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Association of physical capacity with heart rate variability based on a short-duration measurement of resting pulse rate in older adults with obesity

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Abstract

Background

Obesity can limit physical capacity and lower physical activity levels in elderly people. Low physical activity levels may be mediated by autonomic dysfunction with decreased heart rate variability (HRV). However, the relationship between autonomic dysfunction and low physical capability remains unclear. This cross-sectional study investigated the association of low physical capability with HRV in older adults with obesity.

Materials and methods

We recruited 231 old man and 210 old women with a mean (range) age of 65.5 (51–78) and 62.9 (52–76) years, respectively. Physical capability was measured using mobility tasks, including functional reach, single-leg stance (SLS), gait speed (GS), timed up and go, and timed chair rise (TCR), and the scores on these tasks were merged and transformed into a global physical capability score (GPCS). HRV was measured using a 7-min resting pulse-based technique, and the time- and frequency-domain indices of HRV were obtained including standard deviation of normal-to-normal intervals (SDNN), root mean square of successive differences at rest (rMSSD), and high-frequency (HF) power. All HRV indices were natural log (In) transformed for analysis. Participants were divided into high, moderate, and low physical-capability groups according to their physical performance. Multivariate analysis of covariance was performed to test differences in HRV indices among physical-capability groups with participants' characteristics serving as covariates. A stepwise regression model was established to identify the determinants of HRV indices. We used hierarchical regression analysis to identify the association of the GPCS with HRV indices.



Competing interests: All authors have declared that no competing interests exist.

Results

In both men and women, the low physical-capability group exhibited significantly increased heart rate (P < 0.05) and decreased HRV in terms of a decreased ln[SDNN] (P < 0.001), ln [rMSSD] (P < 0.05) and ln[HF] (P < 0.05), compared with the high physical-capability group. GS positively predicted ln[SDNN], whereas SLS, GS, and TCR were determinants of ln[HF], regardless of gender. The GPCS in older men and women independently accounted for 29.9% (P < 0.001) and 23.7% (P < 0.001), respectively, in variance in ln[SDNN].

Conclusions

A low physical-capability level is an independent determinant of decreased HRV in older adults with obesity.

Introduction

Obesity is a burden on the elderly population, and it contributes to an increased risk of many medical problems, such as diabetes mellitus and cardiometabolic disease, that eventually have a substantial negative impact on an individual's health status [1-3]. Obesity is characterized by a proinflammatory state initiated by adipocytes, and the adiposity-engendered systemic inflammation is closely linked to metabolic risk factors such as hyperinsulinemia and hyper-glycemia [3, 4]. These risk factors further impair body homeostasis through a series of hemo-dynamic consequences [2, 4]. In addition, geriatric individuals with obesity may have a high risk of muscle loss and a related decline in physical function, with underlying changes in body composition [5–7].

The autonomic nervous system is believed to play a critical role in mediating the pathophysiology of obesity [8–12]. Autonomic dysfunction can be assessed in terms of heart rate variability (HRV), which has become a marker for the risk stratification of cardiovascular consequences because of its clinical relevance to mortality [13, 14]. HRV can be measured by using an alternative assessment tool based on short-duration measurements of pulse rate variability [15, 16]. Deteriorations in HRV are cholinergic and observed in association with abnormal glucose regulation, adiposity-induced immune responses, and low physical domain values for quality of life [17–19], all of which lead to increased allostatic load and adverse health outcomes [20–23].

Although cardiometabolic impairment (a combination of metabolic and cardiovascular dysfunction) is the hallmark of obesity, studies have suggested that physical function should also be considered in order to fully manage obesity in the elderly population [24, 25]. Impaired physical functioning is a critical determinant of disability and mortality in older adults [26–28], and obesity can further exacerbate the age-related decline in physical function. The risk of adverse physical consequences such as self-reported physical difficulty [6, 7] and reduced physical capability [5, 7, 25], a parameter that can be objectively measured to describe a person's ability to perform free-living activities including walking and rising from a chair [29], is higher in older adults with obesity than in their lean peers. Self-reported physical difficulty or compromised functional capability in older people with obesity can be attributed to reduced cardiorespiratory fitness and impaired muscle function engendered by underlying cardiac autonomic dysfunction and skeletal muscle stress [6, 25, 30–32]. These factors may lead to

further physical inactivity [33] and potentially hinder community-dwelling older people from leaving their houses daily [34].

A large body of evidence reveals an association of HRV with numerous physical domain measures including self-rated physical fitness [35], physical activity levels (particularly moderate-to-vigorous levels) [35–40], physical inactivity [39], and self-reported physical functional status [19]. Nevertheless, the association of HRV with objectively measured physical capability in older adults remains unclear. Considering that physical activity levels in older adults closely depend on performance-based physical function [41–44] and that mobility disability is becoming prevalent in older populations with obesity [25], it is important to understand the relation-ship between HRV and physical capability in elderly people with obesity.

The aim of this study was to determine whether objectively measured physical capability levels have an association with HRV in older adults with obesity. We hypothesized that older adults with higher physical capabilities would have significantly higher HRV than do those with lower physical capabilities, and that physical capability levels would be significantly associated with variations in HRV.

Materials and methods

Design

We conducted an observational, cross-sectional study at the Metabolic Management Center of the Physical Medicine and Rehabilitation Department of Shuang Ho Hospital, Taipei Medical University. Potential participants were sequentially recruited from a health screen admission in the community during a time period from June 2015 to February 2016. The eligibility of all recruited patients was determined through a medical chart review and body fat assessment at screening admission. During the examination, all eligible participants underwent subjective evaluation through questionnaires, and their HRV and physical capability levels were measured. All measurements were performed by a trained research assistant. This study was approved by the Joint Institutional Review Board of Taipei Medical University (protocol number: N201602035), and each participant provided written informed consent before the examination.

Participants

Participants were selected according to the guidelines of the STROBE statement extension for observational studies [45], as outlined in the flowchart in Fig 1. In this study, obesity was measured using the method of Baumgartner [46]. At screening admission, body fat percentage (BF %), which is considered a valid estimator of body composition, was measured using an eight-polar bioelectrical impedance analysis device with a multifrequency current (Inbody 220, Biospace, Seoul, Republic of Korea) [47]. BF% values of >27% for men and >38% for women were considered the cutoff points for obesity in older populations [48].

