

## Exercise Prescription Guideline for Weight Gain in Individuals with Constitutional Thinness: Scoping Review

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### Review Article

#### Abstract

**Introduction:** Constitutional thinness (CT) is a condition where a person is naturally thin without any signs of malnutrition. This study aims to assess the available evidence on the effectiveness of exercise in increasing the weight of people with this type of thinness.

**Materials and Methods:** A search was conducted for articles in both Persian and English languages in national and international databases between October and December 2022 at the Musculoskeletal Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. There was not any time or type of publication limit for the publications. The search was conducted using the keywords "constitutional thinness", "exercise", "exercise training", "fat mass", "fat-free mass", "physical activity", "body mass index", "weight", and "weight gain".

**Results:** It seems that no research has been conducted on the impact of exercise on weight gain and body mass index (BMI) in this population.

**Conclusion:** The potential impact of regular exercise on individuals with CT has been discussed based on the theoretical mechanisms through which exercise affects different bodily systems. It is recommended that clinical studies be designed and conducted to examine the effect of exercise in helping these individuals to gain weight.

**Keywords:** Constitutional thinness; Weight; Exercise; Exercise training; Physical activity

**Citation:** Kazemi M, Namiranian P, Sheikhsosseini N, Saraf-Bank S, Rezaeian ZS. **Exercise Prescription Guideline for Weight Gain in Individual with Constitutional Thinness: A Scoping Review.** J Res Rehabil Sci 2022; 18: 163-9.

Received: 02.10.2022

Accepted: 05.12.2022

Published: 05.01.2023

#### Introduction

The most studies concerning the effect of exercise and diet on body mass index (BMI) are focused on the weight loss for overweight or obese individuals (1-6). However, only a few studies have explored weight gain (7-16). These studies have recruited people with two types of thinness: anorexia nervosa and constitutional thinness (CT) (7). The World Health Organization (WHO) defines underweight as a condition in which a person's BMI is less than 17 (17, 18). CT is a state of thinness with no signs of malnutrition (8, 9). It is considered the opposite of obesity (10). Unlike feeding

disorders related to low weight, such as anorexia nervosa, CT is a non-pathological condition without psychological characteristics such as food aversion (cibophobia), refusal to overeat, low self-confidence, perfectionism, and body dissatisfaction (11). First introduced systematically in 1930, this non-fatal condition has not received much attention in scientific literature (19) possibly due to relatively low prevalence that is less than 0.4% in men and less than 2.7% in women (6).

People with CT are characterized by having no eating or other associated disease/disorder like amenorrhoea

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(6, 8-11, 19-24). The plasma titer of various hormones and hormone-related products like insulin-like growth factor 1 (IGF-1), estradiol, growth hormone, triiodothyronine ( $T_3$ ), cortisol, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) is within normal range although the level of leptin seems to be between anorectic and normal-weight people (20, 23), and higher fasting free  $T_3$  along with lower 24-hour mean cortisol level are recently reported in CT (23). People with CT do not over-exercise and are resistant to weight gain with a quite stable body weight (19-21, 23).

BMI may not specifically differentiate CT (24); while both CT and anorexia nervosa (AN) suffer from low BMI, people with CT are a little less under-weight (23). Conversely, the average food intake by people with CT is similar to that of the normal-weight people, which is significantly higher than individuals who suffer from AN (20). Thus, body composition analysis is the prioritized approach to identify and differentiate CT (19). Body fat mass (body fat percent) regulates energy metabolism (23). For individuals with CT, body fat percent is higher than AN clients (19-23) and lower than average, despite the fact that it still remains within the normal range (9, 20, 23). Therefore, CT clients are underweight, but not under-fat (9, 19-21, 23). Considering similar fat-free mass (FFM) in CT and AN (19, 20, 23), nearly normal fat mass ratio in CT may contribute to their healthy profile (20) and resistance to weight gain (23). Lower FFM possibly explains significantly lower resting metabolic rate (RMR) of people with CT (20). Higher titer of fasting free  $T_3$  in people with CT (23) may reasonably explain significantly higher FFM adjusted RMR and total energy expenditure (TEE) (RMR/FFM and TEE/FFM, respectively) in CT compared to both AN and normal-weight people (20). The untypical body composition phenotype of CT may be the result of the physiological mechanisms integrated with their modified balanced energy metabolism (23). Their normal energy intake along with nearly normal fat mass and significantly lower FFM suggests a different regulation of energy balance in CT compared to that evidenced in AN (19).

