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Resistance Training

Bridging Theory and Practice

*Edited by Luís Branquinho, Ronaldo Vagner Thomatieli
dos Santos, José E. Teixeira, Elias de França,
Pedro Miguel Forte and Ricardo Ferraz*



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Meet the editors



Luis Branquinho holds a Ph.D. in Sports Science from the University of Beira Interior, obtaining the highest final “Approved with Distinction” grade. He currently has over 100 scientific publications distributed among articles, books, and book chapters in the area of Sports Science, and his area of specialization is sports training. He is an editor and reviewer of some of the most prestigious international journals in the field of Sports Science, having also received a research grant and won two awards for his doctoral thesis research project. He was a professor at the Higher Institute of Educational Sciences of the Douro and is currently an Adjunct Professor at the Polytechnic Institute of Portalegre in Portugal, where he also coordinates the management hub of the Life Quality Research Center (LQRC-CIEQV). He is also a technical and scientific consultant for São Paulo FC, Brazil.



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Preface

Resistance training goes beyond the simple goal of increasing muscle capacity and improving athletic performance. Its importance extends far beyond the pursuit of strength and muscle mass, encompassing a wide range of benefits for health, well-being and recovery, both in the context of sports and in the care of individuals with specific health conditions [1]. When prescribed and executed correctly, resistance training can improve physical functionality, prevent chronic diseases, accelerate recovery processes and even promote better mental health [2]. Throughout life, its applications expand, offering significant results for different age groups and profiles [3].

This book was designed to provide a comprehensive overview of the multiple facets of resistance training, aiming to serve as a source of knowledge and a practical guide for professionals, particularly in sports science and health. Based on the latest scientific evidence, several chapters that cover everything from the fundamental principles of strength training to its most recent innovations, emphasising its therapeutic and adaptive applications for different populations, have been compiled.

One of the main objectives of this book is to highlight how the combination of training, recovery and nutrition is essential to optimize the results of individuals in different contexts. For professional athletes, applying resistance training can be the key to achieving high-performance levels, especially when adapted to the different periods of the season and the specific demands of each sport [4, 5]. On the other hand, resistance training can become an essential therapeutic tool for individuals with health conditions, promoting rehabilitation and improving quality of life [6].

Throughout the sections of this book, we explore in detail the most relevant concepts and practices within the field of resistance training, providing a multidisciplinary approach that combines theory and practice. The book's content emphasizes that the benefits of resistance training go far beyond improving aesthetics or increasing strength. Resistance training plays a fundamental role in preventing and treating several health conditions, such as age-related diseases, mental disorders, pulmonary hypertension and bone metastases, providing a solid foundation for a healthier and more functional life [2]. In this context, resistance training is seen not only as a physical practice but also as a comprehensive strategy that involves careful planning, understanding everyone's physiological and psychosocial needs, and an analysis of the interactions between exercise, nutrition, and recovery. By adopting this holistic view, we can maximize the benefits of resistance training, ensuring sustainable results for both elite athletes and those seeking to improve their health and quality of life. Throughout this book, we hope to provide the tools and knowledge needed to improve training practices and inspire new approaches and solutions to contemporary issues facing elite sport and rehabilitation.

Across the three sections of this book, we hope to provide the tools and knowledge needed to improve training practices and inspire new approaches and solutions to contemporary issues facing elite sport and rehabilitation.

Section 1: “Optimizing Strength Training: Balancing Recovery and Performance”

The book’s first section focuses on optimizing resistance training to maximize performance while maintaining adequate recovery. The first chapter, “Considerations Regarding the Management of Resistance Training during Periods of Fixture Congestion in Professional Football Teams”, explores how coaches and strength and conditioning coaches can manage resistance training during intense competition periods, particularly in professional football teams. This chapter provides practical examples that will help coaches make informed decisions in their day-to-day practice, balancing the demands of training and recovery for athletes.

The “Hypertrophy Energy Balance” chapter then delves deeper into the science behind muscle hypertrophy, examining the factors that influence the increase in muscle mass. From biological mechanisms to training, nutrition, and recovery strategies, this chapter provides a detailed overview of the factors that must be considered to achieve optimal hypertrophy results. The interrelationship between resistance training, nutrition, and rest is discussed to provide a holistic approach to maximizing muscle growth.

Section 2: “The Comprehensive Benefits of Resistance Training: From Disease Prevention to Mental Health”

The second section highlights the comprehensive benefits of resistance training, not only for athletes but also for promoting overall health and preventing disease. The “Prevention of Age-Related Diseases” chapter provides a comprehensive approach to healthy ageing, discussing how resistance training can be a key tool in preventing age-related diseases. It also explores how lifestyle interventions, including strength training, can significantly contribute to a better quality of life as we age.

The next chapter, “The Impact of Resistance Training on Mental Health: Neuropsychological and Behavioral Functioning”, addresses how resistance training impacts mental health, focusing on neuropsychological and behavioural functions. This study reveals how resistance training improves physical fitness and positively affects mental health, including benefits for cognition and emotional well-being.

Section 3: “Resistance Training in Special Populations: Therapeutic Approaches for Pulmonary and Cancer Patients”

The third section focuses on resistance training as a therapeutic approach for special populations, such as patients with severe health conditions, including pulmonary hypertension and bone metastases. The chapter “Resistance Exercise as a Therapeutic Benefit for Patients with Pulmonary Arterial Hypertension: Advances and Perspectives” explores the latest developments in the use of resistance training as a therapeutic tool for patients with pulmonary arterial hypertension. The chapter reviews the clinical evidence, discusses implementation practices, and presents perspectives on the future of resistance training treatment for this condition.

The chapter “Resistance Training in Patients with Bone Metastasis” focuses on applying resistance training in patients with bone metastases. It provides an overview of

the pathophysiology of bone metastases and investigates the effectiveness of different types of resistance exercises, including details on prescribing training to ensure patient safety. This chapter provides a crucial insight into healthcare professionals dealing with the rehabilitation and care of cancer patients, illustrating how resistance training can be adapted to their therapeutic needs.

Therefore, we invite readers to discover the latest publications, research, and theoretical references in the area of fundamental resistance training. Resistance training can be the key to transformation – physical, mental and emotional for all individuals, regardless of context, at any stage of life.

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Section 1

Optimizing Strength Training: Balancing Recovery and Performance

Chapter 1

Considerations Regarding the Management of Resistance Training during Periods of Fixture Congestion in Professional Football Teams

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Abstract

Football has changed drastically, and currently teams can play up to 70 games in a season. This means one game, on average, every 4 days, and there is no space for pre-season. However, there may be periods of multiple games every 3 days. This congestion of games increases the incidence of injuries, which has a strong impact on the team's success during the season. Furthermore, it is not possible to develop a methodology to achieve peak performance, but rather development and maintenance of performance. This congestion is unprecedented in football, and there is no literature describing how to manage the workload in teams with this profile. In this chapter, we will present a real case of game congestions and its associated contextual variables. We then make suggestions on how to implement resistance training with the aim of improving/or maintain performance and mitigating the incidence of injuries. This chapter presents practical examples from which coaches and physical trainers can gain insights to apply in their day-to-day professional practice.

Keywords: football, performance, resistance, congested periods, injury prevention

1. Introduction

Football has changed drastically, and currently teams can play up to 70 games in a season [1]. This means one game, on average, every 4 days. Meanwhile, there may

be periods of multiple games every 2–3 days [2]. This congestion is unprecedented in football, and there is no literature describing how to manage the workload in teams with this profile. Not only the number of matches but there has been an increase in the game intensity and volume over the years [3, 4]. This has placed football players under unprecedented physical demands.

With the advancement of effectiveness in transportation and with the means of communication, they helped in the drastic increase in games. Currently, football teams can be qualified to participate in up to 5 competitions per season. Currently, football teams can travel 10,000 km in less than a day, making it possible to schedule up to two games in a week. A fact that did not happen in the past, when a team took months to move from the American continent to the European continent. Furthermore, the increase in means of communication (Internet and streaming) means that the club can sell the broadcasting rights for all its games. This is also a fact that did not happen in the past. Few teams were able to sell part of their games (not all) to the limited media. So, the more I play, the greater financial return for the club. In this sense, professionals involved in physical preparation, recovery (i.e., the athlete's performance and health) must adapt to this new scenario, in which the objective is to prevent the athlete from overtraining and getting injured throughout the season. The literature has shown that game congestion directly impacts the incidence of injuries [5]. Furthermore, injury incidences are strongly associated with success rate in season [6].

At first, we might think that it is just a matter of increasing the squad of players from the usual 22 players (starter and reserve) to 33 (creating a third reserve). And in fact, this has been happening. In Brazil, practically all teams involved in at least three championships this season already have a squad in this regard. A limitation of such a large squad is that the reserve players (especially third reserves) do not reach a level of interaction like the first team. And there is always the problem of the “game level” falling (especially from a tactical organization point of view), as the reserve almost always cannot maintain the level of the starter. As a result, the coach will always use the starter too much (putting him at risk due to overuse) and use too few supplements, also putting them at risk of injury when this athlete has to assume the role of starter for a few games in a row.

When a reserve athlete assumes starting status, they experience a spike and exponential increase in workload. Literature has reported that this acute increase in workload increases the risk of injury by 5–7 times [7]. In this sense, workload monitoring and managing is vital. Monitoring workload can be done well with equipment that measures both the external and the internal load. Internal and external load are two concepts that need to be clear to coaches and physical trainers. In this sense, the external load is all the work done by the athlete (running, jumping, lifting weights, etc.), while the internal load is the response at the physiological/psychological, tissue, or biochemical level, revealing a change in the homeostasis of these parameters. In football, the external load of pitch training or match event is ideally monitored using GPS associated with an accelerometer and gyroscopes. Internal load can ideally be measured with markers of subjective perception of effort and muscle recovery, heart rate, and direct muscle damage (such as creatine kinase, inspection, thermography, ultrasound, and MRI). These markers are necessary to identify the impact of workload on the athlete's body. Below are three common situations that deserve attention:

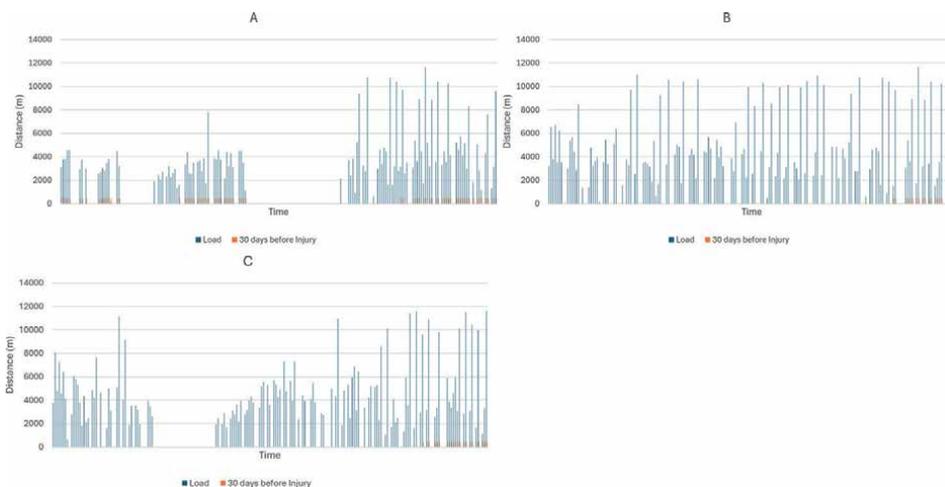


Figure 1. Change in workload and injury over time. In orange in the figure, the period of 1 month before the injury is indicated.

inappropriate load (**Figure 1A**), excessive load (**Figure 1B**), and spike of load (**Figure 1C**).

For example, in **Figure 1A**, we have an example of an athlete who does not tolerate the applied load after a period without training load or games, thus acquiring three injuries during the season. **Figure 1B** is a case of an athlete who was used excessively during the competitive period, and in the pre-injury period he accumulated 2–3 games in a period of 8 days. **Figure 1C** is a case of an athlete taking over as starter, with an abrupt increase in workload. These are cases of athletes who need to be carefully monitored to identify signs of overload. And in addition, ensure that these athletes undergo an injury prevention program.

Resistance training has been convincingly demonstrated to mitigate the risk of injury [8] as well as is a crucial component in improving players' physical fitness and resilience [9]. Therefore, implementing a resistance training program is vitally important. However, effective resistance training to mitigate injuries and thus be applied effectively requires considerable neural demand (causing muscular and central fatigue) and tissue demand (causing microdamage). For teams involved in a congested season, it is extremely difficult to apply this variable to starting athletes. As a last resort, it is even necessary to remove them from games for this variable to be applied. For example, in **Table 1**, we present the extreme case of a sequence of games (every 3 days) of an elite football team. Note that incumbents were only able to train minimally adequate strength in the upper limbs, but not the lower limbs (with only one strength development rate session). Recovery sessions were intensified during this period to help with adaptation, "as tissue that does not recover does not adapt". Even so, several resistance training variables were no longer applied to starting players due to the tissue's inability to receive the load and adapt (i.e., overtraining).

With this scenario in mind, in this chapter we will present real cases of an elite football team subjected to a congested calendar. Next, we will discuss and suggest how a football team subjected to a congested calendar could manage the insertion of resistance training load during the competitive period.

Days of week	Sun	Mon	Tue	Wed	Thu	Fri	Sat	Sun
Week 1								
Field variables	Match (~10 km)	OFF	Pitch training/velocity/tactical (4.0 km)	Pitch training/tactical (2.0 km)	Match (~10 km)	Pitch training/velocity/tactical (4 km)	Pitch training/tactical (2,5 km)	Match (~10 km)
Resistance training	OFF	OFF	Power MMII + preventive exercises	OFF	OFF	OFF	OFF	OFF
Physiotherapist	Recovery session	OFF	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session
Week 2								
Field variables	Match (~10 km)	OFF	Pitch training/tactical (2,5 km)	Match (~10 km)	OFF	Pitch training/velocity/tactical (4,0 km)	Pitch training/tactical (2,5 km)	Match (~10 km)
Resistance training	OFF	RT MMSS1	RT MMSS2	OFF	RT MMSS 1	OFF	RT MMSS 2	OFF
Physiotherapist	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session

Table 1.
Real example of starters in 2 congested weeks.

2. How an elite football team in a congested period manages resistance training load

In football, the dynamics of player utilization within a squad can significantly impact team performance. Coaches often have preferences for certain players based on their playing style, which can lead to some players being overloaded with game time while others are underutilized [10]. This imbalance in player utilization can result in increased risk of injuries, especially for those players who are consistently overworked due to the coach's preferences. For instance, **Table 1** presents a real case from an athlete who played a sequence of six matches and did not perform an adequate regime of resistance training (such as the Nordic hamstrings for the hamstring muscles group and/or Copenhagen for adductor muscles group).

Resistance training plays a vital role in strengthening muscles, tendons, and ligaments, thereby reducing the likelihood of injuries during matches and training sessions [9]. For instance, preventive exercises sessions of 10–15 minutes, two to three times a week, have preventive effect in soccer players [11, 12]. This dose can be an appropriate option in a congestion calendar. In addition to the appropriate dose, the type of exercise must be considered. In this way, exercises programs are potential effective to prevent knee injuries [13, 14], adductor muscle injuries [15], hamstring muscle injury [16, 17], and ankle sprain [18].

However, the insertion of resistance training must be considering the athlete background. For instance, some athletes have a background of resisted training and thus tolerate the insertion of resisted training within a congested period (i.e., **Table 1**). However, other athletes do not have this background, and the insertion of resistance training in this condition can be dangerous (i.e., increase injury risk). This background must be evaluated because the combination of the field workload along with the resistance training can generate an unprecedented load for the athlete (i.e., significantly moving the tissues from the homeostasis) and increases the injury risk.

By incorporating specific training modules focused on injury prevention, football teams can better prepare their players for the physical demands of the sport and minimize the risk of overuse injuries [9]. This proactive approach to injury prevention through resistance training not only safeguards the players' well-being but also ensures that they can be utilized more frequently by the coach without the fear of potential injuries hindering their performance [9].

Moreover, the implementation of resistance training programs must be tailored to the specific needs of football players and can contribute to improving their overall physical fitness and performance on the field [9]. By enhancing players' strength, power, and resiliency through resistance training, coaches can optimize the utilization of their squad members by having a pool of physically resilient and well-prepared players available for selection [9]. This approach aligns with the goal of maximizing player availability and performance while minimizing the risk of injuries that could result from overuse or inadequate physical conditioning [19]. In the context of football coaching, it is essential for coaches to consider the individual needs and physical capabilities of each player when designing resistance training programs [20].

This is particularly important, given that some players will have deficiencies in the hamstrings, while others will have deficiencies in the adductors, and so on. Therefore, training must meet these needs. In addition, some athletes may have deficiencies in speed [21], while others may have deficiencies in strength. In the same sense, training must be designed to address these deficiencies and improve the athlete's muscular power.

Understanding the unique requirements of players based on their position, playing style, and injury history is crucial in developing effective training regimens that target areas of weakness and reduce the likelihood of injury [20]. By personalizing resistance training protocols for players, coaches can not only prevent injuries but also optimize the utilization of their squad by ensuring that all players are physically prepared to contribute effectively on the field [20].

Furthermore, the efficacy of resistance training in injury prevention and player utilization can be enhanced through ongoing education and professional development for coaches [20].

By staying abreast of the latest research and best practices in sports science, coaches can refine their training methodologies and incorporate evidence-based approaches to minimize injury risks and maximize player availability [20]. This continuous learning process empowers coaches to make informed decisions regarding player management, training load, and injury prevention strategies, ultimately benefiting the overall performance and well-being of the squad [20].

Table 2 presents a real case of capacities trained throughout the season in an elite international soccer team. The sets and repetitions are applied to the entire group of athletes (starters, reserves, and those not selected for the game), but it is worth noting that the values for starting athletes should be the minimum suggested in the table (i.e., micro-dosing, providing only neural stimulation to induce muscle power output). This is necessary to avoid tissue damage that could lead to an increased likelihood of inducing injuries during the game. For instance, a strength-training program, composed by four exercise types (horizontal leg press; unilateral lateral leg-press; knee flexion and knee extension) with dose of 3 series of 3–4 repetition (85–95% of 1 maximal repetition), suggested by Duran-Custodio et al. [22], showed to be effective to improve physical fitness and minimize injury incidence and injury burden in semiprofessional soccer players.

To introduce resistance training to induce tissue adaptations (to prevent injuries) in players without the background of resistance training, we suggest that such players have a period of 5–7 days between games. To achieve this, it is necessary to adopt a rotation strategy to introduce resistance training program before the matches [23].

Rotation of players in sports teams is crucial for maintaining athletes' physical health and preventing injuries. By implementing a rotation strategy, teams can evenly distribute playing time among players, reducing the risk of overuse injuries and ensuring all squad members maintain good fitness levels [24]. This approach not only

Capability	Sets	Reps	Exercise per muscle group
Power MMII	2–10	4–12	2–6
Power Whole body	2	5–7	7
Strength MMSS	3	6–10	2–3
RFD	2	3–8	1–4
Preventive ejercicios (resistance exercise)	2–6	5–10	2
Velocity-force	1–9	6	1–4
Core	1–10	10	1–2
Mobility	3	8	1–3

Table 2.
Qualities and loads trained with training in football players in an elite team.

aids in injury prevention but also guarantees that players are consistently available for selection, contributing to the overall success of the team. Research has indicated that neuromuscular training, encompassing strength, flexibility, plyometrics, agility drills, and balance exercises, is effective in preventing injuries in athletes [25]. By integrating such training methods into the rotation schedule, teams can enhance the physical preparedness of all players, decreasing the likelihood of injuries and promoting overall fitness levels [25]. Moreover, individualized training programs based on best practices can further bolster injury prevention efforts and optimize player performance [23, 26]. Successful implementation of rotation strategies can be observed in various teams and sports. For example, professional baseball teams have introduced customized in-season and off-season training programs tailored to individual players, resulting in improved injury prevention and performance outcomes [26]. By adopting similar tailored approaches and incorporating rotation systems, teams can efficiently manage player workload, prevent injuries, and maximize the utilization of their squad members, ultimately enhancing team performance and success.

Table 3 presents a suggestion based on real data from a world elite team that adopted a rotation system to reduce overuse and incorporate resistance training to improve muscle power output and exercise to prevent injuries. Ideally an athlete should play every 7 days, this would drastically reduce the risk of injury [5]. As shown below, the coach (along with the coaching staff: physiology, physiotherapy, and physical trainers) must plan player rotation to create a window so that injury mitigations can be applied. Not only does it lessen injury, but resistance training has also been linked to improving performance [27].

Note that in this model the athlete is banned from a game so that a window of at least 7 days can be created so that it is possible to apply training loads to prevent injuries and enhance physical performance. It is also important to note that when an athlete is removed from a game, the pitch training load must increase so that there is no significant acute change in the workload (i.e., putting the athlete at injury risk due to acute change in the workload, as mentioned in **Figure 1C**). The field training should be of more open fields (to develop speed), not reduced. In addition, the field training needs to be closest to the real situation of games, e.g., friendly matches.

Therefore, coaches can use resistance training to promote equity in physical development and performance within the team [28]. This can be achieved by designing comprehensive resistance training programs addressing each player's specific needs and weaknesses, and thus, coaches can ensure all team members receive adequate training for health, performance, and injury prevention [29]. As presented in **Table 2**, resistance training regimens also must be focused on enhancing balance, stability, and proprioception (i.e., "preventive exercise") that can improve neuromuscular control, reduce the risk of falls, and prevent musculoskeletal injuries [30]. Also, including exercises targeting core stability, lower limb strength, and coordination, coaches can help players maintain balance and decrease injury likelihood during training and competition [31].

Balancing playing time and training loads through personalized resistance training plans can foster a cohesive and competitive team environment while minimizing overuse injuries and burnout [32, 33].

When players are unable to engage in additional training due to demanding game schedules, it can have detrimental effects on their performance and health. Lack of additional training may result in decreased muscle strength, reduced power output, and compromised speed, all of which are vital for injury prevention and overall athletic performance [34, 35].

Days of week	Sun	Mon	Tus	Wed	Thu	Fri	Sat	Sun
Week 1								
Field variables	Match (~10 km)	OFF	Pitch training/ endurance (5.0 km)	Pitch training/ endurance (5.0 km)	OFF	Pitch training/ velocity (4.0 km)	Pitch training/ tactical (2.0 km)	Match (~10 km)
Resistance training	OFF	OFF	Power Whole body + Preventive exercises	Core + Mobility	RFD + Velocity- force	Core + Mobility + Preventive exercises	OFF	OFF
Physiotherapist	Recovery session	OFF	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session
Week 2								
Days of week	Sun	Mon	Tus	Wed	Thu	Fri	Sat	Sun
Field variables	Match (~10 km)	OFF	Pitch training// endurance (5.0 km)	Pitch training/ endurance (5.0 km)	OFF	Pitch training/ velocity (4.0 km)	Pitch training/ tactical (2.0 km)	Match (~10 km)
Resistance training	OFF	OFF	Power MMII + preventive exercises	RT MMSS	RFD + Velocity- force	Core + Mobility	OFF	OFF
Physiotherapist	Recovery session	OFF	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session	Recovery session

Table 3. Optimal distribution of playing and training load in a congested season.

3. Conclusions

Implementing rotation strategies in teams and sports can help manage player workload, prevent injuries, and maintain overall fitness levels. By incorporating resistance training into rotation schedules, teams can ensure that all players receive the necessary physical conditioning to withstand the demands of the sport and minimize injury risks [36]. Monitoring match-play exposure and training load, particularly in professional football players, is a key strategy to prevent injuries and optimize player health [37].

The resistance training must be used to improve performance (by the physical trainer) and to prevent injury (by the physiotherapist). In this sense, the communication between sectors (e.g., physical conditioning, physiotherapy, and medical staff) of the team must be effective, and a communication strategy must be implemented in the club daily basis so that the resistance training program works [23].

A well-designed resistance training program is essential for maintaining players' consistent performance throughout the season. By focusing on exercises targeting key muscle groups involved in football movements, such as the hamstrings, and incorporating periodization principles to vary intensity and volume, players can effectively build strength, power, and resilience to injury. Thus, this approach not only prevents injuries but also helps players maintain their physical condition and performance levels over a demanding season [29]. In conclusion, integrating resistance training into football players' routines is essential for injury prevention, active recovery, workload balance, and consistent performance. Coaches must understand the balance between training load, injury, and performance to manage resistance training effectively. This approach enhances players' physical durability, reduces injury risks, and optimizes performance, ultimately contributing to the team's overall success.

It is important to note that the results presented in this chapter are limited to one team in a specific country, and therefore, the results should not be generalized due to the potential influence of contextual variables (e.g., calendar and training styles) between leagues from different countries.

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Conflict of interest

The authors declare no conflict of interest.

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Chapter 2

Hypertrophy Energy Balance

Pedro José Benito Peinado and Alberto Armero Sotillo

Abstract

The present chapter delves into the topic of muscle hypertrophy in detail, focusing on defining what muscle hypertrophy is, the types of hypertrophy, the mechanisms, and the relationship with resistance training, as well as the variables affecting hypertrophy such as nutrition, rest, exercise selection, training volume, and training frequency, among others. The importance of mechanical tension, metabolic stress, and muscle damage as triggers for muscle hypertrophy is emphasized. Various types of muscle hypertrophy are explored, including connective tissue hypertrophy and sarcoplasmic and myofibrillar hypertrophy. The text also delves into how hypertrophy mechanisms relate to resistance training, highlighting the significance of mechanical tension and metabolic stress as stimuli for muscle hypertrophy. In a practical point of view, the text also discusses factors like nutrition and recovery, highlighting the importance of maintaining a positive energy balance and adequate protein intake to promote muscle growth optimally. Training variables such as exercise selection, exercise order, intensity, volume, frequency, and tempo of execution are discussed in detail, outlining their impact on muscle hypertrophy. The text provides a comprehensive overview of muscle hypertrophy, analyzing various factors that influence the ability to increase muscle mass. It offers detailed information on the biological mechanisms, types of hypertrophy, training strategies, and nutritional and recovery considerations necessary to achieve optimal results in terms of muscle hypertrophy.

Keywords: muscle hypertrophy, energy balance, resistance training, mechanical tension, training variables

1. Introduction

1.1 What is muscle hypertrophy?

Muscular hypertrophy refers to the excessive increase of muscle, more specifically, skeletal muscle. With this definition, it becomes complicated to delimit the term and make muscular hypertrophy measurable, in addition to acquiring a negative connotation on a certain average. We will be able to give a more adequate definition if we look at the concept referred to in the specialized scientific literature when the term muscular hypertrophy is mentioned. Muscle hypertrophy according to Haun and Vann [1] is defined as an increase in the size (volume) of skeletal muscle, accompanied by an increase in minerals, proteins and quantity of energy substrates (e.g., glycogen or intramuscular triglycerides).