The inclusion criteria for participants in this study are outlined as follows: (1) being aged between 50 and 80 years and (2) having a BF% of >27% for men and >38% for women. Participants were excluded if they met the following exclusion criteria: (1) with a BF% not meet the gender specific cut points for obesity; (2) receiving a diagnosis of neurological disorders, orthopedic, or rheumatologic problems that affect the execution of mobility tasks; (3) having history of heart disease, serious arrhythmia, or pacemaker use; (4) habitual smoking or heavy consumption of stimulant beverages such as alcohol; (5) consuming any medication that can presumably influence autonomic functions, such as antihypertensives, anticholinergics, or antidepressants, for at least 1 month prior to the beginning of the study; and (6) having difficulty in lying supine for 10 min.



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During the examination, participants' characteristics, including age and sex, were recorded. Body height, weight, BMI, and BF% were measured using the aforementioned eight-polar bioelectrical impedance analysis device. In addition, the comorbidity status of each participant was evaluated using the Comorbidity Illness Rating Scale (CIRS), which addresses all relevant body systems and was validated for use in older people [49].

Physical capability assessment

Physical capability was assessed through the measurement of functional mobility tasks including functional reach (FR) [50], single-leg stance (SLS) [51], gait speed (GS) [51], timed up and go (TUG) [52], and timed chair rise (TCR) [53, 54]; these tasks have been used as indicators in older adult populations [55] and validated in such populations [51–54, 56]. Each participant performed a practice trial before the test, and two test trials were conducted. The mean score of the two test trials for each task was subsequently calculated for statistical analysis.

Functional reach. FR provides a dynamic measure of balance, regardless of the movement strategy selected [50]. However, previous studies using the FR test have reported that body height is a significant confounding factor for the test results [57, 58]; for example, Isles et al. found that the FR distance increased by 3.3 cm for every 10 cm of body height [58]. Therefore, we used the FR distance-to-participant height ratio (FHR), as described previously by Hageman et al. [57], to minimize the confounding effect engendered by the intragroup variation in body height, according to the following formula: FHR = [FR distance (cm)/height (cm)] × 100.

Single-leg stance. SLS assesses balance control, and the SLS score represents the total time for which a person can stand on his or her dominant leg. In this study, SLS tasks were performed by participants with their eyes open.

Gait speed. GS (in m/s) measures the time required for people to walk for a predetermined distance. In this study, we measured the time taken by participants to walk for 10 m on a track at a self-determined pace [51].

Timed up and go. TUG measures the time required for people to rise from a chair, walk around, and then return to the chair. In this study, TUG was determined as the time taken by participants to rise from their chairs (height, 42 cm; depth, 26 cm), walk for 3 m, turn around, and return to a seated position in the chair at a self-determined speed. A walking aid was used by participants during the test if necessary.

Timed chair rise. TCR measures the ability to get out of a chair. In this study, participants stood upright from a seated position in a chair (height, 45 cm), with their arms folded across their chest, and returned to a seated position as many times as possible within a 30-s period.

Each of the five mobility tests (i.e., FHR, SLS, GS, TUG, and TCR) was attributed a score of 1–4 by using quartiles of performance with the fourth, third, second, and first quartiles being coded as 4, 3, 2, and 1 points, respectively). Participants who performed three or more of the five mobility tasks scored as 1 were classified as having low physical capability, whereas those who performed three or more of the five mobility tasks scored as 4 were classified as having high physical capability. The remaining participants were classified as having moderate physical capability.

In the present study, a global physical capability score (GPCS) was adapted from an approach proposed in previous studies [5, 59]. The scores of all five tests were then summed to produce a GPCS for each participant; scores ranged from 5 to 20. One advantage of the GPCS, compared with individual tests, is that it provides an overall measure of a participant's performance while taking into account several tasks related to daily activities.

HRV analysis

HRV was measured immediately prior to mobility tests. Participants were first asked to rest quietly for 10 min in a supine position; subsequently, they were assisted with attaching the

ANSWatch monitor (Taiwan Scientific Co., Taipei, Taiwan) to their left wrists and were instructed to close their eyes, relax, and remain quiet. A time of approximately 7 min was required in each ANSWatch test to determine the HRV and hemodynamic indices, including blood pressure (BP) and resting heart rate (HR). All data were extracted to a computer by using ANSWatch Manager Pro software.

The ANSWatch wrist monitor, with multiple piezoelectric sensors in the cuff, has been employed to measure BP waveforms in the radial artery [60, 61]. HRV analysis was performed using pulse cycle intervals instead of RR intervals. HRV variables, including time- and frequency-domain variables, were analyzed according to the international standard [62]. The time-domain HRV variables comprised the standard deviation (SD) of normal-to-normal (NN) intervals (SDNN, ms) and the root mean square of successive differences at rest (rMSSD, ms). The frequency-domain HRV variable, namely high-frequency power (HF, 0.15–0.4 Hz, ms²), was determined using a power spectral analysis. All HRV indices were natural log (ln) transformed for analysis.

Sample size estimation

The sample size estimation of this study was based on primary outcomes and SDNN values and was performed using G-Power 3 [63]. At a statistical power of 0.95, an effect size of 0.20 [38], and an alpha value of 0.05, we determined that a minimum of 390 participants were required to identify a difference in the SDNN value of 3 ms² among the three participant groups, assuming an SDNN value SD of 14.4 ms² [38].

Statistical analysis

All analyses were separately performed by gender. One-way analysis of variance and the chisquared test were used to compare participants' characteristics among the three physical capability groups. Multivariate analysis of covariance was also performed to examine betweengroup differences in HRV indices and all mobility measures, with age, BMI, and the CIRS serving as covariates. The Gaussian distribution was tested for all the variables by using the Kolmogorov–Smirnov test. Natural log (ln) transformation was used if data were not normally distributed.

A Pearson product-moment correlation coefficient (*r*) was used to assess the linear relationship between HRV indices and potential factors. When controlling for participants' characteristics, a multiple stepwise linear regression of the collapsed data was established for each HRV index to identify the association between the HRV index and all mobility measures; in this analysis, each HRV index was log transformed and treated as the dependent variable and all the mobility measures (i.e., FFR, SLS, GS, TUG, and TCR) were treated as exploratory covariates for each model.

