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Annals of Sports Medicine and Research

Research Article

Meta-Analysis about the Effect of Caloric Restriction on Functionality

Paulo Roberto Hernandes Júnior[1], Manoel Silva[2], Helena Maia Almeida[3,4], Cláudia Regina Cavaglieri[3,4], Mara Patrícia T. Chacon-Mikahil[3,4], and Amanda Veiga Sardeli[3,4]*

[1]*Faculty of Medicine, University of Vassouras, Brazil*
[2]*Laboratory of Electromyography Studies, Department of Sport Science, University of Campinas, Brazil*
[3]*Gerontology Program – Faculty of Medical Sciences, UNICAMP, Brazil*
[4]*Laboratory of Exercise Physiology (FISEX), University of Campinas, Brazil*

***Corresponding author**
Amanda Veiga Sardeli, Laboratory of Exercise Physiology (FISEX), Faculty of Physical Education, University of Campinas (UNICAMP), Av. Érico Veríssimo, 701 CEP 13083-851, PO Box 6134, Campinas, Brazil, Tel: 55 19 35216625; Email: amandavsardeli@gmail.com

Submitted: 01 April 2021
Accepted: 20 April 2021
Published: 21 April 2021
ISSN: 2379-0571

Keywords
• Caloric restriction; Diet; Health, Performance; Physical fitness; Exercise test

Abstract

There is a concern that a reduction in energy intake would impairs physical performance and functionality in general. However, caloric restriction (CR), a dietary intervention defined as a reduction in energy intake without nutrient deficiency, is able to improve a number of body functions and, thus, could be also able to improve physical functionality. We ran a systematic review in November 2019 that led to inclusion of 9 studies. 15 subgroups were extracted for two main meta-analysis of CR effects on overall functionality: 1) Non-exercise meta-analysis, in which only CR effects were tested by comparison of CR without exercise (CR-NEX) and no diet without exercise (NEX); and 2) Exercise meta-analysis, in which additional CR effects on exercise interventions were tested by comparison of CR plus exercise training (CR-EX) and exercise training (EX). The CR effects on functionality were more evident when CR was the only intervention (SMD: 0.40 [CI95%: 0.015; 0.65], p <0.001), however, the addition of CR intervention for individuals undergoing exercise cause a small but consistent extra improve on functionality (SMD: 0.12 [CI95%: 0.04; 0.19], p <0.001). Among the components of functionality, CR was significantly effective on Balance, daily life endurance and mobility improvements (p<0.05), but not on agility, daily life strength, flexibility or vitality. Therefore, there is no reason for overweight or obese individuals fear functionality loss with caloric restriction.

ABBREVIATIONS

CR: Caloric Restriction; CR-EX: Caloric Restriction with Exercise Group; CR-NEX: Caloric Restriction not with Exercise Group; EX: Exercise Group

INTRODUCTION

The understanding of the human nutritional needs, in different ages to achieve good health and functionality lead to a concern about the use of restrictive diets for children, adolescents and older adults [1,2]. Importantly, caloric restriction (CR), a dietary intervention defined as a reduction in energy intake without nutrient deficiency is able to improve a number of body functions from model organisms to humans [3]. Thus, contrary of what was initially believed, in humans CR have shown a high potential for improving physical fitness, such as cardiorespiratory fitness [4,5] and muscle strength [6].

However, there is no consensus about the effect of CR on different aspects of functionality, such as balance, daily life strength and endurance, agility, flexibility, mobility or vitality. Furthermore, to understand isolated CR effects on functionality, it is needed to compare CR interventions and control groups not combined to exercise interventions or CR interventions and control groups following the same exercise program. In this way, the aim was to meta-analyze previous controlled trial studies in humans testing isolated CR effects on all aspects of functionality.

MATERIALS AND METHODS

The search on PubMed, Web of Science, Embase, Scopus and Cochrane databases, was conducted on at November 16, 2019. It combined the synonyms for CR, physical fitness and clinical trial terms.

We selected controlled trials (CTs) testing CR interventions, with or without exercise training on overall functionality components, including balance, daily life strength and endurance, agility, flexibility, mobility or vitality assessed by a variety of tests.

Studies with one or both of these two types of comparisons, were included:

1) Comparing CR and no exercise (CR-NEX) with no diet and no exercise (control group: NEX), and

2) CR plus exercise training (CR-EX) vs. an only exercise training (control group: EX).