The scientific variables most related to the increase in the volume of muscle (kg) tissue are [2] as follows: Fat-free mass (FFM) was calculated as “all that is not fat”, subtracting fat weight from body weight, or when the measurements were obtained by dual X-ray absorptiometry was calculated as lean tissue plus bone mineral content [3]. Lean muscle mass (LMM), lean mass, lean body mass, bone-free lean body mass or mineral-free lean mass was calculated as the fat-free mass minus the bone mineral content (DXA) or as fat-free mass minus the estimated weight [4] of the live bone by the equation of Heymsfield, Smith [5]. Skeletal muscle mass (SMM) or skeletal muscle was defined as lean muscle and was calculated by anthropometric equations, by proprietary algorithms when using bioimpedance or by estimates based on dual X-ray absorptiometry data [6].

1.2 Types of muscle hypertrophy

If muscle hypertrophy is defined as an increase in the size of skeletal muscle, we must identify which components of muscle tissue produce this increase. A logical and fairly accepted hypothesis is that muscle hypertrophy is primarily due to an increase in the contractile elements of muscle tissue [7]. However, studies have failed to demonstrate that increases in muscle contractile proteins and units (sarcomeres and myofibrils) are proportional to increases in muscle cell area [1]. Two things can be concluded from this: the first is that hypertrophy of contractile elements is not the only one and, moreover, it is not known if it is the one that most influences the hypertrophy of the whole muscle.

We can differentiate three types of hypertrophy or forms of muscle tissue growth [1, 8]:

- **Connective tissue hypertrophy (extracellular matrix):** increase in the volume of the extracellular matrix accompanied by an increase in minerals and protein quantity.
- **Sarcoplasmic hypertrophy:** chronic increase in sarcolemmal and/or sarcoplasmic volume accompanied by an increase in mitochondrial volume, sarcoplasmic reticulum, t-tubules, and/or enzymes or the content of energy substrates such as glycogen and intramuscular triglycerides.
- **Myofibrillar hypertrophy:** increase in size and/or number of myofibrils, accompanied by an increase in the number of sarcomeres or the amount of sarcomeric proteins directly related to the structure and contractile force generation of the sarcomere. Hypertrophy of the contractile elements can be achieved by an increase in the number of myofibrils or the addition of sarcomeres to existing myofibrils. The addition of sarcomeres can occur in series or in parallel, the latter being the most important contributor to exercise-induced muscle hypertrophy [7].

1.3 Muscle hypertrophy mechanisms and their relationship with resistance training

Resistance training (RT) is a popular physical activity recommended for the enhancement or maintenance of musculoskeletal health [9]. It is typically performed with free weights, resistance machines and isokinetic equipment.

In addition, we know that RT is the best training method for increasing muscle mass, superior to aerobic or cardiovascular type training [10]. In turn, RT is the best non-pharmacological method of activating variables linked to hypertrophy and, therefore, the best method for maintaining or gaining muscle mass [11].

Hypertrophy-inducing stimuli are defined as those signals (internally) induced by strength training, which are of sufficient magnitude and duration to trigger hypertrophy of skeletal muscle mass [12]. These signals are recognized by sensors that subsequently trigger muscle protein synthesis through the activation of protein complexes such as mTORC1.

In addition to mTORC1 there are other chemical signaling pathways that induce hypertrophy, such as, among others, insulin and growth factor IGF1, this pathway is also activated with RT, specifically through muscle stretching [13], which is related to the mechanical stress exerted on the muscle during exercise.

Other RT-response pathways that trigger hypertrophy include androgenic markers, myostatin and activin, among others [14].

The main stimuli or mechanisms that trigger the hypertrophic response associated with RT were enunciated by Schoenfeld [7]:

1.3.1 Mechanical tension

When a muscle contraction occurs, whatever the type, it causes an increase in intramuscular pressure captured by mechanical sensors and translated into the corresponding chemical signal at the physiological level. The simple act of walking or running already involves an intramuscular pressure of 200–300 mmHg in the soleus muscle [15]. Therefore, sedentary people who do not practice any type of exercise, simply because they are subjected to the force of gravity on a daily basis, receive sufficient mechanical stimulus to maintain and not decrease muscle mass.

Muscle contraction is not the only way to produce a mechanical stimulus that can result in muscle hypertrophy. Passive muscle stretching can also produce hypertrophy as long as it is very intense or ballasted with resistance [16, 17].

Nowadays, it is considered the main mechanism of hypertrophy since, equalizing mechanical tension, measured as time under tension (TUT), hypertrophy is similar between different types of training protocols [18]. Mechanical tension is load-dependent; the greater the load, the greater the mechanical tension for the muscle, but when in two sets with different percentages of one-repetition maximum (1RM), the same character of effort is reached, which must be high or very high, and the mechanical tension generated in the set is equalized. This is because in the series with higher external load, it will have been possible to perform a small number of repetitions and the TUT will be lower, while in the series with lower load, it will last longer and will reach a similar mechanical stress based on accumulating repetitions of lower mechanical stress [19]. This is why, the mechanical tension and therefore the hypertrophy that we are able to generate through this is dependent on the character of the effort and not so much on the percentage of 1RM used for the series, although obviously both variables are directly related.

1.3.2 Metabolic stress

Metabolic stress induced by weight training could be defined as the accumulation of metabolites, particularly inorganic phosphorus, lactate, H⁺ protons, and associated

muscle hypoxia, which facilitate the increase of these metabolic byproducts and stimulate muscle hypertrophy [20].

One of the most studied metabolites as a signal of metabolic stress has been lactate, a metabolite produced in intense efforts of 30 seconds to 2 minutes duration, times in which the classic RT sets of 6–15 repetitions where anaerobic energy pathways predominate are usually found [21]. It has also been seen how lactate administration in cells *in vitro* promotes anabolism and cell growth [22], and metabolic stress may be a mechanism of muscle hypertrophy in humans.

The two factors that most affect lactate production and the consequent metabolic stress are as follows: the relative load or number of repetitions per set, together with the character of the effort or proximity to muscle failure of these sets [23]. Therefore, the greater the range of repetitions and character of effort, the greater the metabolic stress.

The character of the effort or proximity to failure is also related to the mechanical stress, as this increases notably in the repetitions closer to failure. Therefore, it could be that the increase in muscle mass associated with metabolic stress is a chemical translation of stimuli of a mechanical nature. When attempts have been made to test whether a greater accumulation of metabolic products increases hypertrophy in the absence of mechanical stress, it has been found that this does not occur and that hypertrophy is dependent on mechanical stress [24, 25].

1.3.3 Muscle damage

Exercise Induced Muscle Damage (EIMD) can be defined as a set of alterations or changes at the morphological level that occur in muscle and connective tissue in response to exercise. This muscle damage manifests itself in alterations at different levels in the muscle fiber such as sarcolemma, sarcoplasmic reticulum, loss of structural proteins, necrosis, microtraumas in the contractile elements (discontinuity in the Z bands), as well as in the connective tissue and in the extracellular matrix [26].

As it is sometimes complicated to measure direct markers of muscle damage, muscle damage can also be measured with indirect markers as follows:

- Reduced ability to produce force [27]
- Edema or swelling produced in muscle tissue.
- Delayed Onset Muscle Soreness (DOMS)
- Reduced joint range of motion due to muscle limitations.
- Increased concentration of certain proteins in the blood such as creatine kinase (CK) or myoglobin.
- Increased levels of inflammatory cytokines in blood such as tumor necrosis factor-alpha (TNF- α) or interleukins such as 1 β or 6.

Each of these markers has a specific recovery time [28], but in all of them, the residual effect is affected by the magnitude of the initial damage, and the more the muscle damage, the longer the recovery time.

The association of muscle damage with muscle hypertrophy is due to a series of events and signaling that occurs in the body when muscle damage occurs, such as the inflammatory response, the activation of satellite cells, the cellular swelling, and the production of IGF-1 [29].

Eccentric training has been shown to have greater effects on hypertrophy than concentric training [30]. This could find its explanation in that it is a type of training that generates greater muscle damage or else to that it is a type of training that generates greater mechanical stress. As with metabolic stress, it is difficult to separate the effect of muscle damage on hypertrophy from the effect of mechanical stress on hypertrophy.

Muscle damage decreases as we repeat the type of training that has caused this damage, and this is the effect known in the literature as repeated bout effect (RBE). A few weeks after repeating the training stimulus, the markers of muscle damage diminish to a great extent. If muscle damage was necessary, we would have to find a way to provoke it again once it diminishes with repeated exposure to the same type of training.

This clashes with hypertrophic adaptations that usually occur after 8–10 weeks of exposure to the appropriate stimulus, when muscle damage is already almost nil due to adaptations to training [31, 32]. If muscle adaptations occur when muscle damage is almost nonexistent, it is worth asking whether muscle damage is a direct cause of hypertrophy or whether it is just another means with a small effect on hypertrophy and associated with the main mechanism which is mechanical tension. Without going any further, workouts that involve great muscle damage, as could be eccentric work on slopes, do not generate significant hypertrophy [26]. However, Blood Flow Restriction (BFR) workouts, which barely generate muscle damage, could generate the same hypertrophy as conventional RT [33].

1.4 How much hypertrophy can we expect?

The possible amount of muscle mass (MM) that can be increased depends on the method of measurement and the period of evaluation. Our research in this regard has shown that resistance training can obtain improvements ranged from 1.6 kg in FFM and 1.7 kg in LMM, to 1.1 kg in MM [2]. Regarding the characteristics of the participants, there are no variables (neither the age nor the training status of the participants) that moderate the gains in hypertrophy. In addition, with respect to the characteristics of the training, the only single variable that moderates inversely the gains in hypertrophy is the number of sets per workout, showing that an excess of sets per workouts affects negatively the amount of muscle growth. These muscle mass gains do not include studies that have used anabolic steroids to achieve these increases, and these changes are much greater when pharmacological aids are used [34].

2. Variables affecting hypertrophy

Now that we have to determine which mechanism induces muscle hypertrophy from RT. We can look at the variables that affect how much muscle we can build. When it comes to RT, most people would think first thought in the weight they need to lift, the number of repetitions and series they need to do, or which exercise to execute. All these will have a place in the variables that affect muscle hypertrophy, but in order to study all the edges that have an influence on the hypertrophy process, we need to give it a wider look.

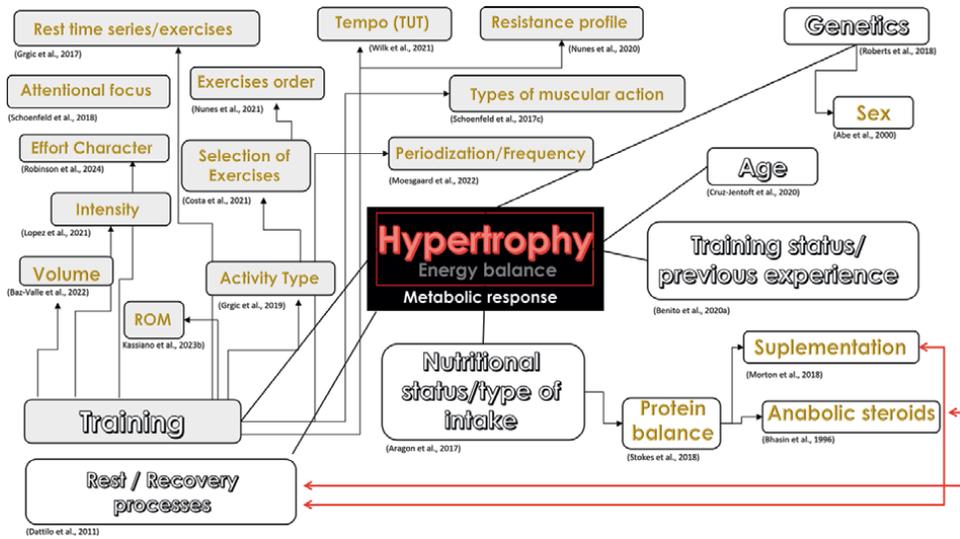


Figure 1.
Hypertrophy map factors.

With this purpose, we have developed a visual map of the variables, backed by science, that a personal trainer should take into consideration when preparing a muscle hypertrophy plan for a client (**Figure 1**).

Within the hypertrophy map, we can gather the factors into different groups by similarity of the factors; by doing so, we obtain three categories of variables:

- Subject-related or non-modifiable variables
- Nutritional and recovery variables
- Training variables

2.1 Subject related or non-modifiable variables

Personal differences between subjects directly affect the ability to generate hypertrophy; some of these variables such as gender, age, or previous training experience are observable to the naked eye or can be known with just one question. On the other hand, the genetics of each individual is difficult to know unless a complex study is performed, which is usually not available when training someone. The main limitation of this group of variables is that although we can know them and know their effects on hypertrophy, we cannot modify them; despite this, it will be essential to take them into account within the hypertrophy program, in order to establish realistic goals for muscle mass gain.

2.1.1 Biological sex

Men and women, due to genetic factors, have different body composition. In the distribution of muscle mass, women have a greater percentage of their muscle mass in the lower part of the body, while men present greater similarity between the lower

and upper part. Likewise, the differences in total muscle mass between men and women are less marked in the lower than in the upper body [35].

Although sex differences exist, there is much evidence available indicating that the relative muscle hypertrophy that can be generated is the same regardless of sex and muscle group. This hypertrophy is relative; in other words, it depends on the initial muscle mass present in the muscle. Therefore, as men generally have greater muscle mass, they can increase their muscle mass to a greater extent than women [36]. But in the case of presenting two subjects of different sexes, with a similar muscle mass in a given muscle, the capacity to hypertrophy said muscle would hardly be affected by gender differences; other variables could mainly influence the differences between subjects.

2.1.2 Age

The peak of a person's muscle mass is reached during youth between 20 and 40 years of age, at which time the maximum values of other health parameters such as bone mineral density are also reached [37]. From that peak point muscle mass decreases at a rate of 0.3% annually if resistance training is not performed [26].

As one advances in age, it becomes more difficult to increase and maintain muscle mass, with age more and more subjects become non-responders to the same training program or hypertrophic stimulus [38]. However, it is always possible to increase muscle mass even in older subjects, especially if they have no previous training experience [39], with the associated health benefits. For trained subjects with a great muscular development during their youth, it will be very difficult to increase muscle mass, reaching a point where it will be impossible for them to increase hypertrophy and they will have to focus on losing muscle mass as gradually as possible [40].

2.1.3 Genetics

There is a limit to the amount of muscle mass that a person can increase over a lifetime, but each person has a different genetic limit or potential. When the same training load is applied to people who apparently have a similar training status, we see that they respond very differently in terms of muscle mass gains [41].

These genetic differences allow us to divide subjects into cluster groups of high responders, low responders, non-responders, etc. Depending on how much hypertrophy, they can build from a same stimulus.

Following this methodology, it has been identified that there are certain genetic polymorphisms and variants that are associated with greater gains in muscle mass, strength, power, or VO_{2max} [42].

2.1.4 Previous training experience

The training level of the subject is also a parameter to take into account, not so much because of its direct involvement but because it is a reference for the use of other variables. In the early stages of training, when one goes from not controlling any of the variables that affect hypertrophy to starting to perform activities and behaviors that enhance it, the change is so great that it means an increase in muscle mass even when the training and nutrition parameters are not optimized, as a little is better than nothing. Given this premise, one would expect that, after this initial stage of improvement, the adaptations would be reduced by the appearance of RBE, but nothing could

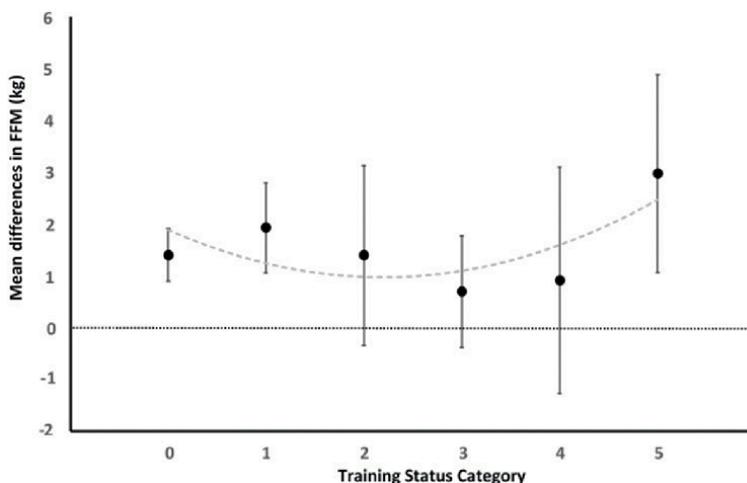


Figure 2. Differences in hypertrophy (kilograms of fat free mass) as a function of level in years of training experience [2].

be further from the truth. Benito, Cupeiro [2] determined that the hypertrophic response depending on the training experience could be equally large in novice and experienced subjects, with less response from those subjects between 2 and 4 years of RT experience (**Figure 2**).

This increase in the capacity to generate hypertrophy as the subject becomes more experienced could be explained not so much by physiological factors but also by the optimization of known and controllable variables. As one gains experience in training, one also learns to train and feed better or more in accordance with the physical objective set. This, added to other factors such as the time invested in achieving the objective and the importance of training in the lives of those who practice it, makes the very experienced optimize their possible gains in muscle mass as opposed to those who, despite having a greater margin for improvement, are not able to take full advantage of the variables that affect the increase in muscle mass. In addition to these implications of experience on the hypertrophy variables, we also found that previous experience with the same type of hypertrophic stimulus affects the stimulus response, which is why it must be taken into account when conducting and analyzing studies if the subjects are subjects without previous experience in RT or if on the contrary they are subjects with experience in RT. This nuance affects not only the magnitude of the effect of the intervention but also the implications that the intervention may have on the subject. The epigenetic response to RT stimuli such as, among others, muscle stretching is dependent on the subject's level of training [43].

2.2 Nutritional and recovery variables

Within the factors that can influence the hypertrophy process are the group of nutritional factors which, in turn, are related to the recovery from the training sessions. The protein balance, where there is a sufficient excess of proteins, necessary for the construction of muscle mass, which is directly related to the need or not of protein supplementation, and on the other hand, those processes that accelerate the recovery processes or enhance the reconstruction of muscle mass, such as the use of anabolic steroids. The effect of these nutritional factors, on the processes of recovery

and energy availability, has a direct connection with the metabolic response that any training stimulus may produce.

It would appear that a slightly hyperproteic, incorporating at least 1.6 g of protein per kilogram of body mass, is appropriate in hypertrophy interventions [44], although it is true that this value may change depending on other variables such as sex, training status, previous training experience, and the use of anabolic steroids.

What is clear and beyond doubt is that a negative energy balance can reduce or even eliminate the ability to hypertrophy in humans, even when weight training with high loads. A slightly positive energy balance and a diet rich in amino acids (2 to 3 times the RDA recommendations) is needed to promote maximal muscle growth [45, 46].

When it comes to nutritional intake, a slightly hypercaloric diet, made of whole foods or high-calorie supplements, combined with RT increases FFM [47]. The calorie surplus just needs to be slight, as if it is too big nor only will there be a MM increase if not also a body fat increase [48], especially in advanced lifters who have small chance of taking advantage of aggressive hypercaloric conditions [49].

There is a wide variety of nutritional intakes, low carbohydrates, high fats, intermediate fasting, etc. All of them with subtypes within it, while most of them claim to be the most effective to improve body composition, it has been proved that all of them have advantages and drawbacks [50]. Concerning FFM, any kind of nutritional intake could possibly increase hypertrophy when combined with RT, as long as the amount of protein intake is high enough [50]. Regarding the other nutritional parameters that could affect the increase in MM, it should be noted that not all of them affect in the same way; it depends on the individuals following the diet program. This should be taken into consideration when designing nutritional plans, as the response is inevitably individual.

The use or not of nutritional supplements will depend on the nutrient intake of each person, so before providing any supplement, it is necessary to analyze whether or not they are necessary to maximize the process of muscle hypertrophy.

Referring to recovery process, in the past few years, there has been a huge increase in recovering methods, cryotherapy, foam rolling, pressotherapy, ice baths, etc. As always, we tend to forget the most simple but effective methods, in this case, sleep. To optimize muscle hypertrophy, sleeping time, and quality needs to be considered, as it is the main time when the muscle will recover from training and grow as a response to the given stimulus [51]. The lack of sleeping time and or quality, could negatively affect hypertrophy, not only the new MM increases but also the already existing MM, what would lead to muscle atrophy and, in worst case, scenarios, sarcopenia, and cachexia. This is due to the effect of sleep deprivation, which causes a decrease in the activity of muscle protein synthesis (MPS) and other anabolic pathways, while also activates catabolic signaling and degradation pathways [51].

Some of the above-mentioned recovery methods have been related to hypertrophy increases, for instance, ice baths or cold water immersions. This method is used right after finishing the training session, with the claim of accelerating the recovery process, but the hypertrophic response clearly does not benefit from it, cold water immersions attenuate the activity and changes in satellite cells, which regulate muscle hypertrophy, therefore reducing the dehypertrophic response of the muscles [52, 53].

In contrast with cold water immersions, we have heat therapy, but despite the change in temperature, there is no change on its effectiveness to increase muscle hypertrophy, same as before, and there was not a difference in MM increments by using or not localized heat pads [54].

Moreover, other recovery methods have not yet been studied along with hypertrophy, and this is the case of pressotherapy. This new method has recently gained prominence among athletes, but its effects on muscle recovery and thus on its possible impact on hypertrophy are not yet clear [55].

That is why, all in all, the main focus of the recovery process should not be on the use of new methods and devices, but to rest properly and according to the personal demands.

2.3 Training variables

2.3.1 Type of activity

Not all types of training are equally efficient in producing muscle hypertrophy, as not all of them involve the principles of mechanical tension, metabolic stress, and muscle damage. In some training methods, even when these mechanisms are present, hypertrophy is not produced, as it is dependent on very specific conditions. The training method that has proven to be most effective and efficient in generating hypertrophy is weight training or RT [10].

2.3.2 Exercise selection

Exercises are usually chosen to work a target muscle, but within the variety of exercises that exist for the same muscle group, not all generate the same hypertrophy, as, depending on muscle involvement, regional hypertrophy of muscle zones can be produced [56]. Small changes in the placement of a joint during the execution of an exercise can lead to small adjustments and changes in the distribution of hypertrophy generated [57]. This can be especially interesting for athletes such as bodybuilders [58], who depend on their physical appearance for their sport performance and where every muscle detail can make a difference.

When we think of different exercises for the same muscle group, one of the first things that comes to mind is the material we can use to perform the exercise, dumbbells, barbells, bars, pulleys, machines, etc. For years, it has been hypothesized whether free weights, being more demanding or harder, generated greater hypertrophy, or whether the use of machines, created for the isolated work of a muscle group, enhanced it to a greater extent. Well, both hypotheses were at least partially wrong. A recent research by Hernández-Belmonte et al. [59] showed that, matching the rest of the training variables such as volume, intensity, etc. There are no differences in hypertrophy generated by the use of free weights or machines. This is due to the fact that the organism does not understand the exercises performed; it simply receives the stimulus signal and triggers the response to this mechanical stimulus in the form of chemical signaling that increases protein synthesis and hypertrophy.

Another point that generates debate within the selection of exercises is whether to use multi-joint or mono-joint exercises, as happened with free weights and machines there are advocates and detractors of both, even so, and as happened with the previous point, no significant differences have been found between using multi-joint or mono-joint exercises [60].

With this we could think that, by selecting the exercise that we like the most for a muscle group, and performing all the corresponding series in this exercise, we could reach the optimal hypertrophy of that muscle group. Despite this logical reasoning, we must remember that there is the RBE or adaptation of the response to the same

stimulus, which is why it is advisable to vary the exercises for each muscle group to maximize hypertrophy [61, 62], this variation of exercises should be more related to biomechanical aspects (resistance profile, muscle activation, etc.) of the exercise than to the material used. Moreover, in general, varying the exercises for the same muscle group helps to increase motivation and avoid monotony [63], which also helps to optimize results.

2.3.3 Order of exercises

Now that we have determined that we must perform several exercises to maximize the hypertrophy of a muscle group, we must order them within the session. Although, as we mentioned before, there are no differences between performing global or analytical exercises, there are differences in how one affects the other, so it is important to know how the order in which they are programmed affects them [64], as the fatigue they generate is not the same. Placing the exercises of the target muscles at the beginning of the session could have slight advantages when it comes to optimizing the hypertrophy of these muscles due to the production capacity and increase in strength available at the beginning of the sessions [4].

2.3.4 Effort character

The character of effort refers to the number of repetitions performed in a set versus those that could potentially have been performed in that same set [65]. Therefore, maximum effort character would be to perform all possible repetitions with the given load, until reaching muscular failure. Muscle failure is the point at which, despite applying all possible force, the concentric phase of the exercise in question cannot be completed [66]. It remains to be determined whether this muscle failure should be considered as the complete achievement of concentric ROM in all exercises, as in very demanding exercises toward the end of the concentric run one might not reach muscle exhaustion but not be able to complete the entire run.

Of all the hypertrophy variables associated with RT, the nature of the effort is one of those with the greatest implication on the muscular hypertrophy that can be generated by RT, and it could be argued that it is the most important, with the exception of training volume. This is due, in part, to mechanical tension, as we saw in the section corresponding to this concept; mechanical tension is the main mechanism of hypertrophy and also increases as the series progresses, when fatigue and the nature of the effort increase.

Indeed, having a high effort character in the series performed is one of the main keys for this series to increase our muscle mass, as demonstrated by the scientific evidence to date [67, 68]. This could lead us to think that performing all sets until muscle failure would be the best way to optimize hypertrophy, but this is not the case, in studies where a high or very high effort character has been compared with muscle failure, it has been observed that there are no significant differences in terms of the hypertrophy produced [69, 70], although muscle failure does lead to greater fatigue, greater accumulation of metabolites and potentially greater muscle damage [71]. Therefore, the use of muscle failure in training should be used as another tool and taken into account when planning.

To measure or estimate the character of effort, there are several tools, such as scales of perceived effort, such as the Borg scale; the repetitions in reserve (RIR), which is the number of repetitions that we leave undone before reaching muscle

failure, if in a series we can perform 12 repetitions and 10 are performed, it would be a series with RIR 2; another option is also the velocity-based training, where the proximity to failure is estimated with the percentage of speed loss of the concentric phase compared to the first repetition. This method is very dependent on the attentional focus on performing the concentric phase at the highest possible speed. All of these are valid ways of estimating the proximity to failure and making a set an effective set for hypertrophy.