The hierarchical regression models were established to explore the association of resting HR and GPCS with each HRV index, after adjusting for control variables related to HRV [64]. Separate hierarchical models were used for each of the 3 dependent HRV variables (i.e., ln SDNN, ln rMSSD, and ln HF). Each model had 3 steps. In step 1, we entered the covariates (i.e., age, BMI, and CIRS). In step 2, we entered resting HR. In step 3, we entered GPCS. Finally, multicollinearity was tested using tolerance and variance inflation factors. SPSS Statistics for Windows (version 17.0; SPSS Inc., Chicago, IL, USA) was used for all analyses, and comparison results with P < 0.05 were considered to represent statistically significant differences.

Results

A total of 461 participants who were referred from the metabolic management center were assessed for their eligibility after they provided informed consent. After excluding 20 participants who did not meet the inclusion criteria (five men and seven women who have a BMI ranging from 24.3 to 25.7 Kg/m²did not match the gender specific cutoff points of BF% for obesity, three had an old onset of stroke, and five were habitual smokers, heavy drinkers, and consumers of coffee), we included 231 old man and 210 old women with a mean (range) age of 65.5 (51–78) and 62.9 (52–76) years, respectively, for further assessment (Fig 1).

Table 1 presents the participants' demographic characteristics and scores on the mobility tasks, according to their group assignment. Overall, both of male and female participants in the high-physical-capability group were younger and had a lower BMI, BF%, CIRS score, and resting HR (all P < 0.05) than did those in the low-physical-capability group. In addition, both of male and female participants in the high-physical-capability group exhibited significantly higher performance in mobility tests compared with those in the low-physical-capability group performance than the male peers in mobility.

Primary data of all HRV indices are presentated in <u>S1 Table</u>. Adjusted mean values for the ln transformed HRV indices of the three physical capability groups are showed in Fig 2. The

	Men									Women								
Items	Low PC			Moderate PC		Hi	High PC		Low PC			Moderate PC			High PC			
	mean	±	SD	mean	±	SD	mean	±	SD	mean	±	SD	mean	±	SD	mean	±	SD
n	68			104			59			65			70			75		
Age (years)	69.9	±	8.1	64.8	±	6.4 ^a	61.9	±	7.2 ^a	68.9	±	5.3	63.8	±	6.4 ^{ab}	61.7	±	5.8 ^{ab}
BMI (kg/m²)	30.4	±	1.6	28.9	±	1.4 ^a	29.1	±	1.7 ^a	31.4	±	2.1 ^b	29.4	±	1.9 ^a	28.5	±	1.2 ^{ab}
BF%	37.3	±	5.6	34.7	±	6.4 ^a	33.5	±	5.4 ^a	39.3	±	6.2	37.6	±	7.1	36.1	±	5.9 ^{ab}
CIRS score	10.4	±	4.6	7.8	±	3.9 ^a	5.4	±	2.1 ^a	13.4	±	7.1 ^b	8.5	±	5.1 ^a	7.3	±	5.9 ^{ab}
BP_SYS (mmHg)	131.8	±	10.1	130.4	±	13.1	128.3	±	11.5	132.3	±	12.1 ^b	130.4	±	13.1	128.3	±	11.5 ^b
BP_DIA (mmHg)	86.5	±	5.4	86.8	±	8.5	87.1	±	6.9	88.1	±	8.4 ^b	85.7	±	8.2	84.5	±	7.9 ^b
Resting HR (beats/min)	71.8	±	6.5	69.2	±	8.2 ^a	66.8	±	7.5 ^a	72.3	±	7.4	69.7	±	8.6 ^a	65.4	±	7.3 ^a
Age group, n (%)																		
<60 years	12		(17.6)	29		(27.9)	29		(49.2)	11		(16.9)	30		(42.9)	33		(44.5)
60–70 years	28		(41.2)	48		(46.2)	19		(32.2)	30		(46.2)	27		(38.6)	28		(37.3)
>70 years	28		(41.2)	27		(26.0)	11		(18.6)	24		(36.9.7)	13		(18.6)	14		(18.7)
Mobility measures																		
FHR	7.3	±	1.9	14.1	±	3.3 ^a	18.8	±	4.1 ^a	6.7	±	2.9	12.1	±	3.8 ^{ab}	18.0	±	2.4 ^a
SLS (s)	9.5	±	2.3	15.2	±	3.6 ^a	20.6	±	1.9 ^a	8.5	±	1.9 ^b	12.2	±	3. ^{ab}	17.5	±	2.3 ^{ab}
GS (m/s)	0.9	±	0.2	1.2	±	0.3 ^a	1.5	±	0.3 ^a	0.8	±	0.2	1.2	±	0.2 ^{ab}	1.4	±	0.3 ^a
TUG (s)	11.1	±	1.6	8.3	±	2.2 ^a	6.6	±	1.9 ^a	11.8	±	1.9	9.0	±	2.1 ^{ab}	5.5	±	1.6 ^{ab}
TCR (repetition)	7.4	±	1.6	14.2	±	3.7 ^a	18.5	±	4.1 ^a	6.2	±	1.4 ^b	11.9	±	3.4 ^{ab}	16.4	±	2.7 ^{ab}
GPCS	7.3	±	0.8	13.4	±	2.6 ^a	18.8	±	0.7 ^a	6.0	±	0.8 ^b	11.8	±	2.4 ^{ab}	18.4	±	0.5 ^a

Table 1. Demographic characteristics of participants stratified on age and gender.

PC = physical capability; BMI = body mass index; CIRS = Cumulative Illness Rating Scale; BP_SYS = systolic blood pressure; BP_DIA = diastolic blood pressure; HR = heart rate; FHR = ratio of the functional reach distance to body height; SLS = single-leg stance; GS = gait speed; TUG = timed up and go; TCR = timed chair rise; GPCS = global physical capability score.

^aA significant difference compared with the low-physical-capability group, P < 0.05.

^bA significant difference compared with the corresponding physical-capability group in men, P < 0.05.

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(A) Men

LOS ONE

(B) Women





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older men with low physical capability exhibited significantly decreased ln SDNN [adjusted mean difference (aMD), -0.83; P < 0.001], ln rMSSD (aMD, -0.74; P = 0.006), and ln HF (aMD, -1.09; P < 0.001), compared with their high physical-capability peers. Similarly, the older women who had low physical capability showed significantly lower ln SDNN (aMD, -0.55; P < 0.001), ln rMSSD (aMD, -0.83; P = 0.008), and ln HF (aMD, -1.18; P < 0.001), compared with the high physical-capability group.