We did not restricted date of publication, specific populations, or language; the only study writing in French was translated by a specialist [7].

Non-original studies such as reviews, conference papers, letters and commentaries were excluded. Details of the selection of the studies are described in (Figure 1).

Functionality average, standard deviation (SD), and sample

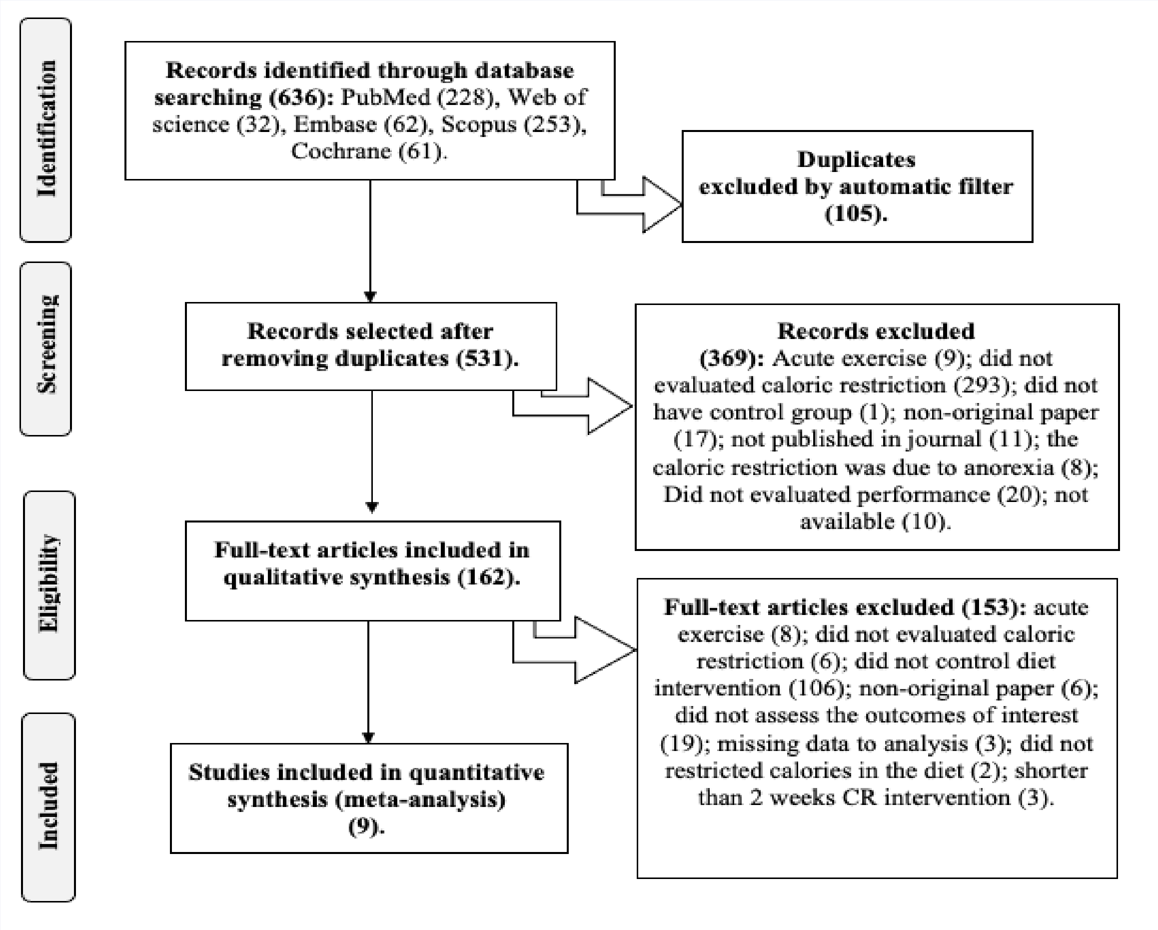

Figure 1 Flowchart of selection of the studies.

size before and after CR and control interventions were extracted for analysis. The components of functionality were also clustered for analysis (balance, daily life strength, daily life endurance, agility, flexibility, mobility and vitality). Furthermore, we shared the studies in two main meta-analysis: the exercise (CR-EX vs. EX) and non-exercise interventions (CR-NEX vs. NEX) (Figure 2A & 2B).

