. H., Gabriel, K. P., & Padhye, N. S. (2017). Association of cardiorespiratory fitness and adiposity with inflammatory biomarkers in young adults. *American Journal of Human Biology*, *29*(3), e22959. https://doi.org/10.1002/AJHB.22959

Plaza-Florido, A., Alcantara, J. M. A., Migueles, J. H., Amaro-Gahete, F. J., Acosta, F. M., Mora-Gonzalez, J., Sacha, J., & Ortega, F. B. (2020). Inter- and intra-researcher reproducibility of heart rate variability parameters in three human cohorts. *Scientific Reports*, *10*(1), 11399. https://doi.org/10.1038/S41598-020-68197-7

Plaza-Florido, A., Migueles, J. H., Mora-Gonzalez, J., Molina-Garcia, P., Rodriguez-Ayllon, M., Cadenas-Sanchez, C., Esteban-Cornejo, I., Solis-Urra, P., de Teresa, C., Gutiérrez, Á., Michels, N., Sacha, J., & Ortega, F. B. (2019). Heart rate is a better predictor of cardiorespiratory fitness than heart rate variability in overweight/obese children: The Activebrains project. *Frontiers in Physiology*, *10*, 510. https://doi.org/10.3389/fphys.2019.00510

Plaza-Florido, A., Migueles, J. H., Sacha, J., & Ortega, F. B. (2019). The role of heart rate in the assessment of cardiac autonomic modulation with heart rate variability. *Clinical Research in Cardiology*, *108*(12), 1408–1409. https://doi.org/10.1007/S00392-019-01486-Y

Plaza-Florido, A., Sacha, J., & Alcantara, J. M. (2021). Short-term heart rate variability in resting conditions: Methodological considerations. *Polish Heart Journal*, *79*(7–8), 745–755. https://doi.org/10.33963/KP.A2021.0054

Sajadieh, A., Nielsen, O. W., Rasmussen, V., Hein, H. O., Abedini, S., & Hansen, J. F. (2004). Increased heart rate and reduced heart-rate variability are associated with subclinical inflammation in middle-aged and elderly subjects with no apparent heart disease. *European Heart Journal*, *25*(5), 363–370. https://doi.org/10.1016/J.EHJ.2003.12.003

Shaffer, F., & Ginsberg, J. P. (2017). An overview of heart rate variability metrics and norms. *Frontiers in Public Health*, *5*, 258. https://doi.org/10.3389/fpubh.2017.00258

Sloan, R. A., Haaland, B. A., Sawada, S. S., Lee, I. M., Sui, X., Lee, D. C., Ridouane, Y., Müller-Riemenschneider, F., & Blair, S. N. (2016). A fit-fat index for predicting incident diabetes in Apparently healthy men: A prospective cohort study. *PLoS One*, *11*(6), e0157703. https://doi.org/10.1371/JOURNAL.PONE.0157703

Sloan, R. A., Sawada, S. S., I-Min, L., Gando, Y., Kawakami, R., Okamoto, T., Tsukamoto, K., & Miyachi, M. (2018). The Association of Fit-Fat Index with incident diabetes in Japanese men: A prospective cohort study. *Scientific Reports*, *8*(1), 1–6. https://doi.org/10.1038/s41598-017-18898-3

Sloan, R. A., Sawada, S. S., Martin, C. K., & Haaland, B. (2015). Combined association of fitness and central adiposity with health-related quality of life in healthy men: A cross-sectional study. *Health and Quality of Life Outcomes*, *13*(1), 1–9. https://doi.org/10.1186/S12955-015-0385-3/TABLES/4

Swainson, M. G., Batterham, A. M., Tsakirides, C., Rutherford, Z. H., & Hind, K. (2017). Prediction of whole-body fat percentage and visceral adipose tissue mass from five anthropometric variables. *PLoS One*, *12*(5), e0177175. https://doi.org/10.1371/JOURNAL.PONE.0177175

Tanaka, H., Monahan, K. D., & Seals, D. R. (2001). Age-predicted maximal heart rate revisited. *Journal of the American College of Cardiology*, *37*(1), 153–156. https://doi.org/10.1016/S0735-1097(00)01054-8

Tarvainen, M. P., Niskanen, J. P., Lipponen, J. A., Ranta-aho, P. O., & Karjalainen, P. A. (2014). Kubios HRV—Heart rate variability analysis software. *Computer Methods and Programs in Biomedicine*, *113*(1), 210–220. https://doi.org/10.1016/j.cmpb.2013.07.024

Task force of the European Society of Cardiology and the North American Society for Pacing and Electrophysiology. (1996). Heart rate variability: Standards of measurement, physiological interpretation and clinical use. *Circulation*, *93*(5), 1043–1065.