Table 2 shows the correlation between the HRV indices and potential moderators. Age, BMI, comorbidity score, and resting HR exhibited significant correlations with all HRV indices with moderate to low correlation coefficients (all P < 0.05) in both older men and women. In addition, all mobility scores in older men were significantly correlated with ln SDNN, ln rMSSD, and ln HF (all P < 0.05) as well as older women did. The GCPS in older men was moderately correlated with ln SDNN and ln HF by a correlation coefficient of 0.61(P < 0.001) and 0.59 (P < 0.001), respectively; similar results was observed in older women.

Table 3 presents the association between the HRV indices and mobility functioning. In older men, increased SLS, GS, and TCR were independent determinants of increased ln SDNN and ln HF, whereas ln rMSSD was positively associated with GS only. In older women, increased ln HF was significantly associated with most of mobility performances, including SLS, GS, TUG, and TCR (all P < 0.05).

Table 4 shows the association of resting HR and GPCS with all HRV indices. In old men, resting HR explained an additional 12.6% [F(1, 226) = 48.73, P < 0.001], 3.6%, [F(1, 226) = 11.33, P < 0.01], and 6.8% [F(1, 226) = 21.56, P < 0.001] of variation in ln SDNN, ln rMSSD, and ln HF, respectively, as well as old women did. The GPCS in old men independently explained an additional 29.9% [F(1, 225) = 232.58, P < 0.001], 2.5% [F(1, 225) = 7.95, P < 0.01], and 10.6% [F(1, 225) = 39.43, P < 0.001] of the variance of ln SDNN, ln rMSSD, and ln HF, respectively; similar results were observed in old women.



Variables ^a		Men		Women					
	In[SDNN]	In[rMSSD]	In[HF]	In[SDNN]	In[rMSSD]	In[HF]			
Age	-0.52***	-0.29***	-0.40***	-0.32***	-0.26***	-0.36***			
BMI	-0.22**	-0.27***	-0.31***	-0.31***	-0.29***	-0.20**			
CIRS score	-0.22**	-0.14*	-0.21**	-0.35**	-0.28***	-0.19**			
Resting HR	-0.43***	-0.32***	-0.38***	-0.33***	-0.43***	-0.30***			
Physical mobility			·						
FHR	0.61***	0.28***	0.46***	0.56***	0.45***	0.53***			
SLS	0.45***	0.17*	0.51***	0.57***	0.22**	0.59***			
GS	0.65***	0.36***	0.53***	0.41***	0.39***	0.51***			
TUG	-0.38***	-0.22**	-0.42***	-0.28***	-0.26***	-0.34***			
TCR	0.55***	0.26***	0.45***	0.50***	0.14*	0.45***			
GPCS	0.61***	0.29***	0.59***	0.53***	0.37***	0.57***			

Table 2. Pearson correlation of HRV indices with potential factors and physical mobility, as assessed through regression analyses.

All HRV variables are nature log transformed (In).

**P* < 0.05

** *P* < 0.01

*** P < 0.001.

^aHRV = heart rate variability; BMI = body mass index; CIRS = Cumulative Illness Rating Scale; HR = heart rate; SDNN = standard deviation of normal-tonormal (NN) intervals; rMSSD = root mean square of successive differences at rest; HF = high-frequency power; FHR = ratio of the functional reach distance to body height; SLS = single-leg stance; GS = gait speed; TUG = timed up and go; TCR = timed chair rise; GPCS = global physical capability score.

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Discussion

The present study investigated the association between physical capability and 7-min resting pulse-based HRV in older adults with obesity. Our results reveal an association of a lower physical capability level with HRV components, including decreased ln SDNN, ln rMSSD, and ln HF in older men and women with obesity. Consistent with these findings, after controlling for potential confounding factors, we observed that the objective measures of functional mobility (i.e., FHR, GS, SLS, TCR, and TUG) were independent predictors of low HRV, and that physical capability (i.e., GPCS) significantly contributed to the variance in the HRV in both older men and women with obesity.

Table 3. Stepwise linear regression analyses for all indices of heart rate variability.

Dependent			Men ^b			Women ^b							
variables ^a	FHR	SLS	GS	TUG	TCR	FHR	SLS	GS	TUG	TCR			
In[SDNN]	0.14	0.45***	0.39***	-	0.67***	0.53***	0.68***	0.34*	-	0.26			
In[rMSSD]	-	-	0.26**	-	-	0.68***	-	-	-	0.51**			
In[HF]	-	0.61***	0.33***	-	0.29*	-	0.93***	0.32**	-0.13*	0.67*			

All HRV variables are natural log transformed (In).

**P* < 0.05

** *P* < 0.01

****P*<0.001.

^aSDNN = standard deviation of normal-to-normal (NN) intervals; rMSSD = root mean square of successive differences at rest; HF = high-frequency power; FHR = ratio of the functional reach distance to body height; SLS = single-leg stance; GS = gait speed; TUG = timed up and go; TCR = timed chair rise. ^bStepwise linear regression variables included mobility task measures. The linear model coefficients are represented as standardized coefficient (β) values. Model was adjusted for age, body mass index, and comorbidity scores.

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Dependent	Step	Independent			Men		Women					
variables ^a	1	variables ^a	R ²	Adjusted R ²	R ² change	F change	df	R ²	Adjusted R ²	R ² change	F change	df
In[SDNN]	1	Age, BMI, CIRS	0.29	0.28	0.29	30.78***	3, 227	0.43	0.42	0.43	51.54***	3, 206
	2	Resting HR	0.42	0.40	0.13	48.73***	1,226	0.51	0.50	0.08	33.74***	1, 205
	3	GPCS	0.71	0.71	0.30	232.58***	1,225	0.75	0.74	0.24	194.54***	1, 204
In[rMSSD]	1	Age, BMI, CIRS	0.24	0.23	0.24	23.48***	3, 227	0.03	0.02	0.03	2.24	3, 206
	2	Resting HR	0.27	0.26	0.04	11.33**	1,226	0.09	0.07	0.06	12.61***	1, 205
	3	GPCS	0.30	0.28	0.03	7.95**	1,225	0.12	0.10	0.04	8.68**	1, 204
In[HF]	1	Age, BMI, CIRS	0.22	0.21	0.22	21.27***	3, 227	0.14	0.12	0.14	10.94***	3, 206
	2	Resting HR	0.29	0.27	0.07	21.56***	1,226	0.21	0.20	0.07	19.22***	1, 205
	3	GPCS	0.39	0.38	0.11	39.43***	1,225	0.35	0.33	0.13	41.73***	1, 204

Table 4. Hierarchical regression analyses for heart rate variability.