Muscle mass is the main modifiable component of FFM. A specific muscle phenotype has been identified in individuals with CT, with muscle biopsies showing defects in energy storage in muscle fibers, which partially contributes to their resistance to weight gain (9). Additionally, compared to individuals with normal BMI, people with CT have a lower muscle mass (13, 14, 20), smaller average cross-sectional area of skeletal muscles and all types of the muscle fibers, with lower oxidative profile

indicated by low capillary supply, low activity of citrate synthase enzyme, low proportion of slow oxidative fibers, high proportion of fast glycolytic fibers (13, 14), and lower glycogen content (13). They also have smaller adipocytes with greater respiratory capacity of mitochondria in their adipose tissue (12). In spite of "equilibrated energy metabolism" and consistent body weight in the lower range of the growth curve and physiological menses for females chart, the BMI for individuals with CT is similar to those with AN (6, 19, 20). People with AN usually report a normal body weight and BMI before the onset of anorectic disorder while in CT, BMI is supposed to be very low throughout the growth period until the age of 18 (20, 22). As FFM is significantly lower than average in CT (19, 20, 23), the muscular phenotype of CT brings their low muscular fitness to the mind. Proper muscle mass is an indicative of health status (25, 26). Obesity and low muscular fitness increase the cardiometabolic risk in adolescents (25), for example, osteoporosis is the main comorbidity with CT (6, 23). Young women with CT are more at risk of low bone mass although they show normal bone turnover (23). The tibia bone of women with CT shows lower bone resistance, smaller bone cross-sectional area, weaker bone configuration, and decreased bone strength against fracture compared to the aged-matched normal-weight women. This is probably due to decreased bone mineral density (BMD) resulting from lower muscle strength in these individuals (15). This fact negatively impacts the quality of life (QoL) of people with CT. Regular exercise, like daily walking, even at a low intensity, can increase BMD and reduce the risk of fractures in thin women (16). However, no study has been found yet that shows the effect of exercise on the bones and other tissues of the musculoskeletal system in people with CT.

Unlike people with AN, individuals with CT are typically dissatisfied with their low weight (6, 9, 19, 20); as a result, they often seek medical advice on how to gain weight (9). As previously confirmed in animal studies, alteration of energetic metabolism balance maintains a stable low weight in CT (20), and dietary modification does not help weight gain in CT (8, 9, 11, 27); individuals with CT exhibit resistance to weight gain despite living in an environment that promotes obesity (11, 20). They do not gain weight even on a high-fat diet (9) although when overfed, their intramuscular triglyceride (TG) reserves increase (7). An increased TEE/FFM ratio differentiates CT from normal-weight individuals and could account for the resistance to weight gain

observed in CT (20). Thus, increasing FFM, may be the key element to optimize weight in CT (19).

The muscle mass alters the weight and BMI (24) and definitely changes the appearance of thinness (21); however, it does not necessarily represent muscle strength (24). Regular exercise has been proven effective in preventing and treating obesity and controlling body weight (1-6, 18). Since body cannot store proteins (27), overfeeding with a protein-rich diet seems not to be the strategy of choice, while muscle-building exercise programs may be a viable option for these individuals. Therefore, a review of the existing literature on the effects of exercise on increasing the BMI and FFM of people with CT was conducted to explore this possibility.

### Materials and Methods

To conduct a comprehensive search across Persian and English language articles, without any restrictions on publication time or type of article, national databases, including MagIran, SID, MOH Thesis, and MOH Journals, as well as international databases such as PubMed, Scopus, and ISI Web of Knowledge were searched. The search was conducted between October and December 2022, using various keywords including “constitutional thinness”, “exercise”, “exercise training”, “physical activity”, “fat mass”, “fat-free mass”, “body mass index”, “weight”, and “weight gain”. This research aimed to find studies that reported the use of exercise in the life plan of individuals with CT and documented the minimum amount of weight or weight change in these individuals.

### Results

It appears that there has been no research conducted on the impact of physical activity on weight gain and BMI in this population. As a result, the potential impact of regular exercise on these individuals was explored based on the theoretical mechanisms of how exercise affected various bodily systems.