The meta-analyses were performed using the comprehensive meta-analysis software version 3.3.070. Since functionality was assessed in different ways, by different unit measures, we calculated standardized mean difference (SMD) based on the difference between the changes in CR and control groups. Fixed and random effects were used, respectively for non-significant (p>0.05) and significant heterogeneity analyses. The risk of publication bias was assessed by Egger's test (p = 0.05). Subgroup analyses were performed to test CR effects within each component of functionality.

RESULTS AND DISCUSSION

From 531 studies found in the highly sensitive search, 9 met the inclusion criteria comprising 15 controlled trials treated as separate studies for analyses. Characteristics of the population and interventions are described in (Table 1). Most studies included overweight and/or obese participants (BMI between 25kg/m^2 and 30 kg/m^2); from both sexes and were non-physically actives. The most studies were carried out in older adults, but a few studies investigate CR effects on children and adolescents. In general CR interventions last from 8 weeks to 3 years, and the magnitude of CR varied from ~250 kcal/day to more than 1000 kcal/day, combining or not with different types of exercise training.

To the authors knowledge this is the first systematic review and meta-analysis to integrate and summarize CR effects on functionality. CR significantly increased functionality in both Exercise and non-Exercise meta-analyses. Within Exercise analysis there was no true heterogeneity (p=0.35), almost null inconsistency (I^2=6.4%), and no risk of publication bias according to Egger tests (p=0.76), However, these precise true CR effects on overall functionality were very small (SMD: 0.12 [CI95%: 0.04; 0.19], p <0.001). On the other hand, within Non-exercise meta-analysis there was true heterogeneity (p=0.02), moderate inconsistency (I^2=46.1%), and a trend to risk of publication bias according to Egger tests (p=0.09), while the CR effects on overall functionality were medium (SMD: 0.40 [CI95%: 0.015; 0.65], p <0.001) (Table 2).

The higher magnitude of effect observed in non-exercise meta-analysis, might be due to the confounding effects of exercise, since exercise intervention might be a more effective