All HRV variables are natural log transformed (In).

**P* < 0.05

** *P* < 0.01

*** P < 0.001.

^aHRV = heart rate variability; SDNN = standard deviation of the normal-to-normal (NN) intervals; rMSSD = root mean square of successive differences at rest; HF = high frequency power; BMI = body mass index; CIRS = cumulative illness rating scale score; HR = heart rate; GPCS = global physical capability score.

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The accuracy levels of pulse-based HRV and ECG-based HRV measurements were compared. The application of pulse-based HRV measurements for assessing healthy individuals at rest was demonstrated to be adequately accurate, whereas mental stress tended to reduce the agreement between two assessment techniques [16]. The current study applied 7-min resting pulse-based HRV rather than ECG-based HRV, which has been used in most of the previous studies evaluating associations between clinical disorders and autonomic dysfunction. Despite being obese with higher BF% values, all of our participants were relatively healthy, after the exclusion of diagnoses of neurological disorders and heart disease. Because we excluded participants who received medications that might influence autonomic activities at least a month prior to this study, we did not assess participants' mental stress; this may bias the results of this study. However, each participant was asked to rest in a lying supine position for 10 min before HRV testing.

Previous several studies have indicated an association of physical activity levels with HRV in older people. Specifically, studies regarding short-term HRV analysis and method have reported that a higher physical activity level was associated with increased SDNN [36, 40, 65], rMMSD [37, 40, 65], and HF [36, 40, 65] in older adults; in addition, previous studies have identified a clear relationship between high physical activity and short-term HRV in individuals with overweight and obesity [36, 66]. The findings of our present study also indicate that physical capability, as derived from objectively measured mobility tasks, was significantly associated with HRV measures, regardless of age, sex, or comorbidities. Despite some discussion [67], the mechanisms through which autonomic dysfunction mediates the physical domain of health (particularly physical function) in individuals with obesity remain unclear. However, in older adults with overweight and obesity, reduced physical capability can be linked to the effect of excessive adiposity on muscles, which plays a crucial role in metabolic adaptation in obesity [68-70]. In addition, the autonomic nervous system dysfunction in elderly individuals with obesity was marked by low muscle mass, which further highlights the relationship between autonomic dysfunction and muscle impairment [66]. Lack of measuring muscle mass did not allow us to directly draw the relationships between low muscle mass and low physical

capability. However, our participants with older age and higher BF% in the low physical-capability group than their high physical-capability peers may be closely associated with muscle attenuation [71]. Taken all of above together, these findings may explain the associations of diminished HRV with low physical capability and low mobility performance.

Another possible exploration involves the adaptation of physical fitness and whole-body energy expenditure indicated by resting HR [72]. A higher resting HR is predictive of poorer physical fitness, which may also be associated with low HRV in older individuals [73]. Compared with the high-physical-capability group, HRV markedly decreased in the low-physicalcapability group, presumably reflecting an adaptation to lower physical fitness in terms of a significantly higher resting HR. In addition, our results showed that both resting HR and GPCS have significant contributions in explaining the variance in HRV. Therefore, our results may indicate that both the state of physical fitness and physical capability are associated with HRV.

Study limitations

The current study has some limitations that should be considered. First, because of the cross sectional design of this study, we could not identify causality within existing associations. However, the participants' current physical capability levels could be assessed, and the associations between physical capability levels and pulse-based HRV were significant after adjustment for age and other confounders. Second, the participants selected for this study were a generally healthy group of older adults. Therefore, our findings may not be generalizable to the whole population in this age range, and this should be considered when examining HRV in people with certain illnesses or diseases such as metabolic syndrome or frailty. Third, there are some potential confounders such as lower limb arthritis which limits physical capacity and sleep-disordered breathing which is prevalent in obese older adults and can have a large effect on daytime functioning and probably daytime HRV; in addition, the participants' mental and cognitive status was not assessed, and no psychological indices were employed in this study; nevertheless, HRV can be simultaneously influenced by various physiological and psychological conditions. Although people who were taking psychological medications were assessed and excluded, subclinical psychological or mental stress can be a potential confounding factor, and the derived associations may thus have then been overestimated. Fourth, we did not have any way to monitor HR and HRV over testing time; therefore, we could not ensure whether participants start to fall asleep, by which a decrease in HR and an increase in HRV can be observed, during the whole testing procedure. Maintaining not to fall asleep during the 10-min pretest rest and the 7-min testing period in a lying supine position may be difficult for older adults. Fifth, all of our mobility tests are related to non-aerobic fitness. It should be accounted that aerobic fitness also has contributions counting for an individual's physical capacity in daily life. Finally, although we identified several significant associations through a series of regression analyses, the level of correlation appeared to be either moderate or weak, with a regression coefficient of < 0.70. The physiological relevance and clinical significance of these associations must be further confirmed.

Conclusions

The results of this study demonstrate that low physical capability levels identified using objectively measured mobility tasks were associated with low resting pulse-based HRV in older adults with obesity. Given the effect of low HRV on the physical domain of health, we suggest that higher emphasis should be placed on the physical fitness and capability of older individuals with obesity with regard to their activities of daily living. The relevance of this study may be its indication of more close associations between physical capability and autonomic cardiovascular function in older individuals with obesity.

Supporting information

S1 Table. Heart rate variability of participants stratified on age and gender. (DOCX)

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References

- Neeland IJ, Ayers CR, Rohatgi AK, Turer AT, Berry JD, Das SR, et al. Associations of visceral and abdominal subcutaneous adipose tissue with markers of cardiac and metabolic risk in obese adults. Obesity (Silver Spring). 2013; 21(9):E439–47. https://doi.org/10.1002/oby.20135 PMID: 23687099.
- Wahba IM, Mak RH. Obesity and obesity-initiated metabolic syndrome: mechanistic links to chronic kidney disease. Clin J Am Soc Nephrol. 2007; 2(3):550–62. https://doi.org/10.2215/CJN.04071206 PMID: 17699463.
- Grundy SM. Obesity, Metabolic Syndrome, and Cardiovascular Disease. J Clin Endocrinol 2004; 89 (6):2595–600. https://doi.org/10.1210/jc.2004-0372
- Grundy SM. Pre-diabetes, metabolic syndrome, and cardiovascular risk. J Am Coll Cardiol. 2012; 59 (7):635–43. https://doi.org/10.1016/j.jacc.2011.08.080 PMID: 22322078
- Bouchard DR, Dionne IJ, Brochu M. Sarcopenic/obesity and physical capacity in older men and women: data from the Nutrition as a Determinant of Successful Aging (NuAge)-the Quebec longitudinal Study. Obesity (Silver Spring). 2009; 17(11):2082–8. https://doi.org/10.1038/oby.2009.109 PMID: 19373219.
- Rolland Y, Lauwers-Cances V, Cristini C, Abellan van Kan G, Janssen I, Morley JE, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. Am J Clin Nutr. 2009; 89 (6):1895–900. https://doi.org/10.3945/ajcn.2008.26950 PMID: 19369381.