### Discussion

Typically, weight gain occurs due to an increase in daily calorie intake. However, combining a proper exercise regimen with a healthy diet can lead to a more aesthetically pleasing body. Since people with CT do not gain weight by modifying dietary calorie intake (8, 9, 11, 27), increasing FFM through muscular hypertrophy, that happens with regular exercise, seems to be a reasonable solution. This review aimed to investigate the effects of exercise on weight gain in individuals with CT. It seems that this

issue has not been adequately studied yet (19, 23). However, health benefits of regular physical activity are widely evident (28). Although American College of Sports Medicine (ACSM) recommended 1-3 sets of 8-12 repetition with external loads between 70%-85% of one-repetition maximum (1RM) for muscle size increase for novice and 3-6 sets of 1-12 repetition with 70%-100% of 1RM for trained ones (29), various exercise profiles are also evident to be as effective as resistance training (26, 30). It seems that muscle hypertrophy depends on the total number of repetitions (exercise volume) that is repetitions per set  $\times$  number of sets (26). Resistance exercises are main physical approach for increasing total muscle mass (28, 31) and muscle fibers size, particularly for fast-twitch ones (32), but should not be combined with strenuous aerobic exercises as they hinder the effect of strengthening exercises (28). Conventionally, various combination of mechanical tension, metabolic stress, and muscle damage may result in muscle hypertrophy (26). If volitional fatigue (indicator of metabolic stress) is not targeted, the minimum intensity threshold ( $> 60\%$  1RM) should be achieved to maximize the muscle hypertrophy (26). From a theoretical perspective, 6 to 12 repetitions of 67%-85% 1RM can effectively increase muscle mass and weight gain in these individuals (28). These exercises are recommended in multiple sets, with a frequency of at least 2 to 3 times a week (28). Additionally, larger muscles should be targeted at the beginning of the exercise and smaller muscles at the end. Thus, exercises that engage multiple-joint muscles should be performed first, followed by exercises targeting single-joint muscles (28, 33).

Exercise-induced muscle tension or strength is the primary stimulus for muscle hypertrophy; significant changes in muscle size can be detected after three weeks of training (38). Over time, the cross-sectional area of the muscle fiber and the contractile proteins, actin and myosin, increase (34). By implementing the principle of overload, that implies progressive mechanical tension (26) through increasing the intensity and duration of the exercise, muscle fiber enlargement and its contribution to muscle hypertrophy will be facilitated. High-loads ( $> 85\%$  1RM) repeated 1-5 times if planned with long enough rest intervals of 3-5 minutes improve both muscle strength and size (26).

Eccentric-only contractions increase muscle mass more than concentric-only counteractions because they facilitate sarcomere production in series that increased fascicle length with limited increases in the pennation angle. In contrast, the concentric-only

actions add sarcomeres in parallel and induce muscle growth mainly by increasing pennation angle with little change in fascicle length (26). The overload training is more effective in stabilizing higher muscle strength if it comprises eccentric muscle fiber contractions (26, 28, 35). Slower tempo of movement, especially during the eccentric phase, decreases the number of repetitions, and increases the time under tension. This way, slower tempos potentially seem to induce greater hypertrophy (26). Energy requirement of eccentric contraction to take a specific load is four times less than that of concentric work; therefore, in spite of greater force capacity of eccentric actions, they induce lower metabolic stress that reduce the expected training effect (26).

Dose-response relationship (26, 31) well describes muscular hypertrophy following repeated sets of exercise. Compared with single-set exercise bouts, multiple sets boost the phosphorylation of the 70-kDa ribosomal protein S6 kinase (p70S6 kinase) and muscle protein synthesis (32) through which, they maximize the muscle hypertrophy. In the same way, higher exercise volume (27-29 sets/muscle/week) significantly improves hypertrophy compared to lower volume (6-10 sets/muscle/week) in both untrained and trained populations (26, 31). However, volitional fatigue hinders anticipated exercise-induced muscle growth (26).

Participating in any exercise is associated with the risk of musculoskeletal injury that is higher when there is direct contact between participants or with the ground, e.g., football, wrestling, etc. (36). Thus, people with CT, who probably are physically weak (15), must avoid over-training; moderate number (~6-12) of repetitions in 3-6 sets of moderate loads (60%-80% 1RM), if separated by short (~60 seconds) rest intervals, may provoke greater metabolic stress and induce more muscle hypertrophy (26). Thus, they should finish the training set and rest when they feel weak and tired to avoid over-training and its local and systemic side effects and save the weekly sequence of the exercise sessions.