In summary, the character of the effort is the parameter that marks whether a series is effective for hypertrophy or not, in general, it is considered that a series of high effort character, which is performed with an RIR 4 or lower, can be quantified as a training series [72]. The degree of effort required in each series will influence the tolerable training volume and the perceived exertion of the training [73].

2.3.5 Relative intensity - load type

Relative intensity refers to the percentage of the 1RM selected in the series to be performed. With each percentage of the 1RM, a certain number of repetitions can be achieved before reaching muscle failure [65]. This number will be different between subjects for the same percentage of the 1RM of each subject [74]. These percentages of 1RM are divided into high loads (1-5RM), medium loads (6-15RM), and low loads (15RM or more) [75].

Current evidence tells us that muscle mass gains can be achieved with either high, medium, or low loads [76–78], as long as some considerations are taken into account for each of them. In all cases, one should have a high or very high effort character, close to muscle failure. Excessively low loads, below 20% of the 1RM, which would be equivalent to 60-70RM, do not produce as much hypertrophy as other load ranges [79]. In the series with low loads is, if possible, even more important, the proximity to muscle failure, as it is the only way to try to match the mechanical stress that occurs in series with higher loads [80]. For its part, the series of high loads, especially if they occur in multi-joint or global exercises, do not require reaching muscle failure if not only to RIR 3–4 [72].

Although, as we have seen, you can conduct hypertrophy with almost any type of load, the use of medium loads is still the recommended for most people and for most of the time, for its efficiency and convenience [81, 82]. High and low loads should be used as a complementary tool within training with which to give variety of stimulus to the muscle.

2.3.6 Volume

The most adequate method used, also in research, for the quantification of volume in RT is the number of effective series per muscle group [83]. Now, not all the series can be considered effective, for this, we return to the character of the effort, as we determined previously the series must have a high effort character, $RIR < 4$, so that this is sufficiently stimulating to generate hypertrophy. Also, this character of the effort should be taken into account depending on the type of load of the series, it is necessary to apply a greater character of the effort when using lower loads so that the series can be effective.

If the character of the effort is the variable that marks if a series is effective for hypertrophy or not, the volume of training is the variable that has more relation with how much can be hypertrophied, but is always more volume more hypertrophy?

In the first studies analyzing training volume in the form of effective sets, such as that of Wernbom, Augustsson [84], it was observed that, for the biceps brachii, the recommended volume was 4–6 sets per session and 2–3 sessions per week, which is equivalent to 8–18 sets per week, while for the quadriceps, it was 8–30 sets to optimize hypertrophy. This review was not misguided, as the latest reviews that study the optimal volume per muscle group, speak of 10 to 20 weekly sets per muscle group [85]. Below 6 weekly sets per muscle group, it is really difficult to produce hypertrophy [86], especially in subjects already trained in RT with hypertrophy objective; possibly for untrained subjects, it is a sufficient stimulus to start but that should quickly approach the 8–10 sets indicated by the reviews.

We already have the limit of the minimum effective volume more or less clear, not to go below 6–8 weekly series and, if possible, to be closer to 10–12, at least. But what about the upper limit?

In some studies such as that of [87, 88], where different groups were compared with different training volumes, it was observed that those who were around 20 weekly sets per muscle group generated greater hypertrophy than those who were closer to 30 weekly sets. On the other hand, the authors of [85] establishes 20–25 sets as the weekly recoverable volume, at which point more fatigue accumulates than hypertrophy is generated, which could be counterproductive for hypertrophy due to a possible subsequent poor recovery. On the other hand, a recent study carried out in men with 5 years of experience in RT, i.e., fairly trained subjects, measured the effect of adding weekly series on the quadriceps, starting from 22 weekly series, an already high volume, until reaching in the case of one of the groups to 52 weekly series. In this study, the group performed a higher volume obtained greater hypertrophy [89]. The results of this study should be taken with caution, due to the nature of the highly trained subjects, the progressive overload approach, and the fact that only the muscle group analyzed was trained during the study. Taking all this into consideration, we cannot say that always more volume is going to be better, there is a point, different for each person and muscle group, where the maximum tolerable or recoverable volume is reached [90]. When this upper limit of the volume is reached not only may it not increase more if not even be a smaller increase than when using a lower volume. This point should be adjusted to each subject and muscle group based on their level of training and ability to adapt and will change as training progresses and based on the approach taken at any given time.

Now that we have the volume in weekly series, it is necessary to distribute it in the workouts, to perform all the series for the same muscle group in the same training session is not optimal, especially if this volume is higher than 8–10 series [91]. The recommended would be around 6–8 sets per muscle group per session, not going below 4 and not exceeding 10 sets per muscle group per session. Therefore, an intermediate or advanced athlete who usually performs 16 weekly sets of a muscle group should divide it into at least two weekly sessions. This is mainly due to the high effort character that must be maintained in the series for hypertrophy.

In the exercise selection section, we already established that it was important to perform more than one exercise per muscle group to provide stimulus variety [61, 62]. Therefore, it will be important to divide the weekly series that are programed in different exercises for the same muscle group. Just as it is not good to perform all sets of the same exercise, it is not good to perform one set in each exercise. Krieger [92] determined that performing 2–3 sets per exercise provided 40% more hypertrophy than performing only one, while performing 4 to 6 sets already diluted this effect and that although greater hypertrophy was generated by greater volume, this did not have

as much increase as in the first sets. Therefore, it is important to perform 2 to 4 sets per exercise.

2.3.7 Training frequency

The training frequency is the number of sessions or days in which training is performed. Taken into RT it is usually referred as the number of days in which a muscle group is trained during a microcycle or week of training; thus, if each muscle group is trained once a week, it will correspond to a frequency of 1 while 2 or 3 days of the same muscle group would be frequency 2 and 3, respectively. Often, the frequency of training does not depend only on physiological factors, as we will explain below, but also on the availability of the subject, which is why the design of efficient training plans is paramount [93].

The frequency is a variable directly dependent on the volume and intensity, I understand this as the character of the effort, the higher the volume and the more intense the training, the higher the frequency must be to be able to tolerate that work. At equal volume and intensity and as long as both are tolerable, the frequency of training does not make a difference on the hypertrophy that is generated [94, 95]. Therefore, we should understand frequency as a tool to regulate training volume.

Frequency has a very high relationship with volume and therefore also with the parameters of optimal volume and tolerable volume, as explained above. As we have seen, the weekly sets that some subjects may require to generate hypertrophy can range from 12 to 25–30 weekly sets [85]; these exceed the 10–12 sets that are tolerable in a single training session [91]. Therefore, for those weekly volumes that exceed the tolerable daily volume, it will be necessary to increase the frequency [96, 97], not so much because this will have an effect on hypertrophy but to tolerate and distribute the volume required to hypertrophy.

As we have also mentioned above, the volume increases as one progresses in training and in the development of muscle mass, therefore, in novice subjects, a low volume may be assumable with a frequency 1, while in more advanced subjects, a type 2 frequency will be required, being able to reach frequencies 3 and 4 at specific times or specialization mesocycles for a specific muscle group in advanced subjects.

The frequency of training is also closely related to the type of training routine, those fullbody routines, where the whole body is worked in each session, tend to have a higher frequency than Split or Weider routines, where the frequency is usually 2 or 1. This distribution of muscle groups in different training days has not been shown to have an influence on hypertrophy [98, 99] provided that the volume is the same. In cases where volume is not well controlled, a higher frequency usually leads to greater hypertrophy, but this is linked to the fact that a higher training volume is usually produced.

In conclusion, the variable that determines the amount of hypertrophy is the volume, the frequency is dependent on it and must be used to maximize the gains generated by the optimal training volume.

2.3.8 Execution time (tempo) and time under tension

The Time Under Tension (TUT) is the time it takes to perform a series, formed by the time of each of its repetitions; adding all the series of the same muscle group, we obtain the TUT of each muscle group in the session.

In RT, each repetition is composed of four phases: concentric, eccentric, and two transition phases, from concentric to eccentric and from eccentric to concentric. The duration of each of these phases is what is known as movement tempo or cadence of execution. The time spent in each of these phases directly affects the number of repetitions that can be performed in the series and therefore the character of the effort of the series, since, against the same external load, performing a given number of repetitions will not involve the same effort, this is due to the tempo in which these repetitions are performed. Therefore, it is essential to set the tempo of execution of each phase in the RT.

Regarding the effects of movement tempo on muscle hypertrophy, as long as the total time of the repetition is between 0.5 “and 8”, hypertrophy is not negatively affected [100], so the margin of time we have to perform a repetition is quite wide. Seen that the total time of the repetition does not have excessive influence on hypertrophy, one might ask whether the time in each phase of the repetition does.

Hypertrophy benefits from increased TUT in the eccentric phase, due to the increased mechanical tension and muscle damage that this generates, so it is interesting that, within stretch-shortening cycles, the eccentric phase is slowed down to maximize hypertrophy [30]. This is due, among other things, to the fact that the load used during the series is always the same regardless of the phase, while muscle strength is not the same in concentric as in eccentric [101]. Therefore, increasing the intensity in the eccentric phase with increasing the time in that phase has effects on hypertrophy, because it intensifies the series by increasing the character of effort.

On the other hand, increasing the time in the concentric phase does not seem to have clear benefits on muscle hypertrophy [102]. Therefore, it is not advisable to deliberately slow down this phase but to allow it to slow down when the character of the effort at the end of the series requires it [103].

The movement tempo that is paused must be in accordance with the level of demand of the repetitions. It must take into account the character of effort and the type of load. When working with high loads or when already close to failure, it is not always possible to follow the stipulated cadence, as the acyclic muscular resistance will have been exceeded. A point from which the speed of execution cannot be modulated at pleasure, especially that of the concentric phase. Despite the fact that the established cadence is not met, the series must continue to ensure the proximity to muscular failure.

Movement tempo is an important variable to be taken into account when RT is patterned. As we will see later, where the attentional focus is placed during a set has implications on the resulting hypertrophy. Although in the first repetitions of a set a stipulated cadence can be met, maintaining a specific tempo and focusing the attention on it can affect the quality of the set when proximity to failure is approaching [104].

2.3.9 Rest time

It is the time that elapses between sets or exercises of a workout. Despite the classic recommendation to use short rest times (60”) to elevate hormonal values and thus maximize hypertrophy, today it is known that there is no relationship between these variables [105]. Rather the other way around, too short rests can negatively affect the hypertrophic response such as muscle protein synthesis (MPS) [106].

This is why new trends, guided by scientific evidence, recommend longer rest times, seeing that hypertrophy generated with 3-minute rests is superior to 1 minute

[107] and that, in general, 2-minute rests can be optimal for hypertrophy [108]. There is no scientific support for shortening rests when hypertrophy is the goal. The feeling of higher intensity from training more often does not trigger greater muscle mass gains [109].

2.3.10 Range of movement

The range of motion (ROM) refers to the distance in degrees that are covered in a particular joint during the execution of an exercise. If all possible degrees of freedom of that joint are traversed for a given exercise, it is called full ROM, whereas if only part of the possible degrees of movement is performed, it is called partial ROM [110].

Current scientific evidence tells us that, the main key to the selection of a ROM for an exercise is that this ROM goes through muscle stretch [111] either through the use of a full ROM or through a partial ROM in the area of muscle stretching or elongation [112]. The latter option of partial repetitions in stretching has taken quite a bit of traction in the scientific literature recently, sometimes surpassing full ROM in terms of the hypertrophy produced [112, 113].

This effect, known as stretch-mediated hypertrophy, whereby hypertrophy is produced by stretching a muscle, either with very demanding passive stretches or RT where the muscle is brought to the stretch, has been shown to have effects on increasing muscle mass [16, 114]. This is because muscle stretching within RT increases mechanical tension to a greater extent than RT in muscle shortening, thereby also increasing TUT intensity [17].

The effects of muscle stretching on hypertrophy can be seen not only in ROM comparisons but also between exercises with the same ROM. Those exercises in which at the beginning or the end of the ROM have a greater muscular stretch produce greater hypertrophy than those with a more reduced ROM in which the muscle is not taken to maximum possible stretch [115, 116]. By this same principle, the use of ballasted stretching between sets of RT could have positive effects on hypertrophy [117]. In this case, it would be mainly due to the fact that, by maintaining tension on the muscle at the end of the series with load, the TUT and the training volume are increased, and it would be necessary to study whether at the same volume and TUT these ballasted stretches between sets would have superior effects on muscle hypertrophy.

2.3.11 Resistance profile

The resistance profile is the result of putting together the torque that a joint undergoes throughout the course of an exercise, with the capacity of the muscle to produce force during that same course. This capacity of the muscle to produce force as a function of its length reduces as muscle shortening occurs [118]. This shows us that, depending on the position of the body segment which is being trained and how the external forces affect it, an intensity curve will be produced during the ROM reflecting how demanding the exercise is along its ROM [119], this curve is known as resistance profile.

This training variable has, to date, little scientific support behind it, which is why it has not yet been possible to determine whether there is an optimal endurance profile when seeking to maximize hypertrophy [120]. However, we do know that once an exercise has been selected, it is important that the ROM passes through the zone of greatest mechanical demand of the exercise [121], or what is the same, to pass through

the highest zone of the resistance profile curve, as that is where the mechanical stress produced by the exercise is greatest.

2.3.12 Muscle action type

As mentioned above, the most common way to generate hypertrophy is through muscle contraction, although as we have seen, muscle stretching can also induce hypertrophy. Within muscle contraction, the use of concentric or eccentric contraction can also have an effect on the hypertrophic outcome.

When comparing the use of only concentric versus eccentric contractions, it has been found that strength gains are specific to the type of contraction while in hypertrophic gains, while both contractions can generate an increase in muscle mass, eccentric contractions generate a greater increase in hypertrophy [122], with the increase in muscle mass in eccentric being very similar to when concentric and eccentric phase are used at the same time [123]. Eccentric overload training generates great muscle damage, accumulates a lot of fatigue, and usually requires supervision and specialized equipment [124], so although it has a place in RT, especially in cases of sports performance, its use when the objective is hypertrophy is not indispensable and, if used, a greater control of the character of the effort should be taken as in this case the eccentric muscle failure is not the same as the concentric and can lead to much more fatigue [125] in addition to possible muscle injuries.

As purely eccentric work has similar results to using concentric and eccentric work in the same set, it will be more interesting in general to use a classical RT work, where the concentric phase is performed in the time required by the load demand and the eccentric phase is slowed down and controlled slightly in order to take advantage of the eccentric work [30]. By doing this, we will increase the TUT and mechanical tension produced by patterning a movement tempo that spends more time in the eccentric than concentric phase [104].

2.3.13 Attentional focus

In the world of bodybuilding and strength training in general, it has long been believed that focusing attention on the muscle being worked during the set increased muscle mass gains, and this attentional focus is referred to as the mind-muscle connection.

Indeed, focusing attention on a muscle can lead to slight increases in the activation of that muscle [126]. Given that, when approaching near failure, it is difficult to maintain attentional focus on anything other than generating force as best one can. We have also investigated how external assistance with verbal instructions affects maintaining that muscle focus and mind-muscle connection. The result was the same as above, and verbal instructions have a slight effect on muscle activation of the target muscle [127, 128].

Despite the fact that there is the ability to improve muscle activation by focusing attention on the muscle, we know that, if the muscular disposition in front of the load is correct, the nervous system itself is responsible for recruiting the muscles with greater mechanical advantages to carry out the demanded movement [129]. This is why, even more important than focusing on the mind-muscle connection, it is essential to select exercises that put the target muscle in an ideal biomechanical position to exert force.

In summary, it has been evidenced that, focusing attention during the series on an internal focus, such as the mind-muscle connection, generates more hypertrophy than focusing on external factors [130]. This does not mean that one should slow down the concentric phase of an exercise looking to maximally notice the muscle, as we saw earlier. This has no positive effect on hypertrophy [102].

During a set, the focus should be on moving the load in the plane where the target muscle is most efficient and moving the load at a controlled speed that allows us to ensure we work the target muscle, without slowing down voluntarily. At the end of the series, when it is difficult to maintain this focus, we should seek to be close to failure, keeping the repetitions as homogeneous as possible to avoid the intervention of other synergistic muscles that would take work away from the target muscle.

3. The effects of energy balance on muscle hypertrophy

The process of building muscle mass is a process that costs energy (endergonic), which means that if we provoke an increase in this type of tissue, it will be at the cost of obtaining the energy necessary for it.

As mentioned above, what is clear and beyond doubt is that a negative energy balance can reduce or even eliminate the ability to hypertrophy in humans, even when weight training with high loads. A slightly positive energy balance and a diet rich in amino acids (two to three times the RDA recommendations) is needed to promote maximal muscle growth [45].

In the mathematical models proposed so far that attempt to predict muscle growth, the energy balance is one of the most essential [131–133]. In the model proposed by Torres, it is clear that the path that muscle growth can develop is very different depending on whether the intake is hypocaloric, normocaloric, or hypercaloric. For this reason, it is worth asking how much energy will be necessary for this process. An increase of approximately 200 kcal over the normocaloric diet is a good start, and in any case, any desired increase that does not produce an increase in the percentage of body fat, which would make it clear that there is an excess of unnecessary Kcal in that energy balance. It is enough to measure every 2 weeks the percentage of fat, to know that the increase of kcal is being adequate. Recent studies have found that larger energy surplus, 15% above maintenance calories, leads to a bigger body mass increase while also increasing fat mass while smaller surplus, 5% above maintenance, will lead

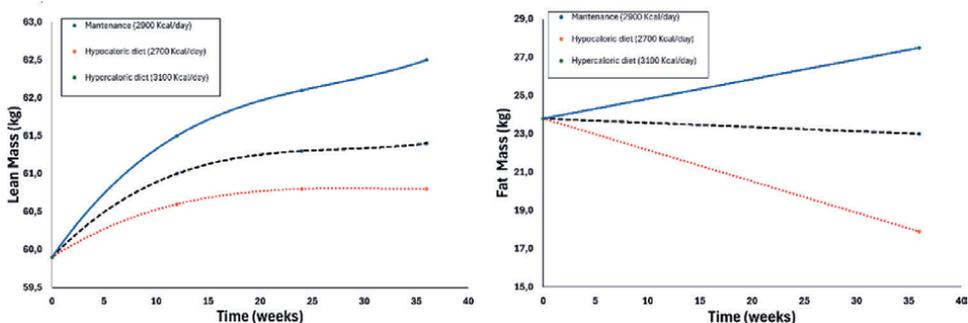


Figure 3. Effects of three types of diets on the growth of muscle mass (left side) and fat mass (right side) in mathematical models proposed by Torres et al. (figure modified with permission of the author).

to a smaller body mass gain while nearly reaching the same MM gains [134]; therefore, just a slight surplus above the normocaloric diet should be enough to optimize muscle hypertrophy while limiting the increase in fat mass (**Figure 3**).

3.1 Body recomposition

One of the questions that we, personal trainers and physical trainers, are often asked is whether it is possible to produce an increase in muscle mass while producing a reduction in the fat mass, which has been called body recomposition. In the light of science, we must say that this process has been moderately studied and that it possibly exists [135].

Body recomposition is especially useful in individuals with high fat percentage, low MM, and low RT experience, as in these kind of individuals, any change for the better will have a positive impact on body composition. As a result, the research done in postmenopausal women has proven that, in this kind of population body, recomposition is possible [136, 137]. Same for the elderly, starting RT and dieting at any age has an impact of increase of MM and decrease on fat mass [138, 139].

Although it might seem that this is a process that only occurs in people with a low level of fitness, it has been shown that it can also occur in people with previous experience in RT, even when not following a nutritional plan [140, 141]. The problem in these cases is that although changes occur, they are pretty small, the amount of time used during a body recomposition to lose 1 kg of fat mass and gain 1 kg of MM might be enough time for a bigger decrease in fat mass and a bigger increase in MM if focused only on one goal at a time. When a nutritional protocol is carried out, the changes can be substantially greater than when only training is taken into account [142]. The possibility of producing a body recomposition is given regardless of the level of fitness [143], for both men [144] and women [145]. Body recomposition exists for all populations, only that some of them, can take greater advantage of it while, in others, it would be more interesting to perform classic processes of muscle mass gain and fat loss.

One population that could benefit from body recomposition is elite competitors, not so much because in their case, the effect of recomposition is very large and because they are athletes who must maintain an optimal state of fitness throughout the year, with a low percentage of body fat. Body recomposition may be sufficient to generate the small changes in body composition required by these athletes while maintaining performance [146, 147]. Among these athletes, we could also find bodybuilders; in their case, this body recomposition occurs when they go from a stage of muscle mass gain to one of fat loss to prepare for a competition. In the first weeks of transition between stages, a body recomposition can occur, and the loss of fat is due to the reduction of calories in the diet while there is still an effect on the increase in muscle mass [148, 149].

It is necessary to say that the process of increasing muscle mass is an anabolic process, and that the process of fat reduction is a catabolic process that can conflict, in fact, we have seen in the previous section as a deficiency of energy in the energy balance can compromise muscle growth. Body recomposition should be taken into consideration as a protocol for some individuals as it can occur in any population [150]; however, sometimes, depending on how much of an increase in MM or decrease in fat mass is required, we believe that an adequate periodization of training by focusing on one goal at a time, could produce more relevant effects than trying to achieve mixed training targets.

3.2 Practical applications

In a practical point of view, in order to be effective in the process of increasing muscle mass, it is necessary to analyze the hypertrophy map individually. Establishing those factors that are not modifiable (with the focus on analyzing the potential hypertrophy for each individual); and adapting those factors that are modifiable within the parameters described in this chapter.

Resistance training has proven to be the most effective training for improving muscle hypertrophy. This is due to the presence of the hypertrophy mechanisms in this type of training. Within the hypertrophy mechanisms, mechanical tension has proven to be the most important one when studying muscle gains, muscle damage and metabolic stress are variables derived from and influenced by mechanical tension, and muscle damage and metabolic stress alone do not induce muscle hypertrophy. Therefore, trainers should seek to optimize mechanical tension within resistance training.

Taken into account the training factors, the variables which have been shown to have the greatest importance on muscle hypertrophy are the character of effort (RIR 4 or lower) and the volume of training (between 12 and 25 weekly series per muscle group), depending on the other factors.

To optimize hypertrophy, it is crucial to sustain a slight positive energy balance, typically around 200 kcal above maintenance levels. This slight surplus supports muscle growth by providing the additional energy needed for effective recovery and adaptation following resistance training.

When it comes to nutritional factors, scientific evidence supports that at least 1.6 g of protein/kg of body weight is necessary to achieve a significant effect on hypertrophy.

4. Conclusions

To effectively enhance muscle mass, it is essential to evaluate the hypertrophy map on an individual basis. This involves identifying non-modifiable factors to assess each person's hypertrophic potential and adjusting the modifiable factors according to the guidelines outlined in this chapter.

Nutritional factors are intrinsically related to recovery. Assuming that hypertrophy always occurs in the recovery phase, poor recovery could be a limiting factor in the muscle growth generated by resistance training.

Although in the field of sports science almost all studies focus on training variables, the present chapter demonstrates that this is only a part of the factors involved in the process of increasing muscle mass.

Maintaining slight positive energy balance is essential to support muscle growth and optimize hypertrophy outcomes during resistance training. Controlling the degree of positivity in the energy balance, by monitoring changes in body fat, and maintaining an adequate protein balance, with or without artificial supplementation, is crucial for optimizing muscle hypertrophy outcomes.

Although body recomposition is scientifically feasible, it might not be the best option for everyone. While obese and overweight people may go through a body recomposition process when initiating resistance training for other subjects such as healthy trained population, it may be more efficient for a periodization process where the goal is to increase muscle mass and then decrease fat mass. Body recomposition

may be also interesting in high performance sports, as these athletes need to maintain a certain body weight during the season.

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Conflict of interest

The authors declare no conflict of interest.

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Section 2

The Comprehensive Benefits
of Resistance Training: From
Disease Prevention to Mental
Health

Prevention of Age-Related Diseases

Nasuh Evrim Acar

Abstract

Healthy aging in elderly adults should be supported by lifestyle factors such as physical activity, nutrition, sleep, and control of harmful habits. Physical activity provides protective effects against age-related problems such as cardiovascular disease, diabetes, osteoporosis, and sarcopenia. Resistance training is particularly effective in maintaining muscle and bone health. It requires attention in terms of nutrition, energy, protein, and water intake. Adequate protein and micronutrient intake in older people can help prevent sarcopenia and frailty. Sleep patterns can change with age and sleep disorders are common; adequate sleep is important for overall health. Controlling smoking and alcohol consumption can reduce the risk of various health problems. Furthermore, access to health services and regular health check-ups are critical for older people to maintain their health and improve their quality of life. Healthy aging requires a comprehensive approach and lifestyle interventions contribute to a better quality of life for older people.

Keywords: health care, lifestyle, nutrition, resistance exercises, physical activity

1. Introduction

Life is a process that begins with birth and ends with death. This adventure continues with the aging phase, which is initially characterized by construction activities, gradually stabilizing, and then by destruction activities. Aging, which constitutes a part of every individual's life, is a natural process and is an indicator of catabolic activities occurring in the body. Increased catabolic metabolism brings about irreversible changes in the organism. The rate at which this change occurs is determined by the genetic factors, environmental influences, and the individual's lifestyle.

The aging process is characterized by a combination of anthropometric, body composition, and metabolic, hormonal, and neuromuscular changes, which result in physical and mental decline in the human body [1]. With increasing life expectancy, the prevalence of age-related noncommunicable illnesses such as diabetes, cancer, overweight, high blood pressure, and cardiovascular disease has risen [2].

Although scientists are constantly conducting research to reduce the negative effects of aging, the aging process is still inevitable. While it is impossible to avoid aging, we can effectively control and improve this natural progression with minor modifications to our lifestyle. Time dedicated to physical activity and exercise, a balanced and adequate diet, regular health checks, and healthy living habits can delay

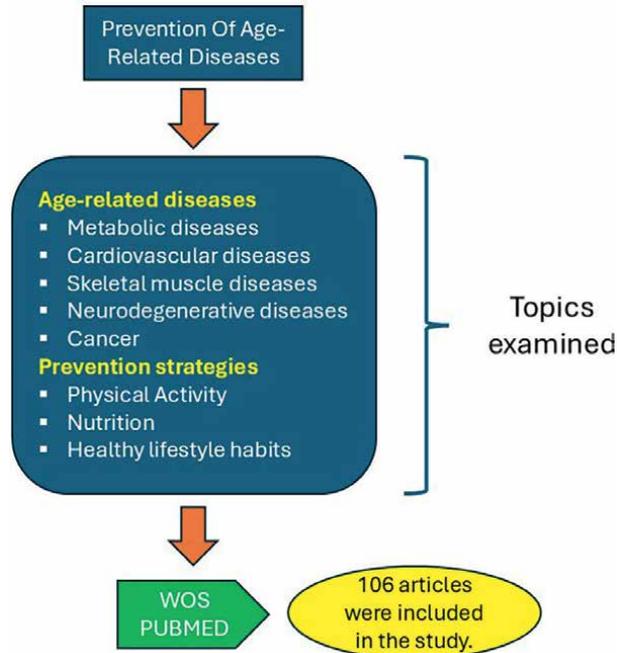


Figure 1.
Flowchart of methodology.

the physical effects of aging and help us maintain our quality of life. This section shows how positive life changes can help us to live healthier lives.