- Lang IA, Llewellyn DJ, Alexander K, Melzer D. Obesity, physical function, and mortality in older adults. J Am Geriatr Soc. 2008; 56(8):1474–8. <u>https://doi.org/10.1111/j.1532-5415.2008.01813.x</u> PMID: 18662211.
- Fidan-Yaylali G, Yaylali YT, Erdogan C, Can B, Senol H, Gedik-Topcu B, et al. The Association between Central Adiposity and Autonomic Dysfunction in Obesity. Med Princ Pract. 2016; 25(5):442–8. https:// doi.org/10.1159/000446915 PMID: 27194294.
- Sant Anna Junior M, Carneiro JR, Carvalhal RF, Torres Dde F, Cruz GG, Quaresma JC, et al. Cardiovascular Autonomic Dysfunction in Patients with Morbid Obesity. Arq Bras Cardiol. 2015; 105(6):580–7. https://doi.org/10.5935/abc.20150125 PMID: 26536979.
- Skrapari I, Tentolouris N, Perrea D, Bakoyiannis C, Papazafiropoulou A, Katsilambros N. Baroreflex sensitivity in obesity: relationship with cardiac autonomic nervous system activity. Obesity (Silver Spring). 2007; 15(7):1685–93. https://doi.org/10.1038/oby.2007.201 PMID: 17636086.
- Skrapari I, Tentolouris N, Katsilambros N. Baroreflex function: determinants in healthy subjects and disturbances in diabetes, obesity and metabolic syndrome. Curr Diabetes Rev. 2006; 2(3):329–38. https://doi.org/10.2174/157339906777950589 PMID: 18220637.
- Lustig RH. Autonomic dysfunction of the beta-cell and the pathogenesis of obesity. Rev Endocr Metab Disord. 2003; 4(1):23–32. PMID: 12618557.
- Huikuri HV, Stein PK. Heart rate variability in risk stratification of cardiac patients. Prog Cardiovasc Dis. 2013; 56(2):153–9. https://doi.org/10.1016/j.pcad.2013.07.003 PMID: 24215747.
- Jorgensen RM, Abildstrom SZ, Levitan J, Kobo R, Puzanov N, Lewkowicz M, et al. Heart Rate Variability Density Analysis (Dyx) and Prediction of Long-Term Mortality after Acute Myocardial Infarction. Ann Noninvasive Electrocardiol. 2016; 21(1):60–8. https://doi.org/10.1111/anec.12297 PMID: 26262922.
- Ahmad S, Bolic M, Dajani H, Groza V, editors. Wavelet estimation of pulse rate variability from oscillometric blood pressure measurements. 2009 IEEE International Workshop on Medical Measurements and Applications; 2009 29–30 May 2009.
- Schafer A, Vagedes J. How accurate is pulse rate variability as an estimate of heart rate variability? A review on studies comparing photoplethysmographic technology with an electrocardiogram. Int J Cardiol. 2013; 166(1):15–29. https://doi.org/10.1016/j.ijcard.2012.03.119 PMID: 22809539.
- Stuckey MI, Kiviniemi A, Gill DP, Shoemaker JK, Petrella RJ. Associations between heart rate variability, metabolic syndrome risk factors, and insulin resistance. Appl Physiol Nutr Metab. 2015; 40(7):734– 40. https://doi.org/10.1139/apnm-2014-0528 PMID: 26140416.
- Saito I, Hitsumoto S, Maruyama K, Nishida W, Eguchi E, Kato T, et al. Heart Rate Variability, Insulin Resistance, and Insulin Sensitivity in Japanese Adults: The Toon Health Study. J Epidemiol. 2015; 25 (9):583–91. https://doi.org/10.2188/jea.JE20140254 PMID: 26277879.
- Lu WC, Tzeng NS, Kao YC, Yeh CB, Kuo TB, Chang CC, et al. Correlation between health-related quality of life in the physical domain and heart rate variability in asymptomatic adults. Health Qual Life Outcomes. 2016; 14(1):149. https://doi.org/10.1186/s12955-016-0555-y PMID: 27765048.
- Kemp AH, Quintana DS. The relationship between mental and physical health: insights from the study of heart rate variability. Int J Psychophysiol. 2013; 89(3):288–96. https://doi.org/10.1016/j.ijpsycho. 2013.06.018 PMID: 23797149.
- Tonhajzerova I, Mokra D, Visnovcova Z. Vagal function indexed by respiratory sinus arrhythmia and cholinergic anti-inflammatory pathway. Respir Physiol Neurobiol. 2013; 187(1):78–81. https://doi.org/ 10.1016/j.resp.2013.02.002 PMID: 23410913.
- 22. Thayer JF, Sternberg E. Beyond heart rate variability: vagal regulation of allostatic systems. Ann N Y Acad Sci. 2006; 1088:361–72. https://doi.org/10.1196/annals.1366.014 PMID: 17192580.
- 23. Kawasaki T, Azuma A, Sakatani T, Hadase M, Kamitani T, Kawasaki S, et al. Prognostic value of heart rate variability in patients with hypertrophic cardiomyopathy. J Electrocardiol. 2003; 36(4):333–8. PMID: 14661170.
- Kalish VB. Obesity in Older Adults. Prim Care. 2016; 43(1):137–44, ix. https://doi.org/10.1016/j.pop. 2015.10.002 PMID: 26896206.
- Vincent HK, Vincent KR, Lamb KM. Obesity and mobility disability in the older adult. Obes Rev. 2010; 11(8):568–79. https://doi.org/10.1111/j.1467-789X.2009.00703.x PMID: 20059707.
- Haapanen-Niemi N, Miilunpalo S, Pasanen M, Vuori I, Oja P, Malmberg J. Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality—16 y follow-up of middle-aged and elderly men and women. Int J Obes Relat Metab Disord. 2000; 24(11):1465–74. PMID: 11126344.
- Nam S, Al Snih S, Markides K. Lower body function as a predictor of mortality over 13 years of follow up: Findings from Hispanic Established Population for the Epidemiological Study of the Elderly. Geriatr Gerontol Int. 2016; 16(12):1324–31. https://doi.org/10.1111/ggi.12650 PMID: 26627681.