Resistance exercises can increase the secretion of testosterone and growth hormone, which can lead to muscle hypertrophy (37). These exercises induce more significant impact on men than women, and their effect on women is still unclear (38). Therefore, exercises that stimulate growth hormone release are recommended to be included in a sport program. Growth hormone secretion is higher in high-intensity exercises, and its secretion depends on the maximum intensity of the exercises performed (28). Nevertheless, excessive growth hormone inhibits its

release (37). Hence, when prescribing exercises to enhance growth hormone secretion in people with CT, it is vital to consider the person's age and the intensity of the exercise. Whole-body metabolism influences synthesis of thyroid hormones. Even though these hormones are not essential for life, they considerably affect QoL. Besides, full expression of growth hormone depends on the thyroid activity to provoke normal growth and development, especially of nervous tissue (28). Regular exercise may harmonize the pituitary-thyroid response resulting in higher turnover of thyroid hormones. Although no evidence to date has reported exercise-induced hyperthyroidism, regular participation in exercise for a long time may surge  $T_3$  turnover through a mechanism different from its normal dynamics (28). Based on a recent meta-analysis, in spite of normal level of  $T_3$  in CT, the fasting level of free  $T_3$  is significantly higher in CT (23), while the RMR is significantly lower (20). This paradox may be imposed by lower FFM in CT as RMR adjusted to FFM is significantly higher in CT compared to that of normal-weight people and anorectic clients (20).

Depressing the metabolic rate directly stimulates thyroid stimulating hormone (TSH) release from hypothalamus and increases thyroid output and resting metabolism (28). For the endurance-trained women, moderate exercise mildly suppresses thyroid function ( $T_3$  and  $T_4$  levels), while more vigorous exercise may release them more. The changes in body composition that accompany a high training volume may contribute to discrepancies in an exercise-induced change in thyroid function in women (28).

Physical activity is known to increase the secretion of cortisol, the stress hormone (39). The level of cortisol secretion depends on the duration and intensity of the exercises, the fitness level of the individual, and their diet (40). Despite normal cortisol titer in CT, the mean 24-hour level has been reported significantly lower than normal-weight people (23). When low-intensity exercises are performed continuously, the cortisol level in the plasma surges, leading to an increase in lipolysis (fat breakdown) to provide energy (41). This process is more prominent in sedentary individuals (28). Therefore, when prescribing exercise, the level of cortisol secretion should be observed, and exercises that increase the level of stress hormone should be avoided for people with CT. Additionally, consumption of herbal and animal proteins and maintaining a balance between the two is important (28). Consuming high amount of animal protein increases the intake of saturated fatty acids and cholesterol, leading to heart diseases (28, 41).

### Limitations

It seems that no study to date has investigated the impact of exercise on the weight of individuals with CT. Consequently, the suggestion to engage in resistance exercises and the link between the exercise regimen and various hormones that aid in gaining weight were only discussed based on the theoretical knowledge available regarding the impact of exercise on metabolism in a healthy human body.

### Recommendations

Since individuals with CT usually use supplements to gain weight, considering the potential complications of these products (42), standard clinical trials are recommended to be conducted, with an adequate follow-up period, to investigate the effectiveness of exercise programs and diets for these individuals.

### Conclusion

Based on the theoretical evidence retrieved from studies on healthy people, it seems that strength training may be recommended for people with CT due to its effect on the volume and cross-sectional area of muscles (fibers) and growth and  $T_3$  hormones. However, to validate this hypothesis, it is necessary to design and implement highly accurate clinical studies in compliance with the required standards.

### Acknowledgments

The authors' deepest appreciation goes to all the participants who assisted us in conducting this research project.

### Authors' Contribution

Project design and ideation: Zahra Sadat Rezaeian  
Providing financial resources for the project: Zahra Sadat Rezaeian

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Maintaining the integrity of the study process from the beginning to the publication and responding to the comments of the referees: Mahsa Kazemi, Parnian Namiranian, Naeemeh Sheikhhosseini, Sahar Saraf-Bank, Zahra Sadat Rezaeian

### Funding

This study had no financial resources and was done at the personal expense of the authors. The Isfahan University of Medical Sciences, Isfahan, Iran, did not interfere in data collection, analysis and reporting, manuscript preparation, and the final approval of the study for publication.

### Conflict of Interest

The authors have no conflict of interest.

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