First author, year (Subgroup)	Functionality component and Test	SMD	LL	UL	p-Value	weight
Bouchard, 2009	BAL: one-leg stand	0.161	-0.658	0.981	0.700	0.84
Bouchard, 2009	DLS: one-leg squat with charge	-0.224	-1.044	0.597	0.593	0.83
Bouchard, 2009	DLS: lifiting 10lb object	-0.076	-0.895	0.742	0.855	0.84
Bouchard, 2009	DLS: climbing satirs	-0.184	-1.003	0.636	0.661	0.84
Bouchard, 2009	DLS: 30s chair stand	-1.194	-2.082	-0.307	0.008	0.71
Bouchard, 2009	DLE: 6min walking test	-0.142	-0.961	0.678	0.735	0.84
Bouchard, 2009	DLE: walking fast speed	-0.097	-0.915	0.722	0.817	0.84
Bouchard, 2009	DLE: walking normal speed	-0.194	-1.014	0.626	0.643	0.84
Bouchard, 2009	MOB : backward walking	-0.077	-0.895	0.742	0.854	0.84
Bouchard, 2009	MOB: put a jacket	0.320	-0.503	1.144	0.446	0.83
Bouchard, 2009	MOB: picking up a penny	0.390	-0.435	1.216	0.354	0.82
Elloumi, 2011	DLE: 6min walking distance	0.613	-0.459	1.685	0.263	0.49
García-Hermoso, 2019	AGI: limb speed	0.271	-0.663	1.205	0.570	0.64
García-Hermoso, 2019	AGI: 10×5m shuttle run	0.489	-0.455	1.432	0.310	0.63
García-Hermoso, 2019	BAL: Flamingo balance	0.266	-0.668	1.200	0.577	0.64
García-Hermoso, 2019	DLS: sit-ups	0.458	-0.484	1.399	0.341	0.63
García-Hermoso, 2019	DLS: standing broad jump	-0.390	-1.329	0.548	0.415	0.64
García-Hermoso, 2019	DLE: 20m endurance shuttle run	-0.265	-1.198	0.669	0.578	0.64
García-Hermoso, 2019	FLE: sit-and-reach	0.502	-0.442	1.446	0.297	0.63
Ghroubi, 2008	DLE: 6min walking test	1.412	0.582	2.242	0.001	0.82
Haywood, 2018 (Mod. CR)	MOB: DEMMI	0.000	-0.450	0.450	1.000	2.77
Haywood, 2018 (Mod. CR)	DLE: 6min walking test	0.360	-0.094	0.814	0.120	2.73
Haywood, 2018 (Int. CR)	DLE: 6min walking test	0.806	0.340	1.271	0.001	2.60
Haywood, 2018 (Int. CR)	MOB: DEMMI	-0.051	-0.499	0.397	0.823	2.80
Melanson, 2004	DLE: timed mile	0.207	-0.208	0.621	0.329	3.27
Nicklas, 2015	DLS: Chair rise time	0.113	-0.259	0.486	0.551	4.05
Nicklas, 2015	DLE: 400m walking time	0.366	-0.010	0.741	0.056	3.99
Nicklas, 2015	DLE: sual gait speed	0.057	-0.315	0.429	0.763	4.06
Nicklas, 2015	MOB: obstacle course	0.375	-0.001	0.750	0.050	3.99
Nicklas, 2015	MOB: SPPB	0.118	-0.255	0.490	0.536	4.05
Nicklas, 2019 (Int. CR)	DLS: chair rise time	0.013	-0.386	0.413	0.948	3.52
Nicklas, 2019 (Int. CR)	DLE: usual gait speed	0.000	-0.400	0.400	1.000	3.52
Nicklas, 2019 (Int. CR)	DLE: 400m walking time	0.001	-0.398	0.401	0.994	3.52
Nicklas, 2019 (Int. CR)	MOB: self-reported disability	0.011	-0.388	0.411	0.955	3.52
Nicklas, 2019 (Int. CR)	MOB: SPPB	0.000	-0.400	0.400	1.000	3.52
Nicklas, 2019 (Int. CR)	VIT: SF-36 Vitality score	0.011	-0.388	0.411	0.956	3.52
Nicklas, 2019 (Mod. CR)	DLS: chair rise time	0.002	-0.389	0.394	0.990	3.66
Nicklas, 2019 (Mod. CR)	DLE: usual gait speed	0.000	-0.392	0.392	1.000	3.66
Nicklas, 2019 (Mod. CR)	DLE: 400m walking time	0.002	-0.390	0.394	0.992	3.66
Nicklas, 2019 (Mod. CR)	MOB: self-reported disability	0.011	-0.380	0.403	0.954	3.66
Nicklas, 2019 (Mod. CR)	MOB: SPPB	0.002	-0.390	0.393	0.994	3.66
Nicklas, 2019 (Mod. CR)	VIT: SF-36 Vitality score	0.013	-0.379	0.405	0.948	3.66
Villareal, 2011	BAL: one-leg stand	0.647	0.100	1.195	0.021	1.88
Villareal, 2011	DLE: one-leg squat with charge	0.269	-0.267	0.805	0.325	1.96
Villareal, 2011	MOB: FSQ	0.340	-0.198	0.877	0.215	1.95
Villareal, 2011	MOB: obstacle course	0.108	-0.427	0.642	0.693	1.97
Summarized fixed effects		**0.119**	**0.044**	**0.194**	**0.002**	**100**

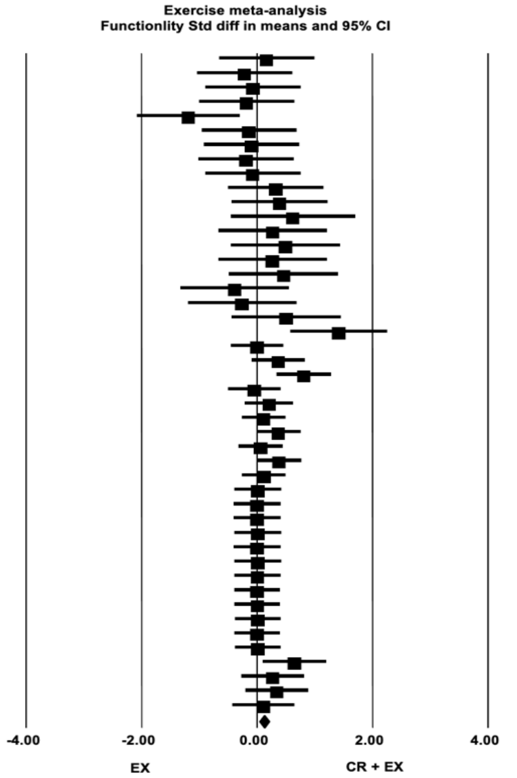

Figure 2a Forest plot of CR effect within the Exercise meta-analysis.