- Idland G, Pettersen R, Avlund K, Bergland A. Physical performance as long-term predictor of onset of activities of daily living (ADL) disability: a 9-year longitudinal study among community-dwelling older women. Arch Gerontol Geriatr. 2013; 56(3):501–6. https://doi.org/10.1016/j.archger.2012.12.005 PMID: 23290919.
- Kuh D. A life course approach to healthy aging, frailty, and capability. J Gerontol A Biol Sci Med Sci. 2007; 62(7):717–21. https://doi.org/10.1017/S0029665113003923 PMID: 17634317.
- Corona LP, Alexandre TD, Duarte YA, Lebrao ML. Abdominal obesity as a risk factor for disability in Brazilian older adults. Public Health Nutr. 2017:1–8. https://doi.org/10.1017/S1368980016003505 PMID: 28112078.
- Buttery AK, Du Y, Busch MA, Fuchs J, Gaertner B, Knopf H, et al. Changes in physical functioning among men and women aged 50–79 years in Germany: an analysis of National Health Interview and Examination Surveys, 1997–1999 and 2008–2011. BMC Geriatr. 2016; 16(1):205. https://doi.org/10. 1186/s12877-016-0377-0 PMID: 27908276.
- Tomlinson DJ, Erskine RM, Morse CI, Winwood K, Onambélé-Pearson G. The impact of obesity on skeletal muscle strength and structure through adolescence to old age. Biogerontology. 2016; 17:467– 83. https://doi.org/10.1007/s10522-015-9626-4 PMID: 26667010
- Kostka T, Bogus K. Independent contribution of overweight/obesity and physical inactivity to lower health-related quality of life in community-dwelling older subjects. Z Gerontol Geriatr. 2007; 40(1):43– 51. https://doi.org/10.1007/s00391-006-0374-6 PMID: 17318731.
- Portegijs E, Rantakokko M, Viljanen A, Rantanen T, Iwarsson S. Perceived and objective entrancerelated environmental barriers and daily out-of-home mobility in community-dwelling older people. Arch Gerontol Geriatr. 2017; 69:69–76. https://doi.org/10.1016/j.archger.2016.11.011 PMID: 27889590.
- Kaikkonen KM, Korpelainen RI, Tulppo MP, Kaikkonen HS, Vanhala ML, Kallio MA, et al. Physical activity and aerobic fitness are positively associated with heart rate variability in obese adults. J Phys Act Health. 2014; 11(8):1614–21. https://doi.org/10.1123/jpah.2012-0405 PMID: 24508687.
- Rennie KL, Hemingway H, Kumari M, Brunner E, Malik M, Marmot M. Effects of moderate and vigorous physical activity on heart rate variability in a British study of civil servants. Am J Epidemiol. 2003; 158 (2):135–43. PMID: 12851226.
- Buchheit M, Simon C, Charloux A, Doutreleau S, Piquard F, Brandenberger G. Heart rate variability and intensity of habitual physical activity in middle-aged persons. Med Sci Sports Exerc. 2005; 37(9):1530– 4. PMID: 16177605.
- Buchheit M, Simon C, Charloux A, Doutreleau S, Piquard F, Brandenberger G. Relationship between very high physical activity energy expenditure, heart rate variability and self-estimate of health status in middle-aged individuals. Int J Sports Med. 2006; 27(9):697–701. <u>https://doi.org/10.1055/s-2005-872929 PMID: 16944398</u>.
- Usui H, Nishida Y. Relationship between physical activity and the very low-frequency component of heart rate variability after stroke. J Stroke Cerebrovasc Dis. 2015; 24(4):840–3. https://doi.org/10.1016/ j.jstrokecerebrovasdis.2014.11.026 PMID: 25680660.
- Soares-Miranda L, Sandercock G, Vale S, Santos R, Abreu S, Moreira C, et al. Metabolic syndrome, physical activity and cardiac autonomic function. Diabetes Metab Res Rev. 2012; 28(4):363–9. https:// doi.org/10.1002/dmrr.2281 PMID: 22238216.
- Stenholm S, Koster A, Valkeinen H, Patel KV, Bandinelli S, Guralnik JM, et al. Association of Physical Activity History With Physical Function and Mortality in Old Age. J Gerontol A Biol Sci Med Sci. 2016; 71 (4):496–501. https://doi.org/10.1093/gerona/glv111 PMID: 26290538.
- Keevil VL, Cooper AJ, Wijndaele K, Luben R, Wareham NJ, Brage S, et al. Objective Sedentary Time, Moderate-to-Vigorous Physical Activity, and Physical Capability in a British Cohort. Med Sci Sports Exerc. 2016; 48(3):421–9. https://doi.org/10.1249/MSS.000000000000785 PMID: 26501232.
- Cooper AJ, Simmons RK, Kuh D, Brage S, Cooper R. Physical activity, sedentary time and physical capability in early old age: British birth cohort study. PLoS One. 2015; 10(5):e0126465. <u>https://doi.org/ 10.1371/journal.pone.0126465</u> PMID: 25961736.
- 44. Reid N, Daly RM, Winkler EA, Gardiner PA, Eakin EG, Owen N, et al. Associations of Monitor-Assessed Activity with Performance-Based Physical Function. PLoS One. 2016; 11(4):e0153398. <u>https://doi.org/ 10.1371/journal.pone.0153398</u> PMID: 27073888.
- 45. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014; 12(12):1495–9. https://doi.org/10.1016/j.ijsu.2014.07.013 PMID: 25046131.
- Baumgartner RN. Body composition in healthy aging. Ann N Y Acad Sci. 2000; 904:437–48. https://doi. org/10.1111/j.1749-6632.2000.tb06498.x PMID: 10865787.