The methodology used in preparing this book chapter is a literature review. In this context, each section listed by title has been screened in the WOS and PubMed literature databases, and articles deemed relevant to the chapter have been included in the study. The flowchart showing the methodology is presented in **Figure 1**.

2. Aging process

Aging is described as the gradual physiological decrease experienced beyond age 30. Although aging is an inevitable process, some variables can affect the speed of this process [3]. Various theories on how and why the aging process occurs are not discussed as they are not the subject of this book and section. Although these concepts exist in theory, in practice there is no single theory but rather the interaction of many external factors that lead to the clinical signs of aging.

While the molecular mechanisms behind the impacts of aging on tissues and organs are the same, the way these effects are observed varies across different types of tissues (**Figure 2**). These markers can lead to impairments in other functions in a domino effect. For example, aging musculoskeletal systems can cause a loss of balance and spatial awareness, resulting in falls. Falls delay the healing of bone tissue and trigger new problems [4]. Since all body systems have age-related physiological changes, the systems in **Figure 2**, which I consider important and summarize, will be briefly mentioned.

	Body composition	Fat Mass (FM) ↑, Fat Free Mass (FFM) ↓, Height ↓, Body mass index (BMI) ↑, Internal adiposity ↑
	Cardiovascular system	Cardiac hypertrophy ↑, Left ventricular muscle hypertrophy ↑, Heart rate (HR) ↓, Stroke volume (SV) ↓, Cardiac output (Q) ↓, Arterial-venous oxygen difference (a-v O ₂) ↓, Systolic blood pressure ↑, Diastolic blood pressure ↓
	Skeletal muscle system	Bone mineral density ↓, Muscle mass ↓, Range of motion of the joint ↓, Skeletal muscle strength ↓
	Nervous system	Nerve cells of the brain ↓, Weight of the brain ↓, Volume of gray and white matter of the brain ↓
	Endocrine system	Estrogen ↓, Testosterone ↓, IGF-1 ↓, Growth hormone ↓

Figure 2.
 Physiological effects of old age.

The process of aging is defined by a rise in overall body fat mass and a related decrease in lean mass and bone density, regardless of fluctuations in weight and body mass index (BMI) caused by general and physiological factors [5]. A 5–25% decrease in basal metabolic rate occurs as we age. This leads to an increase in body weight and body fat, even if diet and exercise habits do not change [6]. Although the extent of increased fat mass (FM) is similar in both sexes, women have higher fat mass than men at all ages [7].

Age is an independent risk factor for cardiovascular disease, and at the same time diseases such as diabetes and hypertension that raise the risk of cardiovascular disease also worsen with age. Arteries thicken and stiffen as we age, increasing the total peripheral resistance and thus the afterload. The left ventricle stiffens and hypertrophies in response to this increase, which lowers the left ventricular reserve, and the pressure needed to fill it and causes left atrial dilatation [8]. When these factors combine, heart failure is inevitable. Heart failure is mostly observed in older adults. A review of the literature shows that adults over the age of 70 account for 90% of heart failure-related fatalities and 50% of heart failure diagnoses [9].

Musculoskeletal aging varies greatly among individuals [10]. Four primary criteria are used to measure this difference: osteoporosis, frailty, sarcopenia, and osteoarthritis [11]. Complex interplay between growth factors, hormones, diet, and principally hereditary factors leads to aging of the musculoskeletal system [12]. As we age, type 2 muscle fibers are replaced by slower type 1 fibers, leading to decreased muscle strength and increased fat accumulation [13].

Another change is in the brain and nervous system. By the age of 85, about 20% of the brain volume is reduced. This reduction is associated with loss of gray matter rather than white matter. Although the number of neurons does not change, axons with shortened myelin are observed with loss of synapses and dendritic spines [14].

As mentioned above, aging has many physiological effects. The magnitude or timing of these effects is directly related to lifestyle. If aging is not managed properly, it brings many diseases that we will discuss.

3. Age-related diseases

Aging is an irreversible and progressive pathophysiological process, which we have already discussed in previous chapters. Decreases in cell and tissue function result from this process, which also raises the likelihood of many age-related illnesses, including immune system disorders, musculoskeletal disorders, metabolic disorders, cardiovascular disorders, and neurodegenerative disorders. Even while medical and technological advancements have increased life expectancy, one of the leading causes of disability and mortality remains chronic diseases [15]. Let us now examine these diseases in more detail.

3.1 Metabolic diseases

3.1.1 Obesity

When FM exceeds optimal levels, men and women are generally considered obese. The most frequently used method in primary care to assess high FM is body mass index (BMI). Adults are usually classified according to BMI thresholds: overweight 25 kg/m² and obesity 30 kg/m². However, BMI may pose some problems for older adults, so these thresholds should be used with caution [16].

In older people, both low and high FM can lead to health problems. However, low FM may be an indicator of physiological reserve deficiencies such as sarcopenia or osteoporosis in the elderly. On the other hand, high FM can increase the risk of health problems and chronic diseases such as obesity and diabetes [17]. These risks include metabolic disorders (hypertension, insulin resistance, type 2 diabetes, and metabolic syndrome), heart disease, musculoskeletal disorders (bone, joint, muscle, and skin diseases), and certain types of cancer [17]. Therefore, as the obesity epidemic spreads today, the prevalence of overweight and obesity among older age groups is also increasing, leading to a number of health and quality of life issues mentioned above [16].

3.1.2 Diabetes

Less physical activity, increased FM, and decreased FFM all contribute to obesity and insulin dysfunction, increasing the risk of diabetes in the elderly. Type 2 diabetes (T2DM) is characterized by hyperglycemia resulting from progressive impairment of insulin-secreting β -cell function and is often associated with varying degrees of insulin resistance [18].

Diabetes is linked to several serious cardiovascular diseases, including heart failure, coronary artery disease, ischemic heart disease, peripheral arterial disease, and stroke, and the risk grows with age [19]. T2DM, which is characterized by insulin resistance and is a precursor to diabetes, is closely associated with chronic kidney disease, eye disease, cardiovascular disease, and other conditions. Patients with T2DM have a higher cardiovascular risk than individuals without diabetes; this risk is two to three times higher, especially in middle-aged and elderly T2DM patients [20]. Due to facilitated lifestyles, the number of older adults with T2DM is rapidly increasing worldwide. This increase is linked to longer life expectancy as well as prolonged exposure to cardiometabolic risk factors such as excess adiposity, skeletal muscle shrinkage, and decreased physical activity [21].

3.2 Cardiovascular diseases

Aging has a substantial impact on the heart and arterial system, increasing the risk of cardiovascular diseases (CVD) such as hypertension, atherosclerosis, myocardial infarction, and stroke [22]. **Figure 3** shows aging-related changes in the heart. The most important change observed in the heart with age is enlargement of the left atrium. This causes changes such as calcification of the aortic main artery, increased fatty deposits in the epicardial region, hypertrophy of the left ventricular muscle, hypertrophy of myocytes, and stiffness (fibrosis) due to increased connective tissue in the heart [23].

3.3 Skeletal muscle diseases

3.3.1 Osteoporosis

Osteoporosis is a condition characterized by loss of bone mineral density and increased bone fragility due to this loss [24]. In aging women, osteoporosis becomes more pronounced due to the effects of decreasing estrogen levels on bone [25]. Primary and secondary osteoporoses are the two basic categories of the disease. Primary osteoporosis is the most prevalent type and includes senile osteoporosis (Type II) and postmenopausal osteoporosis (Type I). Secondary osteoporosis develops due to underlying diseases or medications and increases the risk of fracture with low bone mass [26]. Type I osteoporosis is distinguished by a higher rate of bone loss in comparison with bone formation, which is caused by a decrease in estrogen and androgen levels. Type II osteoporosis involves gradual age-related bone loss [27].

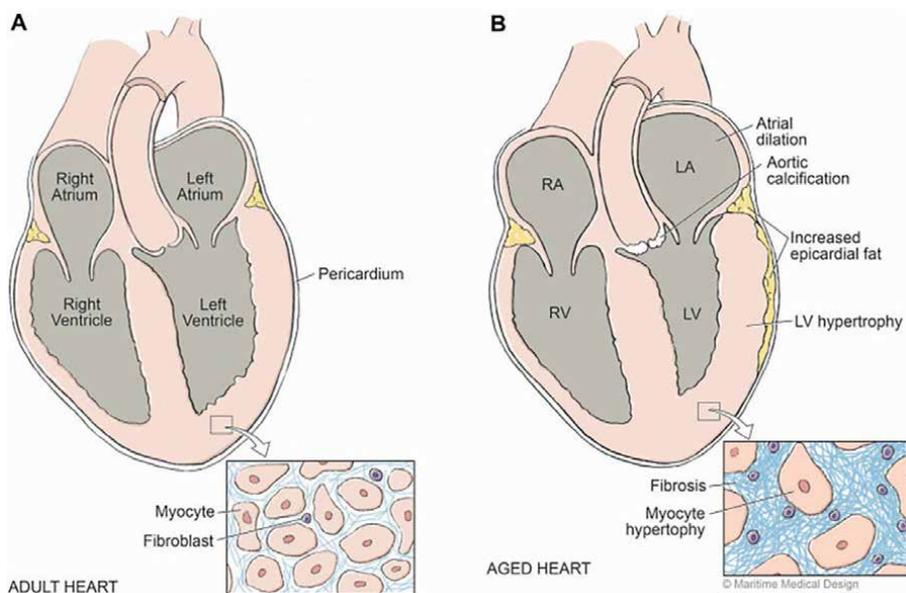


Figure 3.
Physiological changes in the heart with aging [23].

Low bone mineral mass, which is influenced by both modifiable and non-modifiable variables, is the primary cause of osteoporosis. Non-modifiable factors are as follows: age, sex, ethnicity, and genetic conditions. Modifiable factors are diet and eating habits, reduced physical activity, other diseases, and certain medications [28].

3.3.2 Sarcopenia

Sarcopenia is a sickness marked by a gradual and extensive loss of skeletal muscle mass and strength. It is linked to unfavorable consequences of physical incapacity, a low quality of life, and a higher chance of mortality [29]. While the molecular causes of sarcopenia are poorly understood, certain factors such as histologic changes in mitochondria, reduced impact of testosterone and growth hormones as one ages, and denervation of nerve cells can potentially lead to muscle atrophy [30].

Muscle fiber atrophy (shrinkage) is the outcome of aging-related loss of muscle mass. After the age of 30, the rate of muscle mass loss drops by 3–8% per 10 years, with an accelerated rate becoming more pronounced after the age of 65 years [31]. These losses in muscle mass and strength increase the risk of falls and increase the risk of injury in older people [32]. Atrophy is usually more pronounced in fast (Type II) muscle fibers and less common in slow (Type I) muscle fibers [33].

Following trauma and critical illness, critical illness myopathy and cachexia are associated with the most severe muscle loss [34]. This is due to several mechanisms, including reduced nutrition, changes in protein synthesis and degradation, neuromuscular blockade, and increased insulin resistance [35].

3.4 Neurodegenerative diseases

3.4.1 Alzheimer's disease

Alzheimer's disease (AD) is a neurodegenerative disease that occurs with age and is characterized by difficulties in learning, memory, and communication. It is responsible for 60–80% of dementia cases globally [36]. AD is a degenerative neurological condition that primarily affects adults 60 years of age and beyond. It causes issues with thinking, memory, and behavior. The disease causes abnormal deposition of amyloid β -protein ($A\beta$) and the formation of senile plaques, with progressive neuronal loss in the cerebral cortex and hippocampus [37].

One of the major causes of Alzheimer's disease is DNA mutations and defects in DNA repair mechanisms. Exceeding the repair capacity of DNA damage can lead to the development of neurodegenerative diseases through mistranslation by DNA polymerase [38]. Aging and reduced DNA repair capacity lead to increased DNA damage and accumulation in neurons. As a result, there is a rise in cellular oxidative stress and inflammatory reactions, which contribute to the development of age-related neurodegeneration and Alzheimer's disease [39].

Research shows that physical activity and exercise can improve cognitive performance to a certain degree in patients with cognitive impairment [40]. Individuals in the age range of 70–80 who engage in physical activity for a minimum of 30 minutes per day (totaling 150 minutes or more) on at least 5 days per week have been discovered to have a 40% lower risk of developing Alzheimer's disease compared to their inactive counterparts [41]. However, there is no clear information on which type of training should be practiced and for how long and with what intensity.

3.4.2 Parkinson's disease

After Alzheimer's disease, Parkinson's disease (PD) is the second most prevalent neurological illness that impairs the quality of life for many elderly people [42]. The prevalence of Parkinson's disease increases approximately tenfold between the ages of 50 and 80 [43]. The main clinical symptoms include limb tremor, shuffling gait, slowness, stiffness, and postural instability. These symptoms may be accompanied by additional symptoms such as autonomic nervous system dysfunction, depression, dementia, and psychosis [44].

Exercise is considered an important preventive measure in the aging process. Resistance exercises for Parkinson's disease patients have been shown to have positive effects on improving disease symptoms [45, 46]. It is essential to consider balance and gait impairments that occur with cognitive impairments in exercise planning in these patients. Exercise programs should be tailored to meet these specific needs.

3.5 Cancer

Undoubtedly, the risk of cancer increases with age. Approximately 60% of cancers occur in people aged 65 and over, and about 70% of cancer deaths occur in this age group. Cancer is therefore considered a disease of old age [47]. Although genetics plays a role in cancer risk, environmental and lifestyle variables account for the majority of the variance in cancer risk among populations and people. There is compelling evidence that lifestyle habits, including obesity, smoking, alcohol consumption, and bad diets, have a major influence on the development of cancer [48].

Smoking [49] and alcohol consumption increase the risk of many cancers [50]. The main cause of insulin resistance, low-grade inflammation, and many cancers is the accumulation of excess body fat caused by consuming too much energy and not engaging in enough physical activity [51, 52].

Cancer cachexia is a potentially fatal condition that affects older cancer patients. It is characterized by a loss of mass and strength in the skeletal muscles [53]. Reduced consumption of calories and aberrant metabolism brought on by tumor-induced variables are the causes of cancer cachexia [54]. As people age, sarcopenia aggravates cancer cachexia, which raises cancer mortality in senior populations [55]. For this reason, maintaining or increasing muscular mass and strength is essential for older cancer patients to increase their chances of survival.

4. Prevention strategies

The process of aging is intricate and affected by individual-specific factors such as genetics, as well as external factors like environmental conditions and lifestyle choices such as nutrition and exercise. The progressive decline in the health of adults as they grow older is a crucial issue in public health. Nevertheless, there is significant diversity among individuals in the degree of age-related alterations, and numerous changes that were previously considered unavoidable can now be averted, delayed, and even reversed [56].

Preventive strategies for age-related diseases primarily aim to hinder the occurrence or advancement of diseases, specifically in older individuals who are in good health or have long-term diseases. These measures encompass maintaining optimal

body weight, adhering to a well-balanced diet, engaging in regular physical activity, refraining from smoking and restricting alcohol intake [57]. Lifestyle choices have a significant role in the risk of developing age-related diseases. Nutrition, physical activity, and other lifestyle measures (**Figure 4**) are especially essential for the prevention of age-related diseases [58].

It is important to consider an older adult's degree of fragility when regulating their lifestyle. Diabetes is linked to a greater loss of muscle mass, a lower quality of muscle, and a lessened strength of muscle in the aging population. These conditions may cause osteopenia or sarcopenia to develop [59]. Frailty is known to be independently risk-factored by diabetes. A reduction in physical performance and a higher chance of negative health outcomes because of physiological weakness and functional or psychosocial stressors are the characteristics of frailty. Inadequate consumption of certain nutrients, particularly insufficient protein, may raise the risk of frailty and sarcopenia in the elderly [59].

The management of frailty in individuals with diabetes necessitates a workout routine that includes aerobic, weight-bearing, and resistance training, alongside optimal nutrition that includes sufficient protein consumption. Structured exercise programs in frail older adults offer several advantages, such as decreasing sedentary behavior, preventing mobility impairment, and reducing frailty [60].

Research has indicated that the probability of developing various forms of cancer can be decreased by adopting the following lifestyle modifications [57, 61, 62]. Adopting these beneficial practices enhances both physical and mental capabilities and postpones the need for assistance.

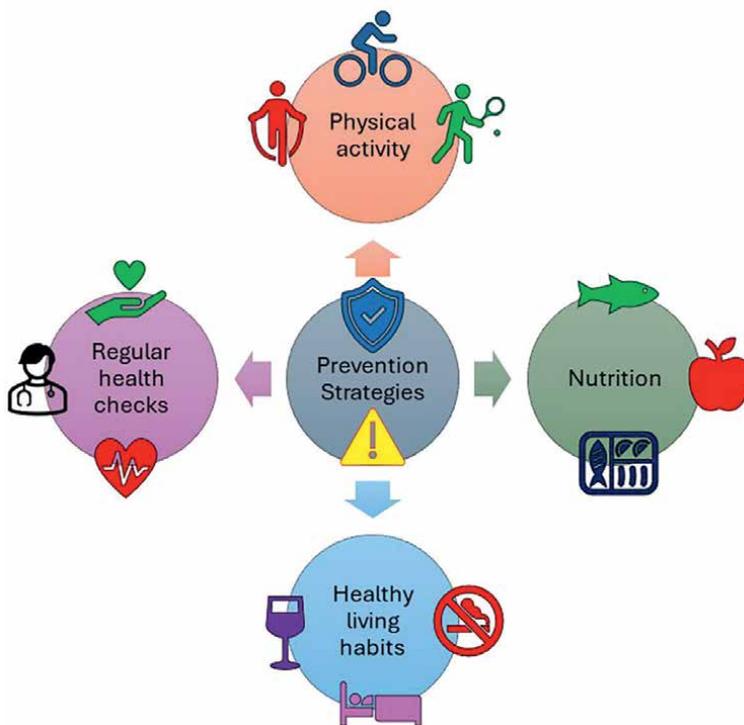


Figure 4.
Prevention strategies.

4.1 Physical activity

Engaging in physical activity (PA) is a highly effective strategy to combat health issues associated with aging. Daily physical activity can aid in the prevention of degenerative diseases such as osteoporosis and osteoarthritis, as well as cardiovascular and type 2 diabetes [63]. Regular physical activity is highly recommended as the most efficient non-pharmacological approach to enhance and sustain bone mineral density (BMD) and decrease the possibility of falls [64].

While certain pharmacological interventions have displayed potential in treating sarcopenia and osteoporosis, the most effective approach to address musculoskeletal aging is prevention through enhanced weight-bearing training and targeted training programs [65]. Physical activity has been found to impact the majority of bone cells and affect various aspects of bone remodeling [66] directly or indirectly. Resistance training specifically enhances both muscle and bone mass in older individuals [67]. Weight-bearing exercises, such as resistance training (RT), are employed as a method to prevent or decrease the loss of bone mineral density (BMD). These exercises enhance bone mineral content by creating tension in the bones, as stated in Ref. [68].

Furthermore, it is also critical to remember that multi-joint activities significantly affect older persons' bone mineralization. For instance, extended-duration resistance training protocols lasting 4–6 months, consisting of three sessions per week, with moderate-to-heavy weights (50–80% of a maximum repetition, 1 RM), two to three sets per exercise, and including squat and deadlift exercises, have been proven to significantly enhance bone mineral density (BMD) in the upper limbs, spine, and hip [69]. Indeed, free weight exercises with high loads (>70% 1 RM) show the greatest increase in BMD [70]. Multiple longitudinal studies have consistently demonstrated that resistance training (RT) is the most suitable form of exercise for enhancing bone health. RT effectively prevents the decline in bone mineral density (BMD) over time and even leads to modest increases when performed for a period of 3–12 months [71, 72]. An optimal resistance training program should include 4–5 exercises for the trunk, upper limbs, and lower limbs. Each exercise should consist of 2–3 sets, with 8–12 repetitions per set. The exercise intensity should be set between 70 and 90% of the individual's one repetition maximum (1 RM). Rest periods between sets should range from 60 to 120 seconds. The recommended frequency for these training sessions is three times per week, for duration of 12–52 weeks [73].

Resistance exercise training is challenging to incorporate into the exercise routines of older adults living in the community. This is because it requires specialized equipment and supervision, may not be suitable for certain health conditions commonly found in older patients (such as hypertension and stroke), and may not be appealing to sedentary older adults. Despite these obstacles, resistance exercise training has proven to be highly effective in increasing muscle mass, strength, and function.

4.2 Nutrition

Insufficient food consumption often leads to malnutrition, which is a prevalent issue among older individuals [74]. Malnutrition is associated with muscle atrophy. Research has indicated that as individuals age, there is a gradual decline in the amount of food they consume, leading to an increased risk of developing energy-protein malnutrition [75].

The energy expenditure declines as individuals age, primarily because of a reduction in both resting energy expenditure (REE) and physical activity [76]. A

study on energy requirements in elderly individuals found that women required 1520–2280 kcal, and men required 1840–2760 kcal [77]. When considering individual factors, the resting energy expenditure (REE) was determined to be 19.4 kcal/kg body weight per day in healthy elderly individuals and 20.4 kcal/kg body weight per day in sick elderly individuals [78]. The study indicated that a variation of 5 kg in body weight over the past 6 months, in either the positive or negative direction, is a sign of malnutrition [79].

The hydration status of the elderly is also a significant limitation. The diminished thirst perception that occurs with aging, in conjunction with multiple factors such as excessive alcohol and coffee intake, as well as the use of diuretic medications, makes older individuals more susceptible to dehydration. Hence, it is important to ensure that elderly individuals consume a minimum of 2000 mL of water at regular intervals, irrespective of their thirst sensation [80].

Protein consumption derived from macronutrients is equally significant. Elderly individuals may choose to decrease their consumption of protein in order to adhere to diets that have lower levels of fat and cholesterol. Recent research indicates that the protein needs of older individuals may be higher, approximately 1 gram per kilogram per day, compared to the recommended level of 0.8 grams per kilogram per day [81].

When assessing carbohydrate intake, which is one of the other macronutrients, a sufficient amount is considered to be 55–60% of the daily energy requirement [82]. When selecting carbohydrates, it is important to prioritize complex carbohydrates with a low glycemic index and avoid simple sugars as much as possible [79]. Reduced energy requirement is a fundamental aspect of maintaining energy balance. Therefore, it is essential for older individuals to exercise caution when consuming macronutrient fats that have a high caloric content. Therefore, the recommended maximum amount of fat intake should be 30% of the energy requirement, with no more than 10% coming from saturated fats [82].

The primary micronutrients that are of particular concern for the elderly are vitamins B₆ and B₁₂, calcium (Ca), and vitamin D [74, 80]. These vitamins and minerals are crucial for promoting optimal health as one ages. Ensuring sufficient vitamin D supplementation, particularly in conjunction with calcium intake, is essential for maintaining optimal bone health [79]. Upon investigating the connection between neurodegenerative diseases and nutrition, it becomes evident that deficiencies in vitamins B₆ and B₁₂ are particularly noticeable. Vitamin deficiencies tend to become more pronounced as one gets older. Furthermore, factors such as excessive alcohol consumption, adherence to a vegan diet, age-related digestive problems, and increased drug use contribute to insufficient intake of these essential vitamins [83].

4.3 Healthy lifestyle habits

Lifestyle interventions are crucial in preventing numerous non-communicable diseases [84]. The conventional elements of these lifestyle interventions primarily consist of physical activity, nutrition, and education for individuals who are at a substantial risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease [85].

Establishing and adhering to healthy lifestyle habits is crucial for preserving health and enhancing the overall well-being of individuals as they age. These habits are as follows:

4.3.1 Sleep

Sleep is essential for maintaining a healthy lifestyle, similar to the importance of proper nutrition and regular physical activity. Changes in sleep patterns are part of the normal aging process. Age is one of the most crucial factors determining the need for sleep. Physical changes occur with aging and sleep patterns change as part of this process. It has been found that sleep disorders increase with increasing age. Older people have difficulty falling asleep and staying asleep because they wake up frequently. In fact, the total amount of sleep required remains almost constant throughout adulthood. It is only sleeping pattern and depth that change with aging [86].

Adults aged 18–64 need seven to nine hours of sleep per night. Adults over 65 need 7–8 hours of sleep. From the age of 60, the onset of sleep is pushed back by 1 hour every 10 years [87]. The elderly tend to go to bed early in the evening (around 19.00–20.00 pm) and wake up early in the morning (around 04.00–05.00 am) [88]. The most serious sleep problem for the elderly is insomnia [89].

Insufficient sleep can lead to various issues including reduced appetite, tiredness, inability to concentrate on tasks, heightened risk of accidents and falls, restlessness, changes in mood, difficulty in focusing, and impaired decision-making abilities. Improving sleep habits, employing relaxation methods, and using therapies to reduce sleep duration have proven to be successful in treating sleep disorders [90].

4.3.2 Control of smoking and alcohol consumption

Smoking is a significant cause of numerous respiratory diseases and is now recognized as a critical risk factor for cardiovascular diseases, various types of organ cancers, and other pathological conditions [91]. Smoking significantly increases the risk of osteoporosis development in older individuals. Research has indicated that individuals who smoke have a higher likelihood of developing osteoporosis [92].

The elderly population is also adversely affected by alcohol consumption. Elderly individuals exhibit heightened susceptibility to the impacts of alcohol and diminished tolerance [93]. Research has indicated that consuming a moderate amount of alcohol, ranging from 1 to 6 drinks per week, is linked to a decreased likelihood of developing dementia [94]. Additionally, this level of alcohol consumption is also associated with a lower risk of cardiovascular disease, coronary heart disease, stroke, and overall mortality [95].

Guidelines for the Regulation of Smoking and Alcohol Consumption:

- *Smoking Cessation Programs:* It is advisable to motivate older smokers to engage in support programs aimed at assisting them in quitting smoking. These programs may comprise nicotine replacement therapies, pharmaceutical interventions, and counseling services [96].
- *Alcohol Consumption Restriction:* It is imperative to arrange educational and awareness initiatives aimed at diminishing or ceasing alcohol consumption altogether. Encouraging light-to-moderate alcohol consumption (1 to 6 drinks per week) is acceptable, but excessive consumption should be avoided [94].
- *Routine Medical Examinations:* It is advisable to undergo regular medical examinations to closely monitor and address the health hazards linked to smoking and alcohol consumption. These may encompass cancer screenings, cardiovascular risk evaluations, and bone health examinations [97].