First author, year	Subgroup	SMD	LL	UL	p-Value	weight
Bouchard, 2009	BAL: one-leg stand	0.530	-0.302	1.363	0.212	5.34
Bouchard, 2009	DLS: one-leg squat with charge	0.356	-0.469	1.180	0.398	5.40
Bouchard, 2009	DLS: lifiting 10lb object	-0.102	-0.921	0.716	0.807	5.45
Bouchard, 2009	DLS: climbing satirs	-0.133	-0.952	0.686	0.750	5.44
Bouchard, 2009	DLS: 30s chair stand	0.073	-0.745	0.892	0.860	5.45
Bouchard, 2009	DLE: 6min walking test	0.226	-0.595	1.046	0.590	5.43
Bouchard, 2009	DLE: walking fast speed	-0.346	-1.171	0.478	0.410	5.40
Bouchard, 2009	DLE: walking normal speed	-0.983	-1.849	-0.117	0.026	5.09
Bouchard, 2009	MOB : backward walking	0.407	-0.419	1.234	0.334	5.39
Bouchard, 2009	MOB: put a jacket	0.819	-0.033	1.670	0.060	5.20
Bouchard, 2009	MOB: picking up a penny	0.563	-0.271	1.397	0.186	5.33
Elloumi, 2011	DLE: 6min walking distance	1.232	0.079	2.385	0.036	3.45
Ghroubi, 2008	DLE: DLE: 6min walking test	0.599	-0.158	1.356	0.121	5.95
Villareal, 2011	BAL: one-leg stand	0.925	0.358	1.491	0.001	7.85
Villareal, 2011	DLE: gait speed	0.416	-0.128	0.960	0.134	8.10
Villareal, 2011	MOB: FSQ	0.746	0.189	1.303	0.009	7.96
Villareal, 2011	MOB: obstacle course	1.047	0.473	1.622	0.000	7.76
Summarized random effects		**0.402**	**0.153**	**0.651**	**0.002**	**100**

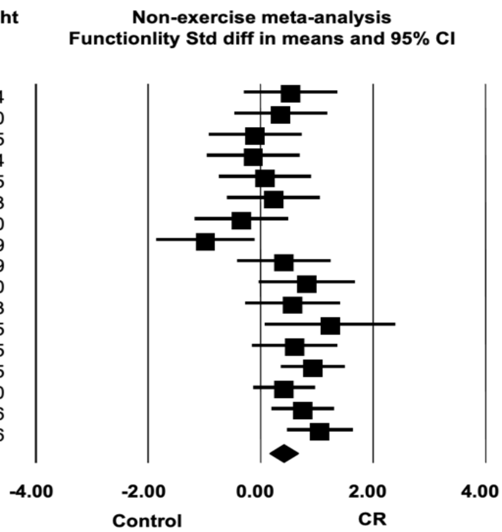

Figure 2b Forest plot of CR effect within the Non-exercise meta-analysis.

type of intervention to increase functionality. In fact, a meta-analysis testing exercise and dietary interventions on health of adults with sarcopenic obesity showed, despite all interventions led to body composition improvements, only exercise led to improvement of gait speed and grip strength [8].

The participants of the included studies underwent substantial weight loss with CR, and despite CR has been shown to improve health through a different physiological mechanism that could improve functionality, it is likely that the reduced body mass facilitates the improved performance following interventions. Indeed, obesity has been associated with functional decline [9,10] and weight loss has been associated with improve in muscle quality, strength, and general functionality assessed by SF-36's physical functioning and vitality dimensions [11-13].

Table 1: Characteristics of the studies included.