- Anderson LJ, Erceg DN, Schroeder ET. Utility of multifrequency bioelectrical impedance compared with dual-energy x-ray absorptiometry for assessment of total and regional body composition varies between men and women. Nutr Res. 2012; 32(7):479–85. <u>https://doi.org/10.1016/j.nutres.2012.05.009</u> PMID: 22901555.
- Zamboni M, Mazzali G, Fantin F, Rossi A, Di Francesco V. Sarcopenic obesity: a new category of obesity in the elderly. Nutr Metab Cardiovasc Dis. 2008; 18(5):388–95. https://doi.org/10.1016/j.numecd. 2007.10.002 PMID: 18395429.
- 49. Abizanda Soler P, Paterna Mellinas G, Martinez Sanchez E, Lopez Jimenez E. Comorbidity in the elderly: utility and validity of assessment tools. Rev Esp Geriatr Gerontol. 2010; 45(4):219–28. <u>https://doi.org/10.1016/j.regg.2009.10.009</u> PMID: 20488585.
- Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. J Gerontol. 1990; 45(6):M192–7. https://doi.org/10.1093/geronj/45.6.M192 PMID: 2229941.
- Takacs J, Garland SJ, Carpenter MG, Hunt MA. Validity and reliability of the community balance and mobility scale in individuals with knee osteoarthritis. Phys Ther. 2014; 94(6):866–74. <u>https://doi.org/10.2522/ptj.20130385</u> PMID: 24557649.
- Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. Phys Ther. 2000; 80(9):896–903. <u>https://doi.org/10.1007/s12199-010-0154-1</u> PMID: 10960937.
- Gill S, McBurney H. Reliability of performance-based measures in people awaiting joint replacement surgery of the hip or knee. Physiother Res Int. 2008; 13(3):141–52. <u>https://doi.org/10.1002/pri.411</u> PMID: 18697226.
- Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. Res Q Exerc Sport. 1999; 70(2):113–9. <u>https://doi.org/10.1080/02701367</u>. 1999.10608028 PMID: 10380242.
- Liao CD, Lin LF, Huang YC, Huang SW, Chou LC, Liou TH. Functional outcomes of outpatient balance training following total knee replacement in patients with knee osteoarthritis: A randomized controlled trial. Clin Rehabil. 2015; 29(9):855–67. https://doi.org/10.1177/0269215514564086 PMID: 25552523.
- Choi YM, Dobson F, Martin J, Bennell KL, Hinman RS. Interrater and intrarater reliability of common clinical standing balance tests for people with hip osteoarthritis. Phys Ther. 2014; 94(5):696–704. https://doi.org/10.2522/ptj.20130266 PMID: 24557648.
- Hageman PA, Leibowitz JM, Blanke D. Age and gender effects on postural control measures. Arch Phys Med Rehabil. 1995; 76(10):961–5. PMID: 7487439.
- Isles RC, Choy NL, Steer M, Nitz JC. Normal values of balance tests in women aged 20–80. J Am Geriatr Soc. 2004; 52(8):1367–72. https://doi.org/10.1111/j.1532-5415.2004.52370.x PMID: 15271128.
- He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens. 2002; 16(11):761–70. <u>https://doi.org/10.</u> 1038/sj.jhh.1001459 PMID: 12444537.
- Liao CD, Rau CL, Liou TH, Tsauo JY, Lin LF. Effects of Linearly Polarized Near-Infrared Irradiation Near the Stellate Ganglion Region on Pain and Heart Rate Variability in Patients with Neuropathic Pain. Pain Med. 2016. https://doi.org/10.1093/pm/pnw145 PMID: 27452896.
- Wang YJ, Hsu CC, Yeh ML, Lin JG. Auricular acupressure to improve menstrual pain and menstrual distress and heart rate variability for primary dysmenorrhea in youth with stress. Evid Based Complement Alternat Med. 2013; 138537:1–8. https://doi.org/10.1155/2013/138537 PMID: 24416063.
- Electrophysiology TFotESoCtNASoP. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Eur Heart J. 1996; 17(3):354–81. <u>https://doi.org/10.1161/</u> 01.CIR.93.5.1043 PMID: 8737210.
- Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007; 39(2):175–91. <u>https://doi.org/10.3758/BF03193146 PMID: 17695343</u>.
- Sammito S, Böckelmann I. Factors influencing heart rate variability. Int Cardio Forum J. 2016; 6:18–22. https://doi.org/10.1016/j.pcad.2013.07.003
- Buchheit M, Simon C, Viola AU, Doutreleau S, Piquard F, Brandenberger G. Heart rate variability in sportive elderly: relationship with daily physical activity. Med Sci Sports Exerc. 2004; 36(4):601–5. PMID: 15064587.
- Baek J, Park D, Kim I, Won JU, Hwang J, Roh J. Autonomic dysfunction of overweight combined with low muscle mass. Clin Auton Res. 2013; 23(6):325–31. https://doi.org/10.1007/s10286-013-0215-9 PMID: 24221882.

- Laederach-Hofmann K, Mussgay L, Ruddel H. Autonomic cardiovascular regulation in obesity. J Endocrinol. 2000; 164(1):59–66. https://doi.org/10.1016/S0167-8760(98)90292-6 PMID: 10607938.
- Amarya S, Singh K, Sabharwal M. Health consequences of obesity in the elderly. J Clin Geronto Geriatrics. 2014; 5(3):63–7. https://doi.org/10.1016/j.jcgg.2014.01.004
- Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. Lancet Diabetes Endocrinol. 2014; 2(10):819–29. <u>https://doi.org/10.1016/S2213-8587(14)70034-8 PMID: 24731660</u>.
- Oh KJ, Lee DS, Kim WK, Han BS, Lee SC, Bae KH. Metabolic Adaptation in Obesity and Type II Diabetes: Myokines, Adipokines and Hepatokines. Int J Mol Sci. 2016; 18(1). <u>https://doi.org/10.3390/</u> ijms18010008 PMID: 28025491.
- Bjordal JM, Johnson MI, Lopes-Martins RA, Bogen B, Chow R, Ljunggren AE. Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of randomised placebo-controlled trials. BMC Musculoskelet Disord. 2007; 8:51. https://doi.org/10.1186/1471-2474-8-51 PMID: 17587446.
- 72. Strath SJ, Swartz AM, Bassett DR Jr., O'Brien WL, King GA, Ainsworth BE. Evaluation of heart rate as a method for assessing moderate intensity physical activity. Med Sci Sports Exerc. 2000; 32(9 Suppl): S465–70. PMID: 10993416.
- Jensen MT, Suadicani P, Hein HO, Gyntelberg F. Elevated resting heart rate, physical fitness and allcause mortality: a 16-year follow-up in the Copenhagen Male Study. Heart. 2013; 99(12):882–7. https://doi.org/10.1136/heartjnl-2012-303375 PMID: 23595657.