Regulating smoking and moderating alcohol intake are crucial measures for enhancing the overall health and well-being of elderly individuals. Controlling these habits is a crucial element of maintaining good health as one gets older.

4.3.3 Health applications

While aging is unavoidable, successful aging is defined by minimal decreases in physiological functioning, while unhealthy aging is linked to a higher occurrence of illness and a decrease in quality of life as one gets older [98].

Around 80% of individuals aged 65 and above suffer from at least one chronic ailment, while 50% have two or more chronic conditions. Chronic diseases have emerged as the primary cause of escalating healthcare expenses, posing a substantial burden on our society [99]. Hence, an efficient healthcare sector that offers easily obtainable medical services is imperative. As the health services improve, the activity rate among older people also increases. These findings indicate that public health policies have a significant impact in the context of population aging [100].

Incorporating regular medical and laboratory exams and screening techniques to identify and address any abnormal processes at an early stage is a crucial aspect of maintaining good health as one ages. The elderly population must inevitably transition toward a more initiative-taking, integrated, and structured healthcare approach in order to sustain functional performance and independent living. Therefore, the objective of preventive medicine is to maximize the productivity and well-being of the aging population while minimizing the period of compromised health and functioning prior to death. Within this particular framework, prioritizing preventive measures rather than solely concentrating on treatments for the elderly is a crucial approach in effectively managing the aging population [98].

Recommendations for Healthy Aging:

- *Regular Health Check-ups*: Older people should be encouraged to have regular health check-ups. These check-ups enable monitoring of important health indicators such as blood pressure, blood sugar, and cholesterol levels [101].
- *Early Diagnosis and Treatment*: Participation in screening programs for early detection and treatment of diseases should be encouraged. Regular screenings should be conducted for common diseases such as breast cancer, prostate cancer, and colon cancer [102].
- *Preventive Health Services*: Vaccinations are important for older people to protect against diseases such as influenza and pneumonia. Regular immunizations should be encouraged [103].
- *Chronic Disease Management*: Individuals should be provided with education and support for the management of chronic diseases such as diabetes, hypertension, and heart diseases. Regular use of necessary medications and lifestyle changes are important for disease management [104].
- *Psychosocial Support*: Support should be provided for the psychosocial needs of elderly individuals. Awareness should be raised about mental health problems such as depression and anxiety and professional help should be sought when necessary [105].

- *Accessibility and Quality of Health Services:* It plays a critical role in improving the quality of life of older individuals. Healthy aging strategies can help individuals live a longer and better-quality life by protecting both their physical health and mental health [106].

4.4 Practical applications

- *Physical Activity:* “Promoting regular physical activity in older adults can significantly reduce the risk of chronic diseases and enhance overall physical and mental well-being.” For instance, extended-duration resistance training protocols lasting 4–6 months, consisting of three sessions per week, with moderate-to-heavy weights (50–80% of a maximum repetition, 1 RM), 2–3 sets per exercise, and including multi-joint activities (squat and deadlift exercises, etc.) [69].
- *Nutrition:* “Ensuring a balanced diet rich in essential nutrients is crucial for preventing malnutrition and chronic conditions in aging populations.” Energy requirements in elderly individuals found that women required 1520–2280 kcal, and men required 1840–2760 kcal [77]. Consume a minimum of 2000 mL of water at regular intervals [80]. The protein needs of older individuals are approximately 1 gram per kilogram per day [81].
- *Sleep:* “Encouraging good sleep hygiene practices can help mitigate the cognitive decline and physical health issues associated with aging.” Individuals over 65 should sleep 7–8 hours a day [87].
- *Control of Smoking and Alcohol Consumption:* “Reducing smoking and alcohol consumption in older adults is vital for preventing respiratory, cardiovascular, and other age-related diseases.” Encouraging light-to-moderate alcohol consumption (1 to 6 drinks per week) is acceptable [97].
- *Health Applications:* “Utilizing health applications for monitoring and managing lifestyle habits can empower older adults to maintain their health and prevent disease.” Health Monitoring Applications can provide personalized feedback and reminders, helping individuals stay on track with their health goals.

5. Conclusion

Engaging in physical activity is a highly effective strategy to combat health issues associated with aging. Engaging in regular physical activity provides a safeguard against degenerative diseases, including cardiovascular diseases, type 2 diabetes mellitus (T2DM), osteoporosis, and osteoarthritis. Resistance training specifically decreases the possibility of falls by enhancing bone mineral density and maintaining muscle mass. Nevertheless, the impact of aerobic training on bone health is relatively restricted. Resistance training plays a crucial role in preserving muscle and bone health among older individuals.

Proper nutrition is essential for the well-being of elderly individuals. Malnutrition is prevalent among older adults and can result in muscle atrophy. Elderly individuals should prioritize their consumption of energy, protein, and water. Consuming protein aids in preserving muscle mass by promoting the process of muscle protein

synthesis. Furthermore, crucial micronutrients for the elderly encompass vitamins B₆ and B₁₂, calcium, and vitamin D. These vitamins and minerals are crucial for promoting a healthy aging process.

The adoption of healthy lifestyle habits significantly contributes to enhancing the overall health condition of elderly individuals. The fundamental elements of healthy aging are sleep, nutrition, and physical activity. Sufficient and high-quality sleep is essential for preserving the physical and mental well-being of elderly individuals. Regulating smoking and alcohol intake provides a safeguard against various health issues, including osteoporosis and cardiovascular diseases. Effective stress management and prioritizing mental health have a beneficial impact on the overall health of older individuals.

Finally, accessibility and quality of health services play a critical role in improving the quality of life of older individuals. Regular health examinations, effective management of long-term illnesses, and timely identification of medical conditions are essential components of strategies aimed at promoting healthy aging. The objective of preventive medicine is to optimize the productivity and well-being of the aging population. To achieve this, it is essential to offer initiative-taking, integrated, and organized health services specifically tailored for older individuals.

Enhancing the health and quality of life in older individuals necessitates a comprehensive approach to lifestyle management. Physical activity, nutrition, sleep, stress management, and access to health services are essential elements in the process of promoting healthy aging. By taking into consideration these factors, older individuals can achieve a more robust and more contented lifestyle.

Conflict of interest

The authors declare no conflict of interest.

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The Impact of Resistance Training on Mental Health: Neuropsychological and Behavioral Functioning

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Abstract

Exercise has long been thought to improve overall cognitive and brain health, and it may protect against dementia by increasing blood flow to the brain. Prospective cohort studies support the idea that starting physical activity as a young adult and continuing throughout life is connected with a lower risk of cognitive impairment. While the presence of a link between physical fitness and overall cognitive health has long been known, only in recent years has research begun to study the role of physical fitness on memory performance. This research focused on the effects of aerobic training on cognition because it has been demonstrated to affect brain plasticity and structure while also improving brain structure. For example, one study found that the presence of a gene linked to brain-derived neurotrophic factors affected learning and individual differences in recognition memory. Thus, the issue remains: would strength training result in neurobiological gains and training effects? Can we discover measurable brain and cognition markers that distinguish between older persons who benefit significantly from resistance training (RT) and those who benefit little or none?

Keywords: resistance training, neuropsychological markers, behavioral functioning, mental processes, neurotransmitters

1. Introduction

Resistance training, defined as the exercise of muscular contraction to increase strength, muscle tone, and anaerobic endurance, has been extensively studied by fitness and medical researchers [1]. Existing empirical evidence has determined that resistance or strength training produces a variety of positive health benefits including, but not limited to, increased bone density [2]; decreased risk of developing sarcopenia (age-related muscle loss) and severe osteoporosis [3]; protection

from injury [4]; reduction of low back pain [5]; improved insulin sensitivity in the elderly [6]; enhanced basal metabolic rate [7]; prevention of diabetes [8]; decreased quantity of visceral fat [9]; and better glucose metabolism, cholesterol profiles, and non-pathological blood pressure levels [10–12]. Further, resistance training also produces marked improvements in self-concept, self-efficacy, self-value, general health perceptions, physical appearance, and social functioning [13]. Taken together, these findings have significant implications for human health and healthcare policy.

Consequently, medical researchers have begun placing greater emphasis on the role of exercise in moderating mental health; both ancient and contemporary societies have noted that exercise “strengthens not only the body but also the mind” [14].

The relationship between resistance training and mental health has garnered increasing attention in recent years, highlighting its potential benefits for neuropsychological and behavioral functioning [15]. Resistance training, often associated with physical fitness and muscular strength, has been shown to exert significant positive effects on mental health outcomes, including reductions in anxiety and depression, improvements in self-esteem, and enhanced emotional regulation [16–18]. These psychological benefits are thought to arise from both biological mechanisms, such as the release of endorphins and neurotrophic factors [19], and psychosocial factors [20], including improved self-efficacy and social interaction through group training environments [21].

Research indicates that regular participation in resistance training can lead to notable improvements in mental health indicators. For instance, a systematic review revealed that resistance training is linked to anxiolytic and antidepressant effects, particularly among populations experiencing high levels of stress or mental health challenges [22]. Furthermore, studies have demonstrated that structured resistance training programs can significantly enhance psychological well-being, as evidenced by improved scores on mental health assessments following intervention periods. Moreover, the impact of resistance training extends beyond immediate psychological benefits; it also fosters long-term changes in self-perception and confidence [23]. Enhanced physical strength often translates into improved self-esteem and a more positive body image, which are crucial for overall mental health. This interplay between physical activity and mental well-being underscores the importance of incorporating resistance training into holistic health strategies aimed at improving both physical and psychological health outcomes [24].

The growing body of evidence suggests that resistance training serves as a powerful tool for enhancing mental health and behavioral functioning, making it a valuable component in interventions designed to address psychological distress and promote overall well-being. However, a comprehensive search of three prominent electronic databases revealed a decline in research activity on this topic, with the percentage of entries related to resistance training and mental health decreasing from 1.8% during the period of 1992–2000 to 1.2% (12,898 entries over 13 years) from 2001 to 2014. This underscores the importance of encouraging researchers to persist in their study on the relationship between resistance training and mental health outcomes, as the potential benefits highlighted by existing studies, such as reductions in anxiety and depression, improvements in self-esteem, and enhanced emotional regulation, warrant further investigation to fully understand and leverage this promising intervention for promoting mental health and well-being.

1.1 Definition and benefits of resistance training

Resistance training, or strength training as it is also known, is a type of physical activity that applies resistance or weights to your body or its limbs [25, 26]. Pertaining to the term of resistance training, this particular text will refrain from using the term “weight” when not absolutely necessary. Resistance training can refer to either anaerobic or aerobic exercise, but this text primarily focuses on the significantly more common category: anaerobic exercise. Some common benefits of resistance training include increased strength and muscle mass, improved mental and emotional well-being, and reduced risk of particular illnesses. Moreover, research shows that incorporating resistance training routines and activities into everyday life can also provide relief from certain mental health conditions such as depression and anxiety [17, 24, 27, 28], as it fosters both mental clarity and emotional stability [29, 30]. Given that well-being is a significant precursor to subjective mental health outcomes such as anxiety, life satisfaction, and generalized psychological distress, resistance training is considered to have a broad influence that may positively impact mental health [31].

Research on the impact of physical activity on neuropsychological and behavioral functioning has pointed out resistance training as a relevant anthropic behavior that can have positive outcomes on cognition and attention. The aim of this paper is to summarize the present knowledge about resistance training, as regards its definitions and protocols currently in use, and to review the most salient neuropsychological and behavioral outcomes and mechanisms through which such impacts on cognition and attention occur. Resistance training protocols vary in accordance with the type of load, intensity, duration, and training frequency. The range of resistance training protocols currently in use includes traditional and circuit resistance training, resistance training based on one’s own body weight, resistance training with elastic bands, and high-velocity resistance training [32]. Each experimental study made use of an intensively supervised training regime across the school semester, with a resistance training frequency ranging from one to five times per week. Training durations ranged from 6 to 22 weeks, and sessions lasting from 30 to 90 minutes were found. In addition, there is great variability in the number of training sessions conducted, which ranged from 6 to over 105 training sessions [33]. The varied implementation of training programs translated into differences in efficacy outcomes. Independent of the design specifics of the resistance training protocols, all of the studies reported significant positive outcomes of training on different variables measuring cognition and attention behavior [34].

2. Neuropsychological functioning

Several studies have investigated the impact of aerobic exercise on cognitive performance, with fewer focusing on resistance exercise [35]. Experimental resistance training programs have found evidence of positive changes in cognitive function, with studies involving young adults and older adults [36].

For instance, young adults who participated in resistance training showed improved cognitive performance, including increased simple reaction time and enhanced executive function tasks. Neuroimaging also revealed increased activation in the anterior cingulate gyrus, a region associated with attentional control [37].

Similar effects were found in older adults who participated in resistance training programs with walking as an active control [38]. However, further research is needed to understand the impact of resistance training on cognition and brain activation, as well as how program characteristics and participant attributes may influence these effects.

2.1 Cognitive function

Cognitive function involves the processes an individual uses to acquire knowledge [39]. Cognitive impairment may occur alongside various neurological diseases, affecting areas such as attention, memory, language, perception, and social skills, as well as sensations like vision, hearing, taste, touch, and smell [40].

Dementia is a significant neurodegenerative disease characterized by cognitive decline, which has severe implications for daily living. Cognitive function can be informally understood as mental acuity or mental sharpness, and impairment may involve some loss of these faculties. Psychosocial and biological mechanisms, including neurotransmitters and neural remodeling, may link resistance training with improved cognitive function [41]. Exercise, including resistance training, is posited to positively affect cognitive function by increasing cerebral blood flow and brain-derived neurotrophic factor (BDNF) levels, potentially leading to improved executive functioning [42]. However, questions remain about the specific types of cognitive function most affected by resistance training and whether the effects are contingent on study design/setting, participant population, or resistance training paradigm.

The impact of resistance training intervention could also be moderated by control/comparison groups or time between interventions and cognitive assessment, and cognitive control measures may confound results and should be investigated further. Thus, given the uncertainty around exercise timing and paradigm effects, resistance training recommendations for improved cognitive function cannot be concretely made. An extensive overview of the design of included studies and the potential for warranted meta-analysis is presented [34].

2.2 Memory and learning

Memory and learning are considered neuropsychological functions that have been explored in relation to the impact of resistance training (RT) [43]. Memory has been defined as the mental faculty of retaining and recalling past experiences. Memory allows for previously perceived ideas and experiences to be retained over periods ranging from seconds to years [44]. The vast capabilities of memory rely on a complex neural infrastructure of multiple brain networks that are tasked with different forms of memory. Research suggests differences between short-term memory (i.e., seconds to minutes) and long-term memory (i.e., days to years). Learning, on the other hand, is defined as the act of acquiring knowledge [45]. Specific knowledge gained *via* learning can enable both prospective and retrospective reasoning. Knowledge is usually tied to specific situational characteristics (e.g., time they occurred) and consolidated into memory.

Using a 12-week randomized controlled resistance training (RT) intervention in healthy late middle-aged adults, cognitive task performance on Verbal Delayed Free Recall was significantly improved post-intervention in the RT group compared to the control group, [46]. These findings are indicative of an RT-related cognitive advantage for memory. Importantly, this change in memory performance was paralleled by a reduction in stress hormones and catecholamines after the intervention [47].

Enhanced memory retention is congruent with findings from studies of delayed recall performance measures following aerobic exercise [48]. However, verbal list-learning measures that tax new acquisition or knowledge of a list of words were not improved by RT. This lack of change in learning is congruent with mixed findings regarding changes in new acquisition performance post-exercise (e.g., improved and no-change verbal learning tasks) [49].

2.3 Executive functions

Several studies have indicated a positive correlation between resistance training and improved cognitive functions such as reaction times on the Stroop Test and Digit Span tasks. However, it is important to note that most of these studies did not utilize a comprehensive neuropsychological battery to assess a wide range of cognitive functions that impact daily functioning [38, 50, 51].

Executive functions, also referred to as higher-level cognitive functions, are proposed in a two-systems model. The decision-making processes in the context of risk are dependent on an understanding of the probabilities of feedback, which has been found to significantly predict performance changes across experimental sessions. The successful implementation of these plans requires the prioritization of the allocation of attentional resources and free time. These attentional control processes also interact with higher-level cognitive functions such as allometric planning and controlling the temporal organization of different epochs [52]. Additionally, procedures of attentional shifting and focusing can be integrated into these planning and controlling activities [53, 54].

3. Behavioral functioning

The influence of resistance training on behavioral functioning has typically been evaluated in regard to mood, anxiety, and the stress response, which includes stress and the stress recovery cycle, as well as sleep. A number of programmatic studies have been undertaken to specifically investigate these behavioral factors in older adults [55].

The majority of initial investigations on the impact of resistance training on mood and anxiety states were conducted by examining older adult populations. These investigations, employing tandem experimental designs, uniformly reported acute resistance training sessions resulted in reductions in negative mood states (feeling tense, nervous, anxious) and increases in positive mood states (feeling energetic, vigorous, active) [56]. As a result, investigations were subsequently conducted focusing on the chronic influence of resistance training on mood states over an extended time period [57]. These studies, again employing tandem experimental designs, reported chronic resistance training (up to 6 months) in older adults was associated with significant reductions in negative mood states and significant increases in positive mood states [58].

In contrast, non-exercise control groups showed significant increases in negative mood states and significant decreases in positive mood states. Given these results, it may be concluded that resistance training can be an effective exercise modality for improving mood states in older adults [17].

The influence of resistance training on anxiety was first investigated in older adult populations with similar findings to mood states. These studies found that a chronic resistance training intervention (up to 16 weeks) resulted in significant reductions in

state and trait anxiety in older women. In contrast, control groups showed no change or an increase in anxiety scores. Importantly, it has also been reported that similar reductions in anxiety scores were achieved using only one resistance training session per week [59].

More recent research has shown that short-term resistance training in depressed older women led to significant reductions in state and trait anxiety levels after only six weeks of training. Therefore, it may be concluded that resistance training is an effective exercise modality for reducing anxiety levels in older adults [60]. However, to date, only a limited number of studies have examined the impact of resistance training extensively across these behavioral functions in middle-aged and older adult populations [61].

3.1 Mood and anxiety

The number of studies examining the effects of resistance training on emotional expression is more limited in contrast to aerobic exercise. The effects of resistance training on mood states or perception of emotional stimuli have been investigated in a group of participants with an explicit focus on weight loss [55].

Short-term resistance training (within one week) produced significant enhancements in mood states related to the state of calmness and anxiety. Enhanced emotional stability (less negative affect) was indirectly supported by findings relating to the perception of emotional stimuli, with resistance training resulting in greater N2 amplitude post-exercise to angry faces in the group with a weekly resistance training schedule [62]. These results are consistent with prior research showing that resistance training can lead to reductions in state anxiety [59]. Further, similar to the present results, in a longitudinal study, Mulligan et al. also observed overall emotional improvements when comparing before exercise and after exercise [63].

The alteration of mood states and emotion regulation that occurs following resistance training is particularly intriguing from a behavioral standpoint, as it provides a potential mechanism to assist weight control efforts, as those who regulate their emotions with food may ultimately become fatter [7]. While effect sizes and significance levels differed between the weight loss program groups, both groups improved emotional functioning in similar ways [64].

Future research should examine if this expectation of mood enhancement would result in a differential affective outcome and adherence to resistance training programs. This is particularly important as resistance training is often combined with aerobic exercise and viewed as supplemental in more general exercise prescriptions [65].

In this case, relative differences in perceived mood enhancement between resistance and aerobic exercise conditions may have clinical relevance for exercise prescription efforts targeting emotional well-being [66].

3.2 Stress response

In human health, homeostasis refers to the dynamic balance of physical, hormonal, psychological, and behavioral systems such that they create a stable condition for functioning optimally. This is efficiently controlled by integrating systems capable of receiving, processing, and providing information on different stimuli resulting from both the internal and external environments. The stress response is a consequence of any stimuli that change the body's homeostasis or equilibrium, called

homeostatic stressors. Out of the stressors that have been studied, physical stressors, or mobilizing stressors, have drawn particular interest [67].

In this regard, it has been documented that strenuous physical exercise can activate identical physiological and neuroendocrine mechanisms to other types of stressors. There is some research on the effects of moderate to high dosage and intensity exercise on the neuroendocrine and behavioral stress response. These studies have focused on examining homeostatic responses to a second challenge stressor after exposure to exercise, specifically behavioral tasks to evaluate anxiety-like behavior, such as elevated plus maze (EPM) and open field (OF) tasks, and on sex and age factors [68].

In general, moderate resistance training has been shown to reduce the hypothalamic-pituitary-adrenal (HPA) axis response to behavioral stressors. Training precondition induces greater circadian fluctuation and a greater peak of the ACTH response to stress in older group females than younger ones [69].

3.3 Sleep quality

It is feasible that resistance training has the potential to affect sleep. Prior community health trials have found a significant correlation between participation in moderate-intensity resistance training and increased self-reported nighttime sleep duration. In a laboratory study conducted by Johnson et al., individuals who participated in high-intensity resistance training during a portion of the nocturnal sleep episode exhibited a sleep onset latency and wake time after sleep onset that was significantly better than individuals who engaged in no activity [70].

Objective sleep quality metrics such as those derived from actigraphy and polysomnography are important to complement self-reported sleep quality metrics. Further, there is a need to examine the potential impact of resistance training on sleep quality in various populations. The resistance training intervention was positively associated with improvements in sleep quality, as determined by self-reported and actigraphy-derived metrics, across analysis sets [71].

Research has demonstrated that sleep deprivation has significant negative effects on both psychological and physiological function and can severely impact performance during exercise, potentially leading to injury. Many experts believe that improvements in health-related quality of life resulting from resistance training are closely linked to enhancements in sleep quality [72].

4. Mechanisms of action

There is a well-established link between cognitive performance and physical exercise. Much less research has been performed regarding physical exercise and plasticity and hence cognition, emotion, and behavior. In addition to the well-recognized peripheral benefits of resistance training such as insulin sensitivity, glucose uptake, and muscle mass, resistance training induces adaptations at the level of peripheral organs, such as the muscles, skeletal system, heart, and respiratory and endocrine glands [73].

It is less well studied how resistance training induces central, or brain, effects on cognition, emotion, and behavior. At the level of the central nervous system, resistance training creates adaptations at the level of function involving cognition and affect, at the level of connectivity involving neural networks, and at the level of structure involving neurogenesis, the expression of neurotrophic factors is enhanced

during several days after resistance training, supporting the homeostatic plasticity of these molecules by counteracting signaling downregulation. Neuroplasticity, neurotrophic factors, inflammation, and oxidative stress are evident mechanisms through which resistance may create beneficial effects on cognition and behavior [51, 74, 75].

Resistance training has been related to increased neurogenesis and synaptic remodeling in the dentate gyrus of the hippocampus and to enhanced arousal caused by catecholamines. Peripheral muscle, adipose tissue, fat, and gut tissues send the brain signals through hormonal pathways. These pathways mainly comprise IGF-1, BDNF, Visfatin, and other neuroactive hormones such as catecholamines and serotonin. Generally, large-scale resistance training interventions reduce cerebrovascular risk, promoting synaptic repair, regeneration, and improvement of cognitive function [76].

4.1 Neuroplasticity

Neuroplasticity is the brain's ability to reorganize and adapt in response to internal and external influences, and it occurs continuously throughout life. Resistance training could impact the neuroplastic ability of both the central and peripheral nervous systems (PNS) [77].

The potential influences of resistance training on the structure and function of afferent sensory pathways, as well as efferent motor pathways, are discussed. Furthermore, changes in the brain, spinal cord, and peripheral nerves that could underlie neuropsychological and behavioral alterations are characterized [78].

Neuroplastic biochemical changes, such as the accumulation of neurotrophins BDNF and NGF, have been observed after resistance training. These changes may contribute to the long-term adaptations and neuroplastic alterations that impact neuropsychological and behavioral function resulting from resistance training. Gaining insights from the referenced studies would be valuable in understanding the effects of resistance training on neuroplasticity and behavioral function [78].

4.2 Neurotrophic factors

With respect to the proposed neuroplasticity mechanisms, growth factors were examined to investigate their potential mediating involvement in the putative beneficial effects of the resistance training intervention on the brain [75]. Neurotrophins are a heterogeneous and pleiotropic group of growth factors that exert their biological functions mainly through the activation of specific molecularly distinct receptors. These proteins are widely distributed within the brain at concentrations higher than those found in the periphery and are involved in a wide number of biological functions, such as the growth and differentiation of new neurons and synapses, the development of axonal and dendritic growth, synaptic plasticity, long-term potentiation (LTP) and long-term depression (LTD), neuronal survival, and the regulation of neurotransmitter systems [79].

The neurotrophins brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4 (NT-4) are products of the same gene family, while neurotrophin-1 (NGF) and neurotrophin-2 (NT-2) are two paralogous genes whose products participate in a non-redundant manner in retinal and sympathetic neuron development, respectively. Neurotrophins also exert important actions in the regulation of adult neurogenesis, a phenomenon involving the generation of new neurons throughout life, which occurs under homeostatic conditions and in response to several endogenous stimuli, such as physical exercise [80].

The exercise-induced production of neurotrophins could ultimately promote the preservation of cognitive functions and stimulate neurogenesis in the dentate gyrus of the hippocampus, countering both age-related hippocampal atrophy and peritraumatic cognitive decline, even following the traumatic event in the case of operant conditions. These effects would counteract the negative consequences of physical activity that can occur in extreme life situations and would warrant the extensive use of physical exercise to prevent and treat physical and mental disabilities in the elderly and the pathological population, respectively [81].

4.3 Inflammation and oxidative stress

According to research, resistance training has been shown to reduce inflammatory activity in the elderly, leading to a decrease in levels of the inflammatory cytokines C-reactive protein and interleukin-6. In addition, studies have demonstrated that failure to effectively resolve acute inflammation can lead to prolonged tissue inflammation and chronic diseases, highlighting the importance of understanding the immune system and non-immune cells in the inflammatory response. This is further supported by the involvement of phosphatases and inhibitor proteins targeted to nuclear factor kappa B, Jun N-terminal kinases, p38 mitogen-activated protein kinase, and signal transducer and activator of transcription 3 in controlling the inflammatory signaling network at the molecular level). Overall, the complex and interlinked signaling pathways involved in the inflammatory response indicate the potential of resistance training to mitigate low-grade chronic inflammation in the elderly [82–84].

Chronic low-grade inflammation, also known as “inflammaging,” is a crucial aspect of aging and is characterized by a continuous increase in serum inflammatory mediators. The causes of inflammation in older individuals are not fully understood, but it is believed that a combination of internal and external factors is involved. These pro-inflammatory mediators associated with aging include overtly infectious agents, damage-associated molecular patterns, senescence-associated secretory phenotype, increased levels of adipokines, and changes in the microbiome. The elderly also experience a decline in immune system function, known as immunosenescence, which reduces their ability to effectively respond to infections [85].