First Author, Year	Subgroups (n#)	Age (Years Mean ± SD)	Sex	BMI (kg/m^2)	CR or BM Reduction	Duration (Weeks)	Type of training
Bouchard, 2009	CR+EX (12)	64.4±4.5	F	31.7±2.6	0.5 to 1 kg/week	12	RT
	EX (12)	62.8±3.7		30.8±2.2			
Bouchard, 2009	CR (12)	60.7±4.6	F	31.9±2.7	0.5 to 1 kg/week	12	-
	Control (12)	62.5±3.1		32.3±2.4			
Elloumi, 2011	CR+EX (7)	13.1±1	M	30.3±4.5	-500 kcal/day	8	AT
	EX (7)	13.1±1		30.3±4.6			
Elloumi, 2011	CR (6)	13.3±0.6	M	30.3±2.9	-500 kcal/day	8	-
	Control (8)	13.2±0.2		30.2±2.2			
García-Hermoso, 2018	CR+EX (10)	10.7±0.9	M	27.9±3.9	1500 kcal/day	144	AT
	EX (8)			27.7±2.95			
Ghroubi, 2008	CR+EX (15)	41.41±3.9	NR	37.45±3.68	-25 to 30% of total daily calorie intake	8	CT
	EX (13)	39.77±13.1		37.14±5.7			
Ghroubi, 2008	CR (14)	41.5±11.7	NR	38.74±6.15	-25 to 30% of total daily calorie intake	8	-
	Control (14)	42.36±9.8		39.2±3.7			
Haywood, 2018 (moderate CR)	CR+EX (40)	70 years (65 to 85)	both	≥32	-500 kcal/day	12	CT
	EX (36)						
Haywood, 2018 (Intense CR)	CR+EX (41)	70 years (65 to 85)	both	≥32	-15% of body weight*	12	CT
	EX (36)						
Melanson, 2004	CR+EX (22)	42.6±6	both	31.5±2.8	-500 kcal/day	24	AT
	EX (19)						
Nicklas, 2015	CR+EX (55)	69.5±3.7	both	30.6±2.3	-600 kcal/day	20	RT
	EX (56)						
Nicklas, 2019 (moderate CR)	CR+EX (58)	69.2±3.5	both	34.7±3.7	−250 kcal/day	20	AT
	EX (44)			34.6±3.1			
Nicklas, 2019 (intense CR)	CR+EX (53)	69.2±3.5	both	34.4±3.7	−600 kcal/day	20	AT
	EX (44)			34.6±3.1			
Villareal, 2011	CR+EX (28)	70±4	both	37.2±5.4	-500 to 750 kcal/day	52	CT
	EX (26)	70±4		36.9±5.4			
Villareal, 2011	CR (26)	70±4	both	37.2±4.5	-500 to 750 kcal/day	52	-
	Control (27)	69±4		37.3±4.7			

Abbreviations: #: n = participants that completed the entire study; AT: aerobic training; CR+EX: CR plus exercise training group; CR: caloric restriction group without exercise training; CT: combined training (AT plus RT, and in some cases balance and flexibility exercises too); CR+EX vs. EX: CR controlled trial comparisons with exercise in both groups; EX: only exercise training group; F: female; M: male; CR vs. Control: CR controlled trial comparisons without exercise in any group; CONTROL: no diet group; NR: not reported; RT: resistance training; Δ: (change); SMD: standardized mean difference; * Two meals of the day were replaced with Optifast (Nestle Nutrition), and the third meal could be the same Optifast or a small serve of protein plus two cups of non-starchy vegetables with one tablespoon of oil.

Table 2: Effect of CR on functionality: Main analyses and Function Subgroup analyses.

Non-exercise meta-analysis								
Subgroup	**k**	**CR (n)**	**Control (n)**	**SMD**	**LL**	**UL**	**p-value**	**I^2**
Overall functionality	17	245	262	0.40	0.15	0.65	**<0.001**	46.1
Balance	2	37	39	0.80	0.33	1.27	**<0.001**	0
Daily life strength	4	44	48	0.05	-0.36	0.46	0.82	0.0
Daily life endurance	6	79	85	0.17	-0.37	0.70	0.54	63.2
Mobility	5	85	90	0.77	0.46	1.08	**<0.001**	0