Tayel, M. B., & AlSaba, E. I. (2015). Poincaré plot for heart rate variability. *Journal of Biomedical and Biological Engineering*, *9*(9), 708–711.

Teisala, T., Mutikainen, S., Tolvanen, A., Rottensteiner, M., Leskinen, T., Kaprio, J., Kolehmainen, M., Rusko, H., & Kujala, U. M. (2014). Associations of physical activity, fitness, and body composition with heart rate variability-based indicators of stress and recovery on workdays: A cross-sectional study. *Journal of Occupational Medicine and Toxicology*, *9*(1), 1–9. https://doi.org/10.1186/1745-6673-9-16/TABLES/4

Thayer, J. F., Yamamoto, S. S., & Brosschot, J. F. (2009). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *International Journal of Cardiology*, *141*, 122–131. https://doi.org/10.1016/j.ijcard.2009.09.543

Tian, Y., Huang, C., He, Z., Hong, P., & Zhao, J. (2015). Autonomic function responses to training: Correlation with body composition changes. *Physiology & Behavior*, *151*, 308–313. https://doi.org/10.1016/j.physbeh.2015.07.038

Toomey, C. M., Cremona, A., Hughes, K., Norton, C., & Jakeman, P. (2015). A review of body composition measurement in the assessment of health. *Topics in Clinical Nutrition*, *30*(1), 16–32. https://doi.org/10.1097/TIN.0000000000000017

Triggiani, A. I., Valenzano, A., Trimigno, V., Di Palma, A., Moscatelli, F., Cibelli, G., & Messina, G. (2019). Heart rate variability reduction is related to a high amount of visceral adiposity in healthy young women. *PLoS One*, *14*(9), e0223058. https://doi.org/10.1371/JOURNAL.PONE.0223058

Tsuji, H., Larson, M. G., Venditti, F. J., Manders, E. S., Evans, J. C., Feldman, C. L., & Levy, D. (1996). Impact of reduced heart rate variability on risk for cardiac events: The Framingham heart study. *Circulation*, *94*(11), 2850–2855. https://doi.org/10.1161/01.CIR.94.11.2850

Wang, Z., Wang, Z., & Heymsfield, S. (1999). History of the study of human body composition: A brief review. *American Journal of Human Biology*, *11*(2), 157–165.

Weippert, M., Behrens, M., Mau-Moeller, A., Bruhn, S., & Behrens, K. (2018). Relationship between morning heart rate variability and creatine kinase response during intensified training in recreational endurance athletes. *Frontiers in Physiology*, *9*, 1267. https://doi.org/10.3389/FPHYS.2018.01267/BIBTEX

Williams, D. P., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., Thayer, J. F., & Koenig, J. (2016). Two-week test-retest reliability of the Polar® RS800CX TM to record heart rate variability. *Clinical Physiology and Functional Imaging*, *37*(6), 776–781. https://doi.org/10.1111/cpf.12321

Williams, D. W. P., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., Thayer, J. F., & Koenig, J. (2017). Two-week test–retest reliability of the polar® RS800CX™ to record heart rate variability. *Clinical Physiology and Functional Imaging*, *37*(6), 776–781. https://doi.org/10.1111/CPF.12321

Wong, A., & Figueroa, A. (2021). Effects of acute stretching exercise and training on heart rate variability: A review. *Journal of Strength and Conditioning Research*, *35*(5), 1459–1466. https://doi.org/10.1519/JSC.0000000000003084

You, T., & Nicklas, N. B. J. (2006). Chronic inflammation: Role of adipose tissue and modulation by weight loss. *Current Diabetes Reviews*, *2*(1), 29–37.

How to cite this article: Navarro-Lomas, G., Plaza-Florido, A., De-la-O, A., Castillo, M. J., & Amaro-Gahete, F. J. (2023). Fit-Fat Index is better associated with heart rate variability compared to fitness and fatness alone as indicators of cardiometabolic human health. *American Journal of Human Biology*, 1–11. https://doi.org/10.1002/ajhb.23945