As a result, the elderly are more susceptible to infectious diseases and have higher morbidity and mortality. In addition, inflammaging can exacerbate tissue deregulation processes and raise the risk of developing chronic age-related diseases. For instance, the ratio of pro-inflammatory mediators to anti-inflammatory cytokines rises in the elderly. Furthermore, the elevated levels of the inflammatory cytokine low-density lipoprotein-6 in the elderly are associated with a greater risk of developing Alzheimer’s disease [85, 86].

5. Types of resistance training

This section discusses different types of resistance training by examining various modalities for conducting resistance training. Traditional weightlifting is identified as a common form of resistance training, while bodyweight exercises such as push-ups and squats are also considered as a form of resistance training using one’s own body weight. Additionally, resistance bands are examined as a portable and cost-effective option for resistance training, offering adjustable levels of resistance [87, 88].

Resistance training can be divided into many types of modalities [89]. One of the most common forms of resistance training is traditional weightlifting, which can be done at home or in the gym. Weightlifting can have movements performed with free weights (dumbbells or barbells), machine weights, or a combination of both. With these weights, people can progressively overload their muscles, resulting in improved muscle strength and hypertrophy. A common perceived limitation of weightlifting is the increased risk of injury compared to some alternative forms of resistance training. However, if done correctly with enough recovery between training sessions, weightlifting safety levels are as high as other types of exercise [87].

Another type of resistance training is bodyweight exercises, encompassing many movements (e.g., push-ups and squats) that utilize one's own body weight as resistance [90]. Bodyweight exercises are often seen as a direct alternative to weightlifting, where resistance is harder to manipulate and progressively overload. Instead, these exercises focus on manipulating exercise parameters, including the total number of repetitions, sets, rest intervals, and number of sessions per week [91]. Bodyweight exercise training has been shown to improve muscle strength similarly to traditional weightlifting. These exercises can also be done anywhere, such as at home or outdoors, requiring minimal equipment and space [92].

5.1 Traditional weightlifting

This subsection provides an overview and analysis of resistance training carried out through traditional weights. These include barbells, dumbbells and weight disks that are used to perform lifts targeting different muscle groups. Free weights can be used for both compound and isolation lifts. Most traditional weightlifting programs include foundational lifts such as the deadlift, squats, bench press, bent-over rows and shoulder presses essential prerequisites for effective traditional weightlifting are adequate knowledge of the lifts and how to execute them safely access to weights, racks and benches further requirements are coaching in the beginning stages and an adequate lifting setup because barbell training is equipment and setting dependent, training groups with at least two participants are recommended for safety reasons with one acting as a “spotter” in addition to guidance and coaching from an instructor or knowledgeable peer attention to all of these factors is crucial, particularly for beginners, since traditional weightlifting can be considered a potent training intervention but also a dangerous one if performed incorrectly Importantly, the Fluency Principle states that complex tasks must be built gradually to be executed fluently, preferably with as few hurdles as possible in early stages [93].

Mechanically, traditional weightlifting is a high-intensity activity, with a demand for near-maximal exertion in multiple muscle groups, even with warm-ups included. Participants in this kind of training are advised to maintain other high-impact activities at a low-level intensity, or avoid such activities altogether on weightlifting days [94].

Metabolically, traditional weightlifting is characterized as a glycolytic/lactic system activity promoting neurological adaptations through mechanisms such as increased myogenic regulatory factors (MRFs), shortened muscle contraction times, and greater excitability of motor neurons. Consequently, a potential advantage of traditional weightlifting, at least for untrained populations, is immediate gains in strength. Such gains are advantageous for other activities and might aid in participation in those activities [95].

5.2 Bodyweight exercises

In the past, when it came to strength training, many people conjured up an image of a steel gym with dramatic flourishes of effort—convulsions of muscle-bound men tossing dumbbells around as if they were oranges. It is only in humanity's current chapter of unrest that many are beginning to appreciate that their own bodies could be used as the ultimate gym and be much more accessible than commercial weight exercise equipment. Bodyweight exercises, such as push-ups, squats, lunges, and planks, rely on using one's own mass to achieve the desired resistance instead of traditional weights. Moreover, body mass resistance exercises can enhance muscular strength and cardiovascular fitness through the activation of multiple muscle groups acting on major joints, promoting muscle protein synthesis) [37, 96].

There is more than one way to perform bodyweight exercises. These can be done by simply using a chair or a wall to create leverage or increase resistance, which makes this mode of exercise accessible, adaptable, and appealing to a wide audience [97].

5.3 Resistance bands

Resistance bands are an alternative to free weights or weight machines in resistance training now recognized by the American College of Sports Medicine (ACSM). Resistance band training is increasingly being incorporated into school and community-based exercise, which adopts an active lifestyle focus for children and adolescents. Although some resistance bands are commercially available, courses viewed on the web with recommendations/protocols on how to perform resistance band training exercises can assist with practical implementation [98].

Several resources are available online under the auspices of national organizations that target elements of resistance training and training in general including balance, muscular strength and endurance, and flexibility. Some additional considerations/notes that can assist with planning sessions include the following [96].

Training sessions can be conducted in a group format (e.g., through circuit style) or an individual approach. Youth perform large amounts of unstructured play consisting of mostly low-intensity activities over the day, implying resistance training sessions need to be kept highly active with minimal rest periods. Typically, a session should include five to ten minutes of warm-up (e.g., jogging and dynamic movements) that may add a few minutes of stretching. Each exercise should be performed for 10–15 repetitions followed by a one to two-minute rest before proceeding to the next exercise station [99].

Currently, there are bands with different resistance levels (ranging from very light to extra heavy), but only a small number of band exercises have been confirmed to be beneficial for young people. It is possible that the tension of the bands may need to be adjusted as an individual grows older and develops. In order to maximize the effectiveness, health, fitness, and performance benefits, it is important to incorporate a focus on wholesome nutrition along with strength training in the community [100].

6. Population-specific considerations

Elders, or older adults, comprise various age groups. As one cohort ages, different controllable physiological changes and uncontrollable functions occur due to the influence of factors such as genetics and lifestyle. To better understand these

occurrences, aging can generally be divided into population cohorts. Following age demographic data approximated by the United Nations, those aged 60–69 are considered early elderly (sub-cohort), 70–79 are middle seniors, and those aged 80 and above are regarded as oldest-old. Ultimately, as early elders grow older and progress into the elderly cohort and later become middle seniors, functional capacities whose conditions can be trained also change [101].

Age-appropriate resistance training (RT) can be used as a preventive measure before certain conditions. For instance, a study by Jones et al. states that despite declines in muscle mass and weaknesses, incidental RT can become a viable health promotion effort within this population under carefully developed exercise programs. Still, according to the guidelines provided by the American College of Sports Medicine, certain technical tips/environmental modifications must be followed so that divers can perform aerobic exercise safely and effectively within water environments. Many conditions occur during the early elderly years that can be intervened with task-specific RT. Individuals with cognitive impairments due to dementia and low cognitive function scores are highly susceptible to deterioration in several facets of functioning and flourishing with a low quality of life but can benefit from RT [102].

6.1 Children and adolescents

Incorporating resistance training into the lives of children and adolescents requires careful consideration of their physical and developmental needs. It is important to ensure that proper techniques and safety measures are in place to prevent injury and promote healthy growth. Additionally, understanding the specific benefits of resistance training for young individuals can help educators and parents make informed decisions about its inclusion in their physical activity routines. Therefore, it is essential to insert references in the text to support the recommendations and guidelines for incorporating resistance training into the lives of children and adolescents [103–105].

Historically, there has been a reluctance for strength training to gain acceptance among younger populations, based mainly on the long-debated premise that resistance training will stunt growth, injure, or harm. Several studies have now put the myth of stunted growth to rest. Participating in resistance training with sound supervision improves growth patterns. A great benefit of resistance training in young populations includes an increase in strength and muscle mass (hypertrophy), a decrease in body fat percentage, improved self-esteem and confidence, improved posture and body mechanics, enhanced general athletic performance and increased safety in sport current data suggests that resistance training is both beneficial and safe for healthy, developing children and adolescents when properly monitored by trained fitness professionals. Health professionals should promote weight training to children as a good supplement to enhance general health. Comprehending the developmental implications of resistance training for school-aged children is germane to fitness professionals, parents and the children themselves children cannot be just scaled down adults, and strength-training programs for youths should be adjusted with biological development in mind [106, 107].

Contemporary conditioning protocols have enlarged the spectrum of training regimens available to children. Among these, resistance training is becoming progressively popular. A recent survey of high-school strength-training practices across U.S. states indicates that 60% of campuses have a weight-training program, and 90% of all adolescent athletes engage in formal or informal resistance training. Nonetheless,

safety remains a dominant theme in youth resistance training, and many health care professionals and parent constituencies are wary of allowing children to lift weights. Historically, the premise of defective musculoskeletal growth, that is, growth plate injury, in budding weightlifters has served as the basis for condemning children to show a sedentary lifestyle and eschew restrictive school PE programs. Moreover, gradual conditioning is warranted, because increases in muscular mass, strength, and performance indices are directly linked to physiological adaptation rather than simply replication of young adult training techniques [108].

6.2 Older adults

Fragmentation of the normal progression of cognitive changes with age may limit the consequences for daily life and allow for the continued engagement in desirable, cognitively stimulating activities (e.g., socialization, travel, and work). Relative thresholds of cognitive resilience may vary based on stabilizing factors (e.g., environmental support) or due to a greater availability of compensatory resources (e.g., education) in some older adults relative to others. Therefore, some older individuals may be capable of high levels of cognitive engagement and performance that far exceed those typical of their age or cohort. As with neuroplasticity in young children, there may be a point at which the capacity for cognitive resilience is exhausted, with marked decline in cognitive activity and performance [109].

Resistance training can be a critically important adjunct to aerobic exercise for some older adults. Movement impairment in the elderly is commonly linked to progressive muscle weakness, which tends to accelerate after 50 years of age. Muscle strength declines approximately 15% between the ages of 50 and 70, and after that, a loss of 20–35% occurs each decade. Weakness and losses in the functional independence that accompanies it represent major risk factors for residential placement and death. In developed countries, such declines are associated with significant declines in both physical and cognitive health. Resistance training is the most effective strategy for promoting muscle strength in younger and older adults. The benefits of resistance training for promoting and maintaining functional independence in older adults are widely recognized, yet participation rates remain low. Older adults view resistance training as intimidating or unsafe and may need additional education and outreach regarding its safety and effectiveness, [102, 110–112].

6.3 Clinical populations

Resistance training interventions have shown to be adaptable and have been applied to diverse clinical populations). Evidence supports the efficacy of resistance training in improving physical fitness and health in people with stroke cardiovascular disease multiple sclerosis chronic obstructive pulmonary disease (Parkinson's disease and mental health conditions including post-traumatic stress disorder (PTSD) and anxiety. Additionally, resistance training has been studied in clinical conditions associated with cognitive impairment, such as stroke Parkinson's disease and chronic obstructive pulmonary disease and has potential therapeutic implications for physical and neuropsychological functioning [113, 114].

References have shown the potential of resistance training to improve health, fitness, and cognition in different clinical populations. Moreover, resistance training interventions can be tailored to meet the needs of individual clients and their care teams, especially when client safety is a top priority. For instance, if there are safety

concerns due to concurrent health conditions, resistance training can be modified by avoiding free weights and isometric contractions (e.g., using a machine-based training regime) or by incorporating only aerobic training [115].

7. Practical applications

Future work is warranted to advance knowledge on best practices for RT prescriptions, including frequency, intensity, volume, duration, mode, and exercise progression for maximal neuropsychological and behavioral changes. From an adherence perspective, research employing a mixed methodological quadruple paradigm (combining behavioral, neurobiological, and environmental aspects) should consider a broader inclusion of those factors that could enhance compliance, such as social support, motivation, enjoyment, self-efficacy, perceived challenges, and work-life balance.

In addition, more work is needed to assess the social efficacy of RT partnerships with other outside organizations. Finally, preliminary evidence suggests that RT may be a safe activity for many clinical populations. However, to minimize adverse and contraindicating events, exercise regimes should be completed under professional supervision until safety and capability are established. At all times, caution should be emphasized, particularly during non-structured protocol elements (e.g., home-based exercises).

7.1 Exercise prescription

Exercise prescription involves the integration of resistance training into current exercise regimens and other forms of physical activity. These practical recommendations do not focus on the scientific or pedagogical rationale for the considerations listed but are discussed here simply as suggestions when designing resistance training programs to fit a client's needs and goals.

As in any exercise regimen, safety is the primary concern when designing resistance training programs. Clients must be questioned about any cardiovascular, orthopedic, metabolic, or neuromuscular conditions that could, under provided limits, contraindicate participation in the program. Indications of uncontrolled hypertension, aneurysms, arrhythmia, diabetes, history of stroke, pain or discomfort in the neck, jaw, arms or other areas, and a host of other concerns, warrant medical clearance before starting an exercise program. Clients should also be carefully monitored for any symptoms of over-exertion. Orthopedic concerns, including osteopenia or osteoporosis, arthritis, prior shoulder or knee injuries, nerve entrapment, and differences in limb length, should also be considered before starting any exercise regimen. For clients who are indicated to participate in resistance training programs, safety should be the second-biggest priority.

7.2 Adherence strategies

Many strategies may be applied to enhance adherence to resistance training interventions. With respect to the content of the program, inclusion of progressive “challenges” appears to be effective (e.g., increase in volume or intensity, inclusion of complexity or instability). Challenges can also be achieved by modifying external factors (e.g., environment and equipment). Adoption of such dynamic programming

components is consistent with the guidelines for exercise optimization. Moreover, variation of the resistance training program can provide psychological benefits (e.g., alleviate boredom by enhancing novelty), which would be especially important for older participants being often more conservative in terms of engaging in changes. Broadly, there are three levels of motivational factors recognized to predict engagement in exercise programs. Firstly, there are dispositional or personality factors, with two leading ones being conscientiousness and self-efficacy. The former indicates a tendency to persevere with regard to on-going tasks, and the latter refers to expectations about one's capabilities with the accomplishment of the desired tasks. Second level comprises behavioral history, implying that prior participation in similar activities is important for adherence. Third level encompasses environmentally sensitive or modifiable factors, with education and support systems being the leading ones [24, 28].

7.3 Safety considerations

Research has shown that resistance training (RT), also known as strength training or exercise training, has numerous positive health benefits, such as improved mood, enhanced cognitive function, and reduced anxiety. Many people engage in RT under the guidance of a qualified individual in a safe environment in order to reap these health benefits. However, for certain populations, such as individuals with intellectual disabilities (ID), safety concerns may limit their access to these benefits. It is essential to recognize that ensuring safety and minimizing risks does not have to mean sacrificing the potential positive effects of exercise [29], starting with ensuring proper form and technique is used in all situations and including education on the exercise, proper supervision, individual progression, and adaptation or termination of exercise in the presence of contraindications to resistance training (RT).

8. Future directions

As the evidence base regarding the benefits of resistance training on neuropsychological and behavioral functioning continues to grow, several areas warrant future investigation. What is the cause of the variability in effects? In view of the fact that not all resistance training studies report beneficial changes, what factors underpin the different responses to training? Some obvious variables to consider are type of implement (i.e., free weights or machines), resistance load repetitions and sets, functional vs. structured exercises training volume, and rest periods. However, there are wider causes of variation that merit consideration, including how the resistance training is implemented within the context of the school day, the degree to which resistance training is seen as a health initiative versus a means of improving academic performance, the format and content of interventions and participant factors such as sex, motivation, and expectations. A closer examination of how these factors impact academic outcome would greatly enhance our understanding of the mechanisms by which resistance training impacts functioning.

9. Conclusion

Resistance training has been found to help reduce neurocognitive deficits in different populations). Research supports the idea that resistance training has

a positive impact on neuropsychological functioning. Although there is limited research into the effects of resistance training on neuropsychological functioning, findings suggest that resistance training can help improve neurocognitive, behavioral, and academic performance, especially in adolescents and military personnel. Resistance training can provide protective effects on the brain and behavioral performance after traumatic brain injuries (TBI), including blast TBI. The biomechanical load of the exercise, frequency, and intensity are factors that can impact the outcomes of the neuroprotective effects of resistance training. Importantly, studies show that both moderate and vigorous exercise can improve mood and cognition in children.

There is little research on the neurophysiological responses of resistance training in healthy children and adolescents. Some studies suggest that an acute bout of resistance training can improve attention and cognitive function and also lead to favorable physiological changes. In general, moderate resistance training can yield benefits in both physical and psychological health areas for children and adolescents.

Studies have found that low-to-moderate intensity (60–80% 1RM) exercise lasting between 30 and 90 minutes can yield the best benefits in behavioral performance. However, individual results may vary depending on factors such as age, mental health status, physical health, or external environment.

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Conflict of interest

The authors declare no conflict of interest.

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Section 3

Resistance Training in Special
Populations: Therapeutic
Approaches for Pulmonary
and Cancer Patients

Resistance Exercise as a Therapeutic Benefit for Patients with Pulmonary Arterial Hypertension: Advances and Perspectives

Leôncio Lopes Soares and Antônio José Natali

Abstract

Pulmonary hypertension (PH) is a progressive and severe disease characterized by increased pulmonary arterial pressure and vascular resistance, leading to heart failure. Although physical exercise was historically contraindicated for patients with PH, recent studies have demonstrated that appropriate physical exercise training can improve functional capacity, hemodynamics, and quality of life of patients with the PH subtypes: pulmonary arterial hypertension (PAH); and pulmonary hypertension due to chronic thromboembolic disease (CTEPH). Thus, current guidelines recommend the inclusion of physical exercise in the treatment of PAH and CTEPH. PH induces vascular and hemodynamic changes that overload the ventricles, followed by systemic inflammation, muscle dysfunction, and exercise intolerance. In this context, it is crucial to understand these mechanisms to develop more effective treatments. Studies suggest that low to moderate-intensity resistance training can improve cardiac function and exercise tolerance in patients with PAH, in addition to preventing renal damage and improving bone properties in animal models. However, intense training requires caution due to the potential to increase blood pressure and the risk of adverse events, highlighting the importance of professional supervision to tailor exercise to the individual condition. This chapter explores advances in resistance training as a therapeutic benefit for PAH, reviewing evidence, discussing implementation practices, and presenting perspectives.

Keywords: pulmonary arterial hypertension, cardiac function, inflammation, vascular remodeling, pathological hypertrophy, physical exertion intolerance, musculoskeletal dysfunction

1. Introduction

Pulmonary hypertension (PH) is a rapidly progressive disease that affects more than 25 million individuals worldwide and is often fatal [1]. PH was previously

classified as primary or secondary, based on the absence or presence of an identified causative agent or risk factors [2]. Currently, a clinical classification is established to individualize different categories of PH (**Figure 1**) according to pathological findings, hemodynamic characteristics, and similar treatments. The classification includes the five main etiologies: pulmonary arterial hypertension (PAH); left heart diseases; respiratory diseases and/or hypoxia; chronic thromboembolic disease (CTEPH); and unclear multifactorial mechanisms [3].

Defined as pulmonary vasculopathy, PH is characterized by a resting mean pulmonary arterial pressure (mPAP) above 25 mmHg [3]. It is caused by restricted blood flow in the pulmonary arterial circulation, a combination of endothelial dysfunction, and increased contractility of the small pulmonary arteries. Such condition occurs due to the proliferation and remodeling of endothelial smooth muscle cells, in situ thrombosis, resistance to apoptosis, inflammation, and fibrosis mediated by a dramatic remodeling of the extracellular matrix of the pulmonary arteries and arterioles, leading to increased pulmonary vascular resistance (PVR) and, ultimately, heart failure [2, 3].

Historically, there were concerns that physical activity could exacerbate symptoms in patients with PH. Although physical exercise is still not recommended for patients with PH of certain etiologies, it has emerged as a promising therapeutic approach for managing PAH and inoperable CTEPH through the maintenance of cardiac function.

Group 1 (PAH)
Mechanism: Vascular remodeling of pulmonary arteries Examples: Idiopathic, medications, HIV, connective tissue disorders
Group 2 (Left heart diseases)
Mechanism: Causing backup of blood flow Examples: Left heart failure, aortic valve disease, mitral valve disease
Group 3 (Chronic lung diseases causing hypoxia)
Mechanism: Impaired gas exchange leading to decreased oxygen availability. Examples: COPD, ILD, sleep apnea
Group 4 (CTEPH)
Mechanism: Chronic thromboembolic obstruction of pulmonary arteries leading to increased pulmonary vascular resistance. Examples: Pulmonary embolism
Group 5 (Unclear and Multifactorial)
Mechanism: Diverse pathophysiological processes leading to PH, including inflammatory, hematologic, and systemic factors. Examples: Sarcoidosis, chronic hemolytic anemia, thyroid disorders, sickle cell anemia, splenectomy, mediastinal tumors, chronic renal failure

Figure 1. World Health Organization classification of PH: chronic obstructive pulmonary disease (COPD); chronic thromboembolic pulmonary hypertension (CTEPH); human immunodeficiency virus (HIV); interstitial lung disease (ILD); pulmonary arterial hypertension (PAH).

There is recent evidence that exercise-based rehabilitation can significantly improve physical capacity, as evidenced by improvements in metrics such as the 6-minute walk test distance and peak oxygen consumption [4–6]. These benefits are attributed to enhanced muscle function, better oxygen utilization, and increased cardiovascular efficiency. Additionally, it has been shown that physical training has favorable effects on right ventricular function and pulmonary hemodynamics, suggesting a potential role in modifying the disease progression [2, 3].

Current guidelines, such as those from the European Society of Cardiology and the European Respiratory Society, now include recommendations for incorporating physical training in the management of PAH and CTEPH, highlighting its efficacy and safety. These recommendations are based on a growing body of evidence from randomized controlled trials and observational studies, which collectively demonstrate that physical training is a vital component of comprehensive care for these patients [2, 3].

Although physical exercise has been recognized as a promising tool for the treatment of PAH, guideline recommendations are largely based on research involving patients with PAH undergoing aerobic physical training [7–13], since the number of studies on resistance exercise training (RT) and on combined exercise (i.e., Aerobic plus RT) is limited. Despite evidence suggesting the potential benefits of RT, access to specialized rehabilitation programs that include this type of exercise remains restricted.

This chapter will explore current advances in RT as a therapeutic intervention for PAH, providing an overview of the evidence supporting its use, discussing practical considerations for implementation, and outlining future perspectives in this evolving field.

2. Methodology

2.1 Search strategy

The methodology for this chapter was based on a search and review strategy, focusing on studies that investigated the impact of RT on patients with PH. A comprehensive literature search was conducted across three electronic databases (i.e., PubMed, Scopus, and ScienceDirect), using the descriptors “pulmonary hypertension” or “pulmonary arterial hypertension” and “resistance training” or “strength training.” Studies that evaluated RT alone or combined with aerobic training in PH patients or animal models were considered. We applied inclusion criteria to select studies that focused on exercise interventions targeting improvements in cardio-pulmonary function, skeletal muscle adaptations, and overall quality of life in PH. Randomized controlled trials, observational studies, and experimental animal research were included, while case reports, reviews, and studies not directly related to exercise intervention in PH were excluded. A flowchart (**Figure 2**) was used to outline the study selection process, starting with the initial identification of articles, followed by screening for relevance, eligibility assessment based on predefined criteria, and final inclusion in the review. The extracted data were systematically analyzed and synthesized to evaluate the therapeutic role of RT in managing PH.

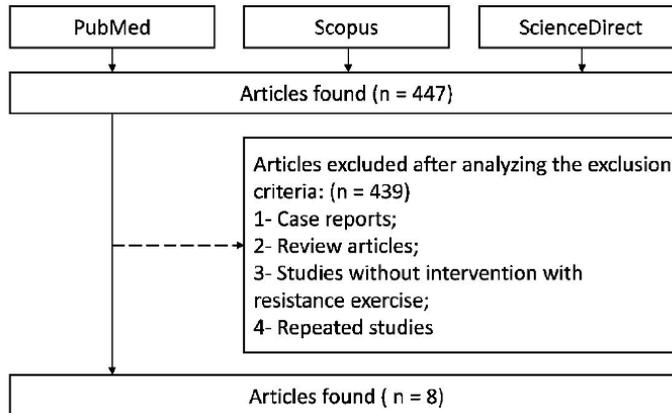


Figure 2. Diagram of the article selection process.

3. Pathophysiology of pulmonary hypertension

The pathophysiology of PH is characterized by complex vascular alterations, including vasoconstriction, cell proliferation, dysregulated apoptosis, inflammation, thrombosis, and disordered angiogenesis. Vasoconstriction in PH involves an imbalance between vasodilatory and vasoconstrictive factors due to endothelial dysfunction. Among the main factors, prostaglandin I₂, which is reduced in PH, leads to decreased smooth muscle cell relaxation and increased platelet aggregation [14]. In addition, nitric oxide (NO) has its bioavailability reduced due to decreased eNOS expression and increased oxidative stress, which reduces vasodilation and increases cell proliferation [15, 16]. On the other hand, endothelin-1 is increased in PH and promotes vasoconstriction and cell proliferation [17].

Cell proliferation and dysregulated apoptosis are hallmark features of PH and cause vascular remodeling (**Figure 3**). Genetic mutations, such as those in Bone Morphogenetic Protein Receptor Type 2, Activin Receptor-Like Kinase 1, and endoglin,

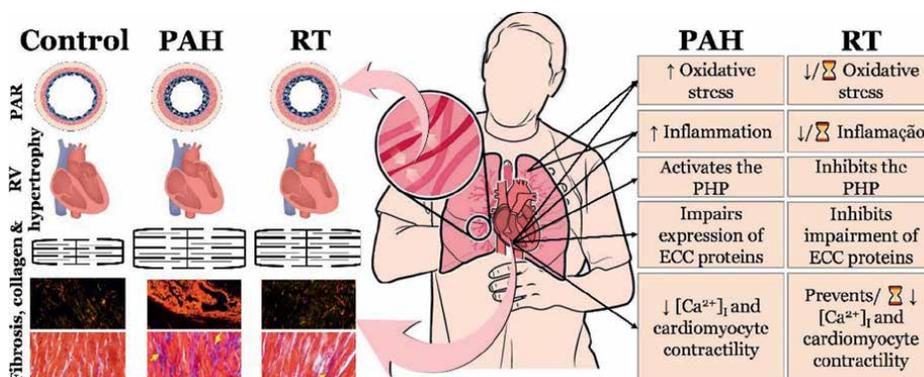


Figure 3. Illustrative diagram of the impact of PAH on the cardiopulmonary system and the contribution of resistance training to the treatment of this condition. Excitation-contraction coupling (ECC); intracellular calcium ([Ca²⁺]_i); pulmonary arterial remodeling (PAR); pulmonary hypertension (PAH); pathological hypertrophy pathway (PHP); resistance training (RT); right ventricle (RV). ↓ = reduces; ↑ = increases; and ⊘ = delays.

are associated with a predisposition to PH [18]. Growth factors, such as vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor, contribute to cell proliferation and resistance to apoptosis [19]. Proteases and elastases modulate the extracellular matrix and release growth factors, while Notch signaling regulates the proliferation and differentiation of smooth muscle cells. The Peroxisome Proliferator-Activated Receptor Gamma receptor, which is reduced in PH, is important for the regulation of cell growth and inflammation [20]. Disordered angiogenesis is present in PH, as evidenced by plexiform lesions. Alterations in endothelial progenitor cell levels in patients with PH suggest a role in maintaining endothelial integrity [21]. These interconnected mechanisms lead to increased PVR and, consequently, PH.