Exercise meta-analysis								
Subgroup	**k**	**CR + EX (n)**	**EX (n)**	**SMD**	**LL**	**UL**	**p-value**	**I^2**
Overall functionality	46	1482	1300	0.12	0.04	0.19	**<0.001**	6.4
Agility	2	20	16	0.38	-0.28	1.04	0.26	0
Balance	3	50	45	0.45	0.04	0.86	**0.03**	0
Daily life strength	9	234	204	-0.04	-0.23	0.14	0.64	12.9
Daily life endurance	16	552	494	0.18	0.06	0.31	**0.003**	37.4
Flexibility	1	10	8	0.50	-0.44	1.45	0.30	0
Mobility	13	505	445	0.10	-0.03	0.22	0.14	0
Vitality	2	111	88	0.01	-0.27	0.29	0.93	0

Abbreviations: CR (n): sample size of only CR group; Control (n): sample size of no diet and no exercise group; CR+EX (n): sample size of CR with exercise group; EX (n): sample size of only exercise group; k: number of controlled groups; LL: Lower limit; p: *p*-value of hypothesis test for CR effects; SMD:standardized mean difference; UL: Upper limit. I^2: inconsistency between studies. Significant p-values were highlighted in bold (p<0.05).

Furthermore, a previous unpublished meta-analysis of our group showed VO_2 max and muscle strength were only increased by CR when the results were relativized by body weight, while absolute values were maintained the same [14].

In the present study, CR led to strong and moderate improvement in balance in both Non-exercise and Exercise meta-analyses, respectively. Since most of individuals included in this analysis were obese and obese individuals have inadequate postural stability (compared to their lean counterparts) [15], it is plausible to speculate that just a reduction in body weight favors the balance control of these individuals.

Daily life endurance, assessed mainly by short distance walking protocols was improved only in the Exercise meta-analysis. It is possible that body weight reduction would not be easily converted to endurance improvements, unless the individuals often experience the walking protocols, and thus it makes sense that just the Exercise meta-analysis was able to capture its true effects. Nevertheless, the smaller number of trials in non-exercise meta-analysis could hinder a true significant effect considering this subgroup analysis was significantly heterogeneous.

Another reason to explain the CR benefits on functionality would be some stimuli of diet in other healthy habit changes more associated to movement, motivation or exercise per se. However, it is not clear whether CR can really affect other habit changes [16,17].

The lack of improvement in flexibility, agility and vitality with CR in the Exercise meta-analysis, could be due to the limited number of trials analyzed: only 1, 2 and 2, respectively. Unfortunately, there were not enough studies to be analyzed within the Non-exercise meta-analysis for these variables. As seen, these functional improvements might be associated with other functionality improvements, it is likely that our results were due just to a lack of power and future studies should investigate these topics.

There was also no improvement in daily life strength, assessed by different tests such as lifting weights, climbing stairs and stand and sit. The loss of muscle mass following CR in most studies might explain at least part of the absence of improvement in daily life strength. It is noteworthy that an additional resistance training intervention to CR might prevent CR-induced muscle loss [18], offering additional benefit for overweight/obese individuals.

It is importantly to the outcomes should not extrapolate to athletes and healthy physically active individuals, since the few studies including these populations had too short CR intervention to distinguish acute CR from chronic CR effects. Thus, future studies should investigate the effects of CR interventions on the performance of lean and highly physically active individuals such as athletes. Another limitation of this study was the overlapping of samples within the overall functionality meta-analysis (Exercise and Non-exercise), since different components of functionality were included as separated studies for analysis.

CONCLUSION

We confirmed that caloric restriction led to significant small improvements in functionality. Although the effects of CR on functionality are more evident when CR was the only intervention, such findings should be considered with caution. The addition of the CR intervention to individuals undergoing exercise causes a small but consistent extra improvement in functionality. Among the components of functionality, CR was significantly effective on Balance, daily life endurance and mobility improvements, but not on agility, daily life strength, flexibility or vitality. Therefore, there is no reason for overweight or obese individuals fear functionality loss with caloric restriction.

ACKNOWLEDGEMENTS

The authors thank the contribution of Natalia Salvatierra Lima, Kellen Cristina da Cruz Rodrigues and Guilherme Francisco Peruca.

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Cite this article

Hernandes Júnior PR, Silva M, Almeida HM, Cavaglieri CR, Chacon-Mikahil MPT, et al. (2021) Meta-Analysis about the Effect of Caloric Restriction on Functionality. Ann Sports Med Res 8(2): 1180.