Chronic elevation of PVR leads to an increase in the afterload of the right ventricle (RV). Such overload generates an adaptive response or adverse remodeling of the RV, resulting in hypertrophy associated with increased passive tension in the sarcomeres, collagen deposition in the extracellular matrix, myocardial fibrosis, inflammation, and cellular apoptosis, and consequently, contractile dysfunction [22]. This condition leads to RV failure as structural and functional damage progresses (**Figure 3**). Heart failure is the leading cause of death among patients with PH [23].

In addition to these changes in pulmonary circulation, studies [24–26] have shown that right ventricular hypertrophy and dilation induces interventricular septum flattening, which negatively impacts the structure and function of the left ventricle (LV). Patients with PH frequently exhibit altered LV geometry (i.e., reduced ventricular cavity due to cardiomyocyte atrophy) [27] that, in turn, impairs ventricular filling, thus reducing end-diastolic volume and cardiac output [28–30].

At the cellular level, various elements contribute to the pathological remodeling of the RV and LV, including increased levels of reactive oxygen species, activation of apoptotic pathways, neurohormonal activation (e.g., adrenergic pathways) [31], increased beta to alpha myosin heavy chain ratio (β/α MHC), cell proliferation, inflammation, and apoptosis, all of which are evidenced in PH [32]. Studies involving humans or animal models support the role of inflammation in the RV under pressure overload, showing that neutrophils and macrophages may be involved in the remodeling of the RV and LV during the development of PH [32, 33].

Right ventricular myocytes in PAH models commonly exhibit abnormalities in excitation-contraction coupling [34, 35]. A negative contraction-frequency relationship [9, 12], which is associated with a decrease in the amplitude of intracellular calcium ($[Ca^{2+}]_i$) transients [12, 35, 36] has been observed. In right heart failure induced by PAH, dysregulation in the $[Ca^{2+}]_i$ cycling contributes to reductions in the amplitude and time course of the $[Ca^{2+}]_i$ transients, which leads to mechanical dysfunctions and reduced capacity to respond to contractile demands [37]. The alterations in excitation-contraction coupling present in PAH are associated with disturbances in the expression of Ca^{2+} regulatory proteins, such as phospholamban (PLB), sarcoplasmic reticulum Ca^{2+} ATPase, type 2 ryanodine receptor, and sodium-calcium exchanger [34, 35].

The structural and functional impairments in the cardiovascular system caused by PH cause edema in the lower limbs and pre-syncope/syncope due to reduced cardiac output (CO) [38, 39]. In fact, muscle loss, that boosts exercise intolerance, has been attributed to low CO and the consequent reduction in the availability of oxygen and other nutrients to peripheral tissues [40]. The reduction in oxygen availability results in elevated inflammatory responses [i.e., Interleukin (IL)-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, and tumor necrosis factor- α], which contribute to abnormalities in the mitochondrial function [41]. Such changes result in an imbalance between the synthesis and degradation of myofibrillar proteins, overcoming proteolysis mediated by the

ubiquitin-proteasome system [41, 42]. Additionally, these inflammatory markers alter and suppress the insulin receptor substrate-phosphoinositide 3 kinase-protein kinase B (Akt) pathway causing thus impairment to the skeletal muscle [43–48].

The complex pathophysiology of PH, which involves a series of vascular, cellular, and molecular changes, assists the progression of the disease and its complications. A thorough understanding of the mechanisms involved in PH is essential for the development of innovative and effective therapeutic approaches. Furthermore, ongoing scientific investigation is crucial for identifying new therapeutic targets and developing treatments that can help improve the patient's quality of life. Moreover, the integration of knowledge on the interaction between the cardiovascular and pulmonary systems, as well as the impact of inflammation and cellular remodeling, can pave the way for holistic and personalized interventional strategies.

In this regard, due to the clinical characteristics and prognosis of the disease, treatments for PH have evolved considerably over the past decade, partly due to advancements in the understanding of the pathobiology of the disease. These treatments aim to reduce pulmonary arterial pressure and normalize CO given the severe hemodynamic disturbances caused by PH. Another important goal is to reverse, or at least prevent, disease progression to improve the survival of patients with PH. Advancements in research in this area increase the possibilities of more effective treatments for such complex diseases.

4. Resistance training as a therapeutic intervention for patients with pulmonary arterial hypertension

Physical exercise has been recognized and recommended as a non-pharmacological therapeutic tool for various diseases, including pulmonary (e.g., chronic obstructive pulmonary diseases) and cardiovascular ones (e.g., hypertension, coronary artery disease, and heart failure) [49].

The aerobic types of physical exercise, also known as cardiorespiratory exercises, are identified by sustained increases in heart rate and ventilation, involving large muscle groups in a rhythmic and continuous manner (e.g., running, cycling, and swimming). According to the American College of Sports Medicine [50], aerobic exercise promotes significant cardiorespiratory adaptations and improves functional capacity and cardiovascular health.

Although the benefits of aerobic exercise on the cardiovascular system are well established, it has been tested whether regular physical exercise can alleviate or reverse the complications imposed by PH. Despite the limitations imposed by the disease, there is growing evidence from both human [51–57] and animal model [7–9, 12, 13, 58] studies that continuous (i.e., 60–80% of VO_{2max}) and intermittent aerobic exercise can provide beneficial effects for individuals with PAH. The overall positive results observed in humans translate into improved quality of life and functional capacity, increased exercise capacity and ventilatory efficiency, improved overall cardiac function, arterial and myocardial elasticity, muscle metabolism, and mitigation of oxidative stress, inflammatory processes, and adverse cardiopulmonary remodeling present.

The resistance exercise training (RT), also known as strength training, refers to a form of physical exercise in which the practitioner uses external loads to obtain muscular and neuromuscular adaptations [59]. The hallmark of RT is the application of a

progressive load to the musculoskeletal system, which enforces the muscles to contract against resistance. As a result of several RT sessions there are muscle mass growth (i.e., hypertrophy), as well as muscular strength and resistance increases [60]. Resistance exercise training is highly versatile and is also essential for maintaining bone health and improving functional capacity in different populations upon distinct conditions [59, 61, 62]. The planning of an RT must consider a training load adjusted according to the individual's goals and fitness level as well as the health condition [50, 63].

From this perspective, the RT could be a promising and effective option for the treatment of patients with PH [64]. Considering the impact of PH on skeletal muscle dysfunction [5], some studies have integrated RT as a complement to aerobic exercise (i.e., Combined exercise training) [65–67]. According to recommendations from the American Heart Association, RT should primarily consist of low-weight dumbbell exercises targeting large muscle groups [61, 65, 67]. Training loads should not exceed 50% of 1 repetition maximum, with 8–12 repetitions per set, and 2–3 sets per exercise [61]. Additionally, the Valsalva maneuver must be avoided [68]. The available literature focused on studying the effects of RT on patients with PAH suggests that this type of exercise should use body weight or dumbbells (i.e., from 0.5 to 1 kg) for 15 to 30 minutes [69] and complement the aerobic exercise training [68].

Recently, our group assessed the impact of low- to moderate-intensity RT (i.e., from 55% to 65% of the maximum load), performed five times a week, on the structure and function of pulmonary, cardiac, skeletal muscle, and bone tissues in a model of stable PAH induced by monocrotaline in the rat. The results indicate that the RT program improves survival and exercise tolerance, slows the increase in pulmonary artery resistance (i.e., TA/TE), and preserves cardiac function (i.e., fractional shortening, ejection fraction, stroke volume, and TAPSE) [24, 70, 71]. Moreover, the RT neutralizes oxidative stress (i.e., CAT, SOD, GST, MDA, and NO) and adverse remodeling in the lung (i.e., collapsed alveoli) and in the biceps brachii (i.e., atrophy and total collagen). Furthermore, RT slows RV adverse remodeling (i.e., hypertrophy, extracellular matrix, types I and III collagen, and fibrosis) and impairments in the contractility of isolated RV myocytes (i.e., amplitude and velocity of peak and relaxation). From a molecular perspective, RT improves the gene expression (i.e., miRNA 214) and regulatory proteins of the intracellular Ca^{2+} cycle (i.e., $\text{PLB}_{\text{Ser16}}$), as well as pathological factors (i.e., α/β -MHC ratio and forkhead box O3) and physiological factors [i.e., Akt, phosphorylated Akt, mammalian target of rapamycin (mTOR), phosphorylated mTOR and B-cell lymphoma extra-large] in the RV [70] (**Figure 3**). Thus, along with increased survival and exercise tolerance, low- to moderate-intensity RT performed during the development of stable PH delays the increase in pulmonary artery resistance and prevents RV dysfunction, adverse remodeling, and deterioration in single myocyte contractility in the rat.

Furthermore, upon investigating whether low- to moderate-intensity RT is beneficial to the LV in the stable PAH model [24], the results revealed that, alongside improvements in survival and exercise tolerance, RT attenuated the contractility dysfunctions in the whole LV and in single myocytes. To illustrate, RT preserved ejection fraction, fractional shortening, the shortening amplitude, and the contraction and relaxation velocities in myocytes. RT also prevented increases in fibrosis and type I collagen in the LV.

Regarding the effects of stable PAH and RT on renal morphometry, bone morphometry, and biomechanical properties [71], it was found that PAH reduces renal glomerular area and volume, which was prevented by RT. However, PAH does not

impair either femoral morphometry or its structural and mechanical properties. Nevertheless, RT improves femoral parameters, such as length, trabecular percentage, and bone marrow, as well as ultimate and yield loads. Collectively, these findings are clinically relevant as they suggest that low- to moderate-intensity RT may positively contribute to the health and survival of individuals with stable PAH.

Despite the evidence supporting the potential benefits of RT to patients with PAH, it is important to highlight that such exercise modality may present certain risks and contraindications, especially for those with severe PAH. Intense RT can exacerbate symptoms or lead to adverse cardiopulmonary events in some patients because increased systemic and pulmonary arterial pressure during intense RT can elevate cardiopulmonary load, potentially resulting in right heart failure in susceptible patients. Therefore, RT should be approached with caution, as it can cause abrupt increases in blood pressure and vascular resistance, which is particularly harmful in patients with PAH. It is essential that exercise programs are carefully tailored and supervised by healthcare professionals with expertise in PAH to mitigate risks and ensure that both type and load of exercise are appropriate for everyone's condition. Comprehensive pre-exercise screening and regular monitoring during exercise sessions are imperative to maximize the benefits of physical activity while minimizing the potential for harm in patients with PAH.

5. Practical applications

The current literature on the pathophysiology of PH emphasizes the urgent need for further research to elucidate its underlying mechanisms and to develop effective therapies aimed at reducing the mPAP, maintaining the cardiac function and thus improving the patient's quality of life and increasing their survival. It is essential to expand our understanding of mechanisms and physiological responses, from systemic to cellular and molecular levels. The complex interactions between pathological processes and the body's physiological responses to identify more precise therapeutic targets and efficacious treatment strategies warrant further investigations.

Regarding RT for patients with PAH, studies are invited to explore its effectiveness at different loads and in combination with aerobic exercises, especially in specific patient subgroups, such as those with severe PAH or with comorbidities. The CTEPH should also be investigated. Further investigations about exercise dose-response and specific protocols would provide valuable insights into how to optimize clinical benefits and minimize risks. Additionally, studies should consider the molecular and cellular mechanisms involved in the physical exercise response, including the regulation of oxidative stress, inflammation, and cardiopulmonary remodeling. Integrating biomarkers and advanced physiological analyses may help personalize interventions and more accurately assess the effects of physical exercise on disease progression. Finally, it is essential that future studies include the evaluation of psychosocial aspects and quality of life to ensure that physical exercise programs not only improve physiological parameters but also promote overall well-being in patients with PH.

From a practical standpoint, healthcare professionals should pay close attention to the recommendations regarding RT and its potential benefits for patients with PAH. Studies suggest that combining RT with aerobic exercises may be an effective approach, especially for patients with more severe conditions or multiple

comorbidities. However, RT has not yet been extensively studied in patients with CTEPH, and future investigations could provide evidence for its application in this group.

Additionally, tailoring interventions based on advanced analyses, such as biomarkers and cellular responses, is critical to enhancing the effectiveness of exercise therapies. Healthcare professionals should also incorporate psychosocial considerations when designing exercise programs to ensure that, in addition to physical improvements, there is a positive impact on the emotional and social well-being of patients with PH. These integrated approaches can lead to more effective and individualized interventions, optimizing both treatment outcomes and patients' quality of life.

6. Conclusion

Supervised aerobic and combined physical training are currently recommended for patients with PAH undergoing medical treatment due to its proven safety and effectiveness. The latest guidelines for the rehabilitation and treatment of patients with PH now incorporate additional evidence that further consolidates the crucial role of supervised physical exercise. Although the guidelines do not formally incorporate RT alone, there is evidence showing that low- to moderate-intensity RT can offer significant benefits for individuals with PAH, such as improving skeletal and cardiac muscle functions, reducing oxidative stress, and mitigating adverse remodeling. Finally, it is important to emphasize that integrating evidence-based strategies for PAH into clinical management can not only enhance therapeutic outcomes but also significantly improve the quality of life of patients affected by these conditions.

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Conflict of interest

The authors declare no conflict of interest.

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Chapter 6

Resistance Training in Patients with Bone Metastasis

Margit Eidenberger

Abstract

Bone metastasis (BM) is a complication in advanced cancer. Symptoms are pain, pathological fractures, hypercalcemia or spinal cord compression. Pain is experienced by 60–80% of patients and has a deteriorating effect on activities of daily life (ADL) and quality of life (QoL). Physical activity is an intervention recommended for early and advanced cancer patients. Resistance training (RT) offers different advantages for BM. It can improve muscle strength, bone density and QoL and prevent loss of functional activity. The question remains: how can RT be delivered in BM patients? Different approaches are possible: supervised in-patient and unsupervised training. Loading to BM sites may be avoided or implemented and certain precautions may be given. Various prerequisites are crucial before implementing RT in BM patient cohorts. This chapter will give an overview of the pathophysiology of BM and a description of various assessments. It will elaborate on the feasibility, safety and efficacy of different types of RT. It will investigate prescription details (intensity, exercise tools and additional requirements) to ensure safety.

Keywords: cancer, bone metastasis, resistance training, pain, strength, quality of life

1. Introduction

Bone metastasis (BM) is a symptom and complication of advanced cancer stages. With solid primary tumors, bone is a common location of metastasis [1]. BM is associated with relevant morbidity and a decline in survival [2]. Various cancer subtypes are inclined to spread into bony structures. Breast cancer (BC) is the most common malignancy in women [3] and prostate cancer (PC) is the most common in men [4]. These both, as well as other cancer types, for example, lung cancer (LC), myeloma and kidney cancer or melanoma, disseminate [5] by entering the circulation system and spreading to the bone marrow [3].

Therapeutical progress led to longer patient survival and shifted cancer diagnosis to chronic disease [6]. It raised the number of patients with long-term cancer [7]. This puts emphasis on health-related quality of life (QoL) during several years of cancer therapy for cancer survivors [8]. After multifaceted treatment, that is surgery, chemotherapy, radiation therapy, targeted therapy, or immune therapy, patients complain of a variety of symptoms such as muscular weakness, musculoskeletal symptoms, fatigue, restriction in range of motion and overall activity. Chemotherapy- and radiation-therapy-induced side effects, for example, polyneuropathy or fibrosis, are

prevalent. In conjunction with BM, patients suffer from pain, pathological fractures with different bones, hypercalcemia, spinal cord or other nerve compressions [9], all of which decline physical activity, mobility and QoL. Fracture risk corresponds to higher mortality; loss of muscle mass increases the risk of falls [10], contributing to further fractures.

The therapeutic goal for BM is most often palliative only. It comprises surgery, radiotherapy and systemic therapy (chemotherapy, hormone therapy, immune therapy) and analgesics according to the WHO suggestions (non-opioids or opioids). Bisphosphonates and denosumab are the mainstay of medical treatment [11].

Physical activity is a type of intervention recommended for cancer patients in early as well as advanced stages [3, 12]. It comprises aerobic training, resistance training (RT) and additional individualized therapeutic goals such as balance training or relaxation therapy [13]. Adhering to physical activity gives patients the possibility to counteract therapy-related side effects and to better cope with the entire situation [12]. The goal of RT is to improve pain, muscle strength, functional activity, bone mineral density and overall QoL. During chemo- or radiotherapy, the safety of RT was already established [14]. RT in BM patient cohorts needs further research and an answer how to accomplish implementation into practice. This chapter will deal with RT in BM only, although a mixed-techniques approach is patient-centered and useful in a multiprofessional setting. Additionally, exercise programs for BM patients must be easily accessible. Barrier factors such as motivational lack or hindrances at reimbursement or travel difficulties to supervised facilities must be surmounted [15].

The question remains: how RT should be delivered in BM patients because different approaches, intensities and sophistications are possible. It will elaborate on the feasibility, safety and efficacy of different types of RT. It will investigate prescription details (intensity, exercise tools and additional requirements) to ensure safety.

2. Methods

Although this was planned as a narrative review, a structured literature search was undertaken and is presented here. The keywords “bone metastas*”, “resistance training” and “strength training” were combined with the Boolean operators AND and OR. Time limits were set for publications between 2004 and 2024 to get an insight on how the topic evolved over the last 20 years. Trials on children with cancer were excluded. To have a broad body of literature, no research design limits were set; also, no language restrictions were introduced. For details, compare **Figure 1**.

3. Bone metastasis

3.1 Incidence and types of bone metastasis

After the lungs and the liver, bone is the third most frequent location of cancer metastasis. The two most common types of cancer, that is BC in women and PC in men, tend to develop BM in the long term [8]. BM has a predictive quality for survival, limiting the range after BM detection to 1–4 years, depending on cancer type [16].

In prostate cancer, the incidence of BM is 65–75%, 69% of BM is in the spine, 41% in the pelvis and 25% in long bones such as the femur [11]. In PC, 90% of deceased investigated patients had BM with a 5-year survival of only 5%. Metastatic PC tends

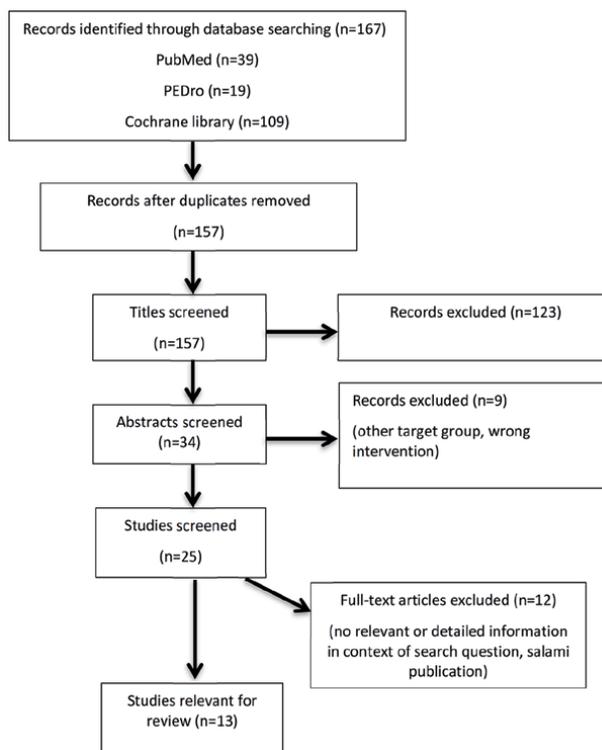


Figure 1.
Flow chart.

to affect the axial skeleton with osteoblastic, that is, bone forming metastasis, but osteolytic or mixed types are also possible [10].

During their course of disease, 70–80% of BC patients develop metastasis. In BC, most BM is of the osteolytic type [1, 3]. Seventy percent of BC patients experience BM and thereof metastatic bone destruction. Breast cancer BM is a sign of an end-stage tumor disease [9]. Both BC and PC have a predominance for BM because of their connection to sexual hormones [10].

In lung cancer, about 20–30% of patients already have developed BM at the time of their diagnosis [2]. About 35–60% of non-small cell lung cancer are diagnosed with BM at some stage of their disease [10]. The median survival of LC patients with BM is about 6–7 months [2].

In pancreatic cancer, which is highly aggressive, the prevalence of BM ranges from 5 to 20%. In this type of cancer, the liver and the peritoneum are the preferred sites of metastasis, with about 45–50% [17].

About 30% of patients with kidney cancer develop BM with an incidence of approximately four skeletal-related events (SRE) per year in this cohort. They mostly belong to the osteolytic type [18].

In an Italian cohort of melanoma patients, 83% presented with BM. The most common site was the spine (90%). Forty seven percent of those patients suffered from at least one SRE. Their mean overall survival after BM detection was less than 11 months [19].

BM can be labeled as osteolytic, osteoblastic or both, depending on cancer type [11]. BC and LC are most followed by osteolytic metastasis whereas PC

predominantly leads to sclerotic, that is, osteoblastic metastasis [8]. In PC all different types can appear in one single bone and even one lesion. Hodgkin's lymphoma, melanoma or thyroid cancer mostly produce osteolytic lesions [16].

Apart from BM, there is cancer-treatment induced bone loss because of several surgical or systemic hormonal therapies in BC and PC such as androgen-deprivation therapy, orchidectomy or long-term tamoxifen. This reduces both testosterone and estrogen levels and comes with the side effect of a reduction in bone mineral density and an elevated risk for osteoporotic fractures [10, 20, 21]. This is another reason to adopt exercise therapy, especially RT.

3.2 Symptoms

Typical symptoms are pain, pathological fractures, hypercalcemia and spinal cord compression [8] or distal nerve compression. They are labeled skeletal-related events [11]. SREs are a widespread complication of BM. They have a negative impact on patients' diagnosis of cancer and lead to elevated healthcare costs [22]. If spinal cord compression occurs through in spite of a multi-targeted therapy, only 50% of patients can walk, and it is doubtful if non-ambulatory will ever walk again [23]. SREs diminish QoL and increase mortality. Early diagnosis and intervention can prevent the development of SREs by evaluating biomarkers and correlating factors such as age >65 years and advanced disease [10].

The leading symptom is bone pain and is experienced in different degrees by 60–80% of patients. Pain can occur in advance of X-ray or otherwise detected bone changes and both pain and pathological fractures can occur earlier than cancer diagnosis [11]. We differentiate between intermittent or later constant pain. It is usually correlated with movement, cumulating at night or following palpation or touch. It can occur as seizures of "breakthrough pain," described as acute, piercing and at a high intensity. Interestingly, approximately 25% of patients do not report pain. Pain has certainly a deteriorating effect on activities of daily life (ADL) and QoL [11].

Hypercalcemia, i.e. calcium levels above normal in cancer patients can occur through abnormal bone resorption or elevated intestinal absorption or renal excretion. Approximately 30% of patients develop hypercalcemia, which ranges from mild cases to life-threatening conditions. Patients present with renal symptoms (polyuria, increase of creatinine), constipation, nausea and vomiting. They also show apathy, fatigue and bone pain, and finally, ventricular arrhythmias and coma. The patient's increasing immobility, coming with the loss of strength and activity, contributes to calcium resorption from the bone and the state of hypercalcemia. Depending on the cause, there are different pathways of therapy, e.g. bisphosphonates, intra-venous rehydration or calcitonin [24].

3.3 Pathophysiology

Under physiological circumstances, bone equilibrium is achieved through regulated new mineralized bone formation and bone resorption, leading to bone homeostasis [1, 2, 16, 25]. The primary tumor first invades the surrounding healthy tissue, new blood vessels are created [2]. After tumor cells have left the primary tumor and entered the circulatory system, they need to survive in this new environment. They achieve self-defense mechanisms by inhibiting the normally ongoing apoptosis [10, 11]. Research showed that e.g. BC tumor cells are capable of changing the normal bone microenvironment by secreting e.g. interleukin-1- β , a proinflammatory

cytokine, which can create a so-called pre-metastatic environment [9] and prepare niches [10]. The fact that bone marrow blood vessels are fenestrated facilitates the migration of tumor cells through the vessel into bone marrow, where they remain through mechanical adhesion [16]. The tumor cells generate new blood vessels, ensuring their own supply and start to dysregulate the normal balanced bone remodeling [2]. After settling in the bone marrow, cancer cells can commence a dormancy which can last years to decades [10]. During this dormancy, they are protected against chemotherapy or immune system engagement. They may terminate this dormancy long after diagnosis and tumor treatment and cause a cancer relapse by the release of certain growth factors [10, 16]. The dormant tumor cells are characterized by slow growing but also dying, holding them stable and awaiting a reactivation through the tumor microenvironment. Also, hypoxia is discussed as an underlying factor to awaken dormant tumor cells [25].

Both osteoblasts and osteoclasts dwell in the bone marrow during their maturation process. There, they start to divide and grow, which, in BM, finally leads to bone damage. By releasing certain mediators, e.g. endothelin, tumor cells stimulate osteoblasts to start proliferation. Proliferation is followed by the formation of new bone. These osteoblasts also release RANK-L (receptor activator of nuclear factor kappa B ligand), which stimulates osteoclasts and leads to bone demineralization and bone instability [11]. The interplay of RANK and RANK-L is the dominant driver for both physiologic and pathophysiologic bone remodeling. The binding of RANK to RANK-L starts the cell differentiation and activity of osteoclasts [2]. Cancer cells can diminish the expression of the RANKL antagonist osteoprotegerin [1].

Cancer cells also can combine with macrophages, giving them osteoclastic properties [10]. BC cells can also promote osteolysis through their interplay with osteoblasts [25]. For osteoblastic metastasis, cancer cells induce osteoblastic activation by e.g. fibroblast growth factors and TGF- β [1]. Osteoclasts also release growth factors such as TGF- β , inducing further tumor growth [10]. In both types, the interaction between tumor cells and bone cells can activate a vicious cycle [10, 25]. The process enters this cycle of destruction (osteoclastic vicious cycle) and/or formation of bone (osteoblastic vicious cycle) [10]. Furthermore, it starts metastasis to other organs [9].

3.4 Imaging methods and biomarkers of bone metastasis

Early detection or prevention of BM is crucial for timely treatment and to enhance QoL and overall prognosis [9], but diagnosis on time remains difficult [16]. Although often applied, radiography has poor sensitivity. Also, bone scintigraphy, which has long been used to detect BM has a limited sensitivity and specificity [8]. Predictive quality is dependent on whether there are osteolytic or osteoblastic lesions, e.g. the sensitivity for PET-CT is better for the former [23]. CT can detect both types in the bone marrow even before X-rays are able to depict any destruction. FDG-PET-CT (fluorodeoxyglucose positron emission computed tomography) is highly sensitive and recommended for an overall skeleton assessment [2]. MRI allows for an accurate anatomical demarcation [23] and is very useful in the suspected spinal cord compression [2]. If there is an acute onset of pain both CT or MRI are recommended [5]. Bone densitometry, dual-energy X-ray absorptiometry, is another means for evaluating BM [26]. If lesions are smaller than 10 mm, which is most often the case and lack soft tissue involvement, they are mostly inaccessible for assessment, which excludes many patients with BM from new drugs in trials [27]. Biopsies would produce a definite diagnosis but are often neglected because of the patients' risks [2].

Several cancer-type specific biomarkers, labeled bone turnover markers (bone resorption markers and bone formation markers, e.g. pyridinium crosslinks or alkaline phosphatase [1]) serve as supporting diagnostic methods [8]. They can identify high-risk patients and predict therapy response. These are protein-fragments which can be detected in both, serum and urine. They are used to predict the metastatic involvement of bony structures [1]. Elevated hypercalcemia serum level is another predictor for BM [9]. Further, a nomogram was developed for pancreatic cancer. Independent factors for prognosis were e.g. age, cancer grading, histological subtype or chemotherapy [28]. Mirels' score (12 points max.) relies on the anatomic site, the BM size, the radiography assessment, and the pain pattern, and it is a tool to predict pathological fracture risk. A score of $\geq 7/12$ was suggested as a cut-off value for the realization of prophylactic surgery for upper limbs and $\geq 9/12$ for lower limbs [29].

Assessment methods for therapy response in BM are rather difficult. Healing only becomes apparent after a minimum of 3–6 months and is challenging to evaluate. It is further doubtful in the predominance of lytic BM [27].

3.5 Treatment

Therapy of BM is palliative, not curative [2]. Several approaches are used, which will be described in the following paragraphs. BM patients need an interprofessional team consisting of an oncologist, radiotherapist, orthopedic surgeon [10, 30], general practitioner, specialized physiotherapist and exercise physiologist [7, 30]. The latter two are the most gifted professionals to prescribe and monitor the training if they have university degrees and additional cancer expertise. At the start of their career, they should be supervised by an experienced colleague [31]. Patients want to exercise at public gyms or sports facilities, and they want to be supervised by physiotherapists but clearly need more and deeper instructions on safe therapy execution. They take part mostly because they hope to improve their pain and enhance or maintain their strength [15].

3.5.1 Pharmacological treatment

Bisphosphonates, i.e. Zolendronic acid, are bone-modifying agents and the mainstay of treatment. They are commonly used to prevent bone resorption in cancer as well as in osteoporosis. They have an apoptotic effect on osteoclasts and provide rapid pain relief and a reduction of SREs [11]. Only 50% of the dose is taken up by the bone, the rest metabolized by the kidneys [1]. Additionally, they provide an anti-tumor effect by e.g. hindering tumor-associated angiogenesis [32]. Bisphosphonates are indicated in lytic and blastic, i.e. sclerotic lesions [2].

Denosumab is a human monoclonal antibody. It effectuates RANKL inhibition, therefore preventing osteoclast maturation [1] and declining osteoclastic bone resorption. This is associated with an enhanced bone mineral density which also improves pain. Both substances mentioned can cause jaw osteonecrosis as a possible side effect if taken in the long term. This is further associated with poor oral hygiene or tooth surgery [10]. Leading symptoms of this osteonecrosis are pain, bone destruction, infections and compromised healing of the maxilla and the mandible [27]. The incidence is rather low (2% in Bisphosphonates or Denosumab) and is influenced by drug dose and cancer type. Because of the tremendous loss of QoL, physicians should be aware of this side effect and take evidence-based decisions [33]. More common, but not as grave side effects of both are nausea, fatigue and diarrhea [1].

3.5.2 Surgery

Surgery is adequate for solitary and small lesions. Accessibility depends on the location. Nailing, plates and locking screws applied by minimally invasive approaches, bone-cemented techniques or endoprosthesis are applicable [23]. If possible, surgery should be implemented as a prophylactic measure for BM. It is certainly indicated in persistent pain after radiotherapy, with the BM being ≥ 30 mm, if $\geq 50\%$ of the cortical structure of a long bone is destroyed [27] and for impending fractures. BM surgery is correlated with poor survival with a median of 3–5 months. It is argued by preserving continence and a better functional ability [2].

3.5.3 Radiotherapy

Radiotherapy can provide sustained pain relief. So-called uncomplicated BM with pain but without fracture or spinal cord compression of every size is the target. The standard dose is a single fraction of 8 Gy [5]. Palliative radiotherapy improves QoL and lowers the incidence of SREs [10] with a positive response rate of about 70–80% and a complete alleviation of pain in about 30% of patients [27].

4. Resistance training

Physical activity is a means to first reduce the risk of developing cancer [34] and second to treat and mitigate various complaints of cancer patients and therapy-induced side effects [35] in their early and late stages. It also contributes to a certain percentage of protection against cancer relapse.

In the past, the medical staff was concerned about prescribing exercise for cancer patients with BM because of fear of bony and neurological complications. Current research has overcome some of those hesitations. Considering various safety precautions, exercise therapy has been established as an important part of the therapeutic regime for BM patients [36]. Health care staff can use e.g. the “International Exercise Guidelines for Cancer Survivors” [37] as a preliminary source, but postural alignment, controlled movements and correct technique need special attention on top of knowledge and consideration of individual bone lesions [30, 31]. Already in 2002, Courneya demanded to incorporate RT in cancer exercise programs, stating that modifications are necessary with comorbidities such as fatigue, lymphedema or metastasis [38]. Bone and muscle loss often take place simultaneously, especially in this cohort. Because of their anatomical proximity and their mechanical connection, exhibited muscle force can trigger anabolic activity in adjoining bones [39], which can be interpreted as a reason for RT.

Patients need evidence-based expertise on how to implement physical activity despite their BM diagnosis. RT offers different advantages for BM patients. RT has the potential to improve muscle strength, bone density and QoL and can prevent additional loss of functional activity [36]. The target group is very heterogeneous, so the diagnosis BM must be divided into subgroups of patients by using radiological and clinical assessments to treat them accordingly and safe. If patients with “unstable” lesions or patients with “moderate to severe bone pain” are excluded from trials and/or training prescriptions, the question arises how to handle them at all. There certainly are functional activities exhibiting similar or even greater forces than a controlled exercise prescription would do, and pain is one of the chief complaints.

Overall, a lack of advice on physical activity from oncologists could be observed, although patients are seeking advice and see their oncologist as the main source to offer it. Nonetheless, results from a survey showed that 89% of oncologic health care providers thought physical activity to be important and 82% to be safe in BM patients. On the other hand, only 43% were confident in their own prescriptions, and 85% wanted further education for doing so or expressed their need for explicit exercise guidelines to follow in the case. Another 57% would not have referred such patients to physiotherapy [7, 30]. These results show a consensus for the need how to firstly treat and guide BM patients and secondly how to meet health providers educational desires. Only recently an exercise guideline for cancer patients with BM was published [31] and awaits to be implemented in daily practice.

4.1 Exercise testing and clinical assessments

An exercise testing in advance of the training is recommended to assess for the possibility of SREs due to exercise, but this risk should not be the reason to restrain completely from exercise. Forty four percent of respondents in a survey answered they would avoid any strength testing, which places stress on the BM, another 37% would use caution therefore [31]. Several factors contribute to a patient's personal risk: the underlying primary tumor and its prognosis, the treatment prescribed, the lesion itself and personal variables. So, exercise testing in this cohort may be neglected at all or at least the test protocol needs modification.

In detail, the health care team must gather the following information: a recent bone scan giving type, size, number and location of lesions, and a CT or MRI for structural bone quality. Furthermore, medical treatments, the use of bone stabilizing drugs or other medication, which may impair bone stability (e.g. Cortison), osteoporosis, fatigue or cachexia as a comorbidity, a diligent pain assessment (intensity, site, medication, triggers), gait/balance disturbances or recent falls, neurological symptoms, impairment of ADLs and cognitive functions and whether there is an exercise history [30, 31]. All this information can help to assess the likelihood of SREs [30]. Concerning spine BM, the Spinal Instability Neoplastic Score (SINS), based on six criteria: location, pain, type of lesion, spinal alignment, presence of vertebral compression fractures, posterolateral element involvement was suggested showing the vertebrae as “stable = 0–6,” “potentially unstable = 7–12” or “unstable = 13–18” [40].

For defining the correct intensity in every RT, exercise testing is useful [41]. Several methods have been described in the past. The one-repetition maximum test (1-RM) is defined as the maximum load a patient can manage during a specific kind of exercise just once and is frequently used in exercise testing [42]. The advantage of 1-RM is an accurate, reliable and valid testing of strength in practice settings [14]. But the average force patients muster is positively correlated to the load charged [43]. The disadvantage is obvious, as it poses several risks for different kinds of patients, e.g. with circulatory diseases or in this case patients with BM. Although some trials and protocols implemented 1-RM tests to define the individual protocol [44, 45], although eventually modified and limb-restricted [46], we should not cut out possible adverse events in weak bony structures. The second method is a multiple-repetition maximum test or submaximal strength test, where a minor load is given to the patient, followed by a calculation of the 1-RM. This is also known as the strength pyramid. Additionally, submaximal strength tests reflect the ability of ADLs better, which may be of relevance in this group.

A case report related to the 1-RM. However, non-metastatic BC for inclusion criterion, no hormone therapy and a specific warm-up, a crackling followed by pain occurred at the leg press. Ongoing assessments revealed a cover-plate compression fracture. This happened, although the patient was instructed in advance. The authors concluded that given a possible pre-exercise osteoporosis, a change to an x-RM test would enhance patient safety [47]. As we can never be sure if patients understand and process instructions correctly, an x-RM seems the right assessment. In patients with BM the risk of an SRE is unproportional to the information gathered by the 1-RM.

4.2 Intensity

The intensity is closely related to the energy the patients need while performing the training. Not only in cancer patients, RT should be preceded by a suitable warm-up (e.g. light aerobic exercise) and followed by a cool-down (e.g. stretching) [41, 48]. Exercise starts with an education on ADL and active movements without any load, progress is only slowly. Jerky, rapid and loaded full range of motion movements must be avoided [31].

Training begins with exercises and muscle groups remote to bone lesions but can move on to lesion sites under consideration of the precautions to be mentioned. As also certain ADLs put considerable load on predisposed bones, patients need education and guidance on these as well. The RT should ideally incorporate major muscle groups. Patients should classify the training intensity as moderate [41], which would be “3” using the BORG scale (0–10) or “11–13” on the 6–20 scale. Adherence rates e.g. in trials were 79 (12 SD) %, accentuating patients’ interest in exercise and its feasibility. For more details, cp. **Table 1**. Unsupervised settings are conceivable if patients in need are supplied with a potential check-up for re-confirmation [49]. Of course, more resources (staff and infrastructure) are necessary when considering supervision.

Modality	Weekly planning	Prerequisites	Location	Muscle activation
Open/closed kinetic chains	2–3x/week; 8–12 weeks minimum or constantly	Warm up/cool down; diligent instruction, positioning, alignment and body control	Limbs without BM; limbs with stable BM, unstable BM very cautious	Isometric
Resistance bands/ free weights	15–45 min per session, 60 min if combined with aerobic training	Medical team consultation and clearance	Cave to potential muscle overflow; shear and compression stress/ strain; movement velocity and joint angle;	Concentric 2 sec per movement
Body weight	4–8 exercises; 2–4 sets plus 1 min rest; 20 or longer sec isometric hold	Oncologist/radiologist clearance, bone scan, CT, MRI, Karnofsky Index, ECOG performance status scale, densitometry, medication, co-morbidities	minimal loading to area in question	Eccentric 2 sec per movement
Resistance machines/ isokinetics	8–12 repetitions; slow increase of weight	Modified strength test; supervision per physiotherapist, exercise physiologist	Focus on ADL dominance; supine, prone, sitting, standing	Great muscle groups; limbs and trunk

Table 1.
Exercise modalities.

4.3 Muscle activity and positioning

Different approaches are conceivable for BM patients. First, exercises with a “no-load philosophy” for the BM sites, where only other parts of the body are exercised. Second, “isometric exercises” explicit for body regions with BM to also include and offer training feasibility for high-risk patients or prior fractures [50]. Other authors suggest a preliminary isometric trunk muscle activity, followed by concentric and eccentric limb movements [45, 51]. Slower movements, i.e. 2 seconds per one contraction [44], are advantageous for movement control. Because the faster the velocity of a contraction is, the less time is given to the body to counteract the force. The authors of a systematic review concluded with the unexpected ability of patients with BM to perform higher intensities than considered earlier and asked for further research of telerehabilitation in this area [49], therefore propagating an unsupervised approach.

Taking free weights allows for eccentric and concentric contractions at different velocities. An increase in velocity would require an enhancement of the force while using the same load. Also, the joint angle is a factor determining the resistance that is applied to a muscle [52] and needs consideration.

Both, exercises using closed or open kinetic chains, e.g. support against a wall or bridging while supine as well as moving free limbs is possible. The chosen mode of exercise significantly affects biomechanical factors such as kinetics, kinematics and muscle activity. Common exercises such as biceps curls or calf raises can be conducted. Adapted squats and lunges are possible in patients without femoral or pelvis BM involvement and are highly functional. Aside from that, upper limb exercises can train muscle strength in this region, BM absence provided.

As adjunctive tools, resistance rubber bands or dumbbells can be used to alternate resistance, but those bands come with several limitations. Firstly, it is questionable if they can always produce the overload needed for exercise-driven muscle changes [14]. Secondly, a disadvantage may be the necessity to overcome the elastic recoil in the movements’ beginning [52]. Isokinetic training facilities regulate the movement velocity during exercise. The accommodating resistance facilitates a maximal dynamic strain at every joint angle and accommodates the person’s expended strength.

As for the starting position, exercises are possible while supine, prone, sitting or standing, depending on the patient’s abilities, constitution and given contraindications for certain positions. Weaker patients can have problems lying down on or get up from the floor. In this case, a living room couch will be sufficient. Prone position e.g. will be contraindicated with adjoining heart conditions and/or breathing problems. The feasibility of e.g. an all-fours position will depend on potential humerus BM.

4.4 Repetitions, sets and intervals

Overall, 4–8 different exercises with 8–12 repetitions were chosen with 2–4 sets. The duration of the intervention was often set at 12 weeks, once at 8 weeks. Given exercises comprised upper and lower limbs or different parts of these and the trunk. Exercises were individualized according to the patients’ needs and the location of their lesions [44, 45, 51, 53, 54]. With the number of repetitions mentioned, a gain in muscle mass can be expected. The velocity of the concentric or excentric training was low, i.e. 2 seconds per movement to enhance movement control. In a real setting and knowing of ongoing muscle atrophy after terminating exercise and ongoing muscle

weakening through therapy-side effects and behavior, a long-term intervention seems appropriate. Interventions must be modified in both directions of intensity if needed according to the disease's progress and the patient's constitution.

It has been shown that lower limb muscles exhibit greater muscle endurance than upper limbs. Therefore, the rest interval may depend on the muscle site with longer resting intervals for upper limb exercises. As the goal in these patients is achieving adaptations in muscular endurance, not maximal strength, the resting intervals may be set at approximately 1 minute. In this, oxygen consumption levels, capillary density and mitochondria are increased to enhance muscular endurance [55]. Only Yee et al. [56] reported on the interval between sets, which was fixed at 1 minute.

Depending on status and constitution, the duration of RT may be 15–45 minutes, if it is RT alone and approximately 60 minutes if RT and aerobic training are combined. RT should be performed two to three times a week on non-consecutive days. The WHO's recommendation to spend at least 150 minutes on moderate physical activity and to work on moderate muscle strengthening involving major muscle groups can be applied in those circumstances.

4.5 Adaptations and precautions

Some researchers recommend supervised in-patient training for security reasons. A meta-analysis recommended supervised and individualized exercise for BM patients [57]. However, during the COVID pandemic arose the need of virtual and unsupervised exercises [31]. A pilot-study subjected 20 patients (BC, PC) with BM to a 3-month supervised RT with a 6 month follow-up assessment. They observed significant improvements in physical function, physical activity and QoL, the latter remained in the follow-up [48].

A combined approach was proposed by another research group. The protocol suggested three clinic-based exercise sessions per 60 min with a supplement of two sessions at home per 15 min from the third week on for 40 PC patients. A similar program was suggested for 40 BC patients with stable spinal BM: spinal isometric training combined with aerobic and flexibility exercises for 12 weeks. The training program included modifications based on BM location. Loads to the lesion were minimized as much as possible through isometric muscle activity after instruction on trunk stabilization, pelvic control and breathing technique [45, 51]. Results are not published yet. Those exercises in different positions (prone, supine, bridge, side-bridge, etc.) were ambitious. Although patients were instructed to pre-activate abdominals it remains questionable if they can perform it correctly, as such exercises are challenging even without BM in e.g. low back pain patients. Teaching patients to pre-activate abdominals does not necessarily include back muscles, but abdominal coactivity can lead to increased forces in extensors and ligaments. The passive system, i.e. ligaments can contribute to instability even at smaller compression loads (< 100 N), which is below several exercises and activities.

Positioning and limbs as a lever are crucial questions because back muscle activity is dependent on where a given load is held during ADLs, that is in front or at sides, with more activity at the latter [58]. The pelvic position can make a difference to enhance or decrease muscle forces and internal loads. It makes sense to ensure that patients know how to stabilize their pelvic region. Adding another 200 N load in front of the body increased the algorithmic calculated stability but resulted in shear and compression forces of approximately 500 and 1200 N at the lumbar spine [59]. So, educating patients on postural alignment and proper instructions is crucial.

Knowledge on possible spinal loads and trunk muscle forces must be considered before designing exercise programs for BM patients. A good proportion of biomechanics is required for adequate training regimes and should be part of the desired aforementioned advanced educational programs for health care providers.

A very recent review showed that unsupervised training can also be applied without increasing unwarranted side effects. The authors concluded that both, aerobic and resistance training are safe for BM patients and bone pain is the chief complaint. Medical staff advising patients should be qualified professionals with expertise and special training in treating cancer patients [36]. A systematic review including 17 trials investigated the feasibility, safety and efficacy of different types of exercise in patients with BM (aerobic, resistance and several control interventions such as stretching or breathing therapy). The training was both supervised and unsupervised. The promising conclusion was that exercise was safe and feasible. It need not necessarily be supervised if it is preceded by a supervised instruction by qualified experts. Adverse events occurred, but in a trial with soccer training and were therefore attributed to the rough body contact during sports [49].

Physicians' clearance should be a prerequisite to guarantee safety [31, 48, 49, 53]. The intensity should be tailored to the patient, low-level resistance is preferable. A sensible decision is the use of several assessments (e.g. Karnofsky performance status >70, ECOG performance status scale 0–2/5; cp. **Table 1**) to establish a minimum physical performance [49]. Karnofsky's index, or Karnofsky Performance Scale, is a widely used assessment to evaluate patients' QoL also in oncologic cohorts. It serves for the classification of functional impairments; the lower the score, the worse the QoL (0 = dead, 100 = no complaints, no evidence of disease) [60]. Score 70 accounts as "cares for self; unable to carry on normal activity or to do active work." ECOG performance status scale differentiates into six grades (0–5; dead-fully active). It is labeled as a standard criterion to measure the impact of certain diseases on ADLs and is widely used in trials [61].

Loading to the area in question, i.e. the BM should be minimized, overflowing pressures from the limbs to spine BM must be considered. To diminish loading of the affected sites [44], exercise selection is restricted so that lesions are subjected to minimal physical forces only [53]. Compressive loads, shear loads, and peak forces similar to walking should be chosen [46]. Using an orthopedic corset during exercise may improve feasibility and safety for the spine.

Miramini et al. reported on fracture healing by combining a model of a plate-locked tibia with a musculoskeletal model of the leg. Both lateral and vertical components of loads were considered, the latter having several detrimental effects on the healing process. The calculations under partial weight bearing of the leg in question stayed below the threshold of a 10% bone strain [62]. It is to note, that this was a calculation model without taking BM into account. Even more, the assumed atrophy of spine muscles can interrupt the former balance between a specific load and a subsequent following muscle contraction and lead to stability loss of several segments. Considering those arguments, even more caution is required in BM patients.

As compressive strains are comparably lower with lesser percent of the maximal voluntary contraction [63], this is a reason for moderate intensity. It was shown that trunk stability was best when pulling upward. Antagonistically, spinal loads peaked under forces at higher elevations and inclinations downward. Abdominals and local lumbar muscles play an important role in maintaining stability while applying horizontally oriented forces [64]. Agonists and antagonists must interact during contraction to ensure (a) driving the movement and (b) protecting the joint and giving accuracy to the movement in question.

Fifty seven PC BM patients at the spine, femur, ribs, humerus, etc., were included in a 12-week intervention program (combined aerobic, RT and flexibility) for trunk, upper and lower limbs involving large muscle groups. Three sets with 10–12 repetitions were executed (chest press, seated row, leg extension, leg curl, etc.) trying to avoid loading of individual bone lesions. The leg-extension 1-RM was omitted in femoral BM and the chest-press 1-RM in humerus/rib/thoracic spine BM. With an adherence rate of 89% and 49 patients at follow-up, no adverse events were observed and bone pain was not exacerbated [44].

Sprave et al. and presumably later Rosenberger et al. subjected the same 60 patients to free spinal stabilization exercises (“all fours, plank, swimmer, shoulder blade TheraBand”) vs. muscle relaxation. The training started with 2 weeks supervised sessions and commenced with three unsupervised months. Patients were advised to hold each position for 20 sec, and the time was subsequently enhanced, if possible. They tested the maximum plank holding time and the handgrip strength, the former showing significant differences in group comparison. No training-related SREs were reported in either group. The exercises needed modification in different percentages because of patients’ inability to perform them (13, 42, 54 and 25%, respectively). Exercises that required moving to the floor were reported to be difficult to perform but could greatly enhance patients’ self-confidence. They concluded that close supervision is indispensable in the beginning [50, 65].

Resistance training vs. passive therapy was tested in patients with spinal BM receiving radiotherapy and led to significant improvements in bone density after 3 and 6 months. Several pathological fractures occurred but could not be related to the intervention and furthermore also in the control group without a difference to the exercise group [54]. The pain was significantly lower in the intervention group after 3 and 6 months, respectively [66]. As the inclusion criteria, the intervention, and the number of patients are astonishingly similar, albeit with different outcomes (bone density, pain, QoL, fatigue, biomarkers), six papers in total, four in the same year, some sort of salami publication must be suspected in these cases.

In a scoping review, 26 studies were screened, 12 of these included patients with BM, and none reported any SRE. Eight trials measured muscle strength and found positive results. They reported that exercise adherence was comparable in supervised and home-based protocols. Pain is the most common symptom of BM and should therefore be a standard outcome [36].

The existence of motor overflow, that is involuntary muscle contractions in other body parts following a voluntary strain deserves some attention in RT for BM patients. Motor overflow is even more pronounced if the task, i.e. contraction proofs to be difficult or if weakness or fatigue is a co-factor [67]. All limitations apply to this patient cohort. Exercise instructors should bear in mind that the intended exercise may give overflowing strain to the bone lesion in question.

5. Measurements

5.1 Pain

Bone pain can be measured by Functional Assessment of Cancer Therapy Bone Pain Questionnaire (FACT-BP) with 16 items where higher scores depict lesser bone pain and better QoL. Another revised version with 20 items tried to include the

potential impact of pain on daily functioning. Also, the Brief Pain Inventory (BPI), which has 11 questions on pain severity, pain site, relief and interferences, can be used as a patient-related outcome. Comparing both reveals that FACT-BP gives more details on function and includes pain-related psycho-social aspects [68]. The Visual Analog Scale can assess pain via a subjectively measured pain level, which should be noted, as well as the analgetic medication dosages taken [65].

5.2 Strength

Manual muscle testing using a 6-point scale (0–5) is commonly used in practice but lacks reliability and differentiation between moderate and normal strength. Furthermore, maximal resistance tests may be contraindicated, as has been shown. Submaximal exercise testing works with percentages of the 1-RM. In this model, eight or 12 repetitions are equivalent to about 80% or 70% of maximal strength, respectively [69]. The gold standard, isokinetic dynamometry, offers better reliability, and both, isometric and isokinetic strength can be measured. It requires of course more time and financial investments. Measuring isokinetic strength is the means to gain insight into the patient's ability to perform ADLs [70].

The evaluation of muscle strength is possible via a handgrip dynamometer [56]. As poor handgrip strength in cancer patients is correlated with poor QoL and cancer-related fatigue, this may be a feasible and inexpensive test for clinical practice [71]. Three repetitions of the test and a calculated mean of these results is the best method. A drawback in BM patients is not only that it should not be performed with lesions in the ulna and radius, which are rare, but patients may also have problems with handgrip because of chemotherapy-induced polyneuropathy. Bioelectrical impedance can objectively inform of body composition, that is, lean mass. It is used to detect sarcopenia in cancer cohorts; it is non-expensive and quick [72].

5.3 ADL

Additional possible measurements should consider the connection between strength and functional activity. Therefore, assessments such as the 5-chair-rise test for lower limb strength and balance, the Timed-up-and-go test (TUAG) as a prediction for falls, or timed walking tests are conceivable in cancer cohorts. The TUAG can assess mobility and dynamic balance not only in older adults but also in cancer patients with similar cut-off values [73]. Although not tested in a cancer cohort, the 5-chair-rise test could inform on knee extensor strength while putting emphasis on a very functional daily activity and is correlated to mobility and potential falls [74].

The deleterious impact of BM with symptoms such as pain, limited strength and QoL leads to impaired activities and social avoidance. Tools such as the original or revised International Physical Activity Questionnaire (IPAC) can be used complementary. The revised version includes people with physical disabilities better, which may be favorable in BM patients [75, 76].

5.4 QoL

VAS can be used to assess QoL in cancer populations [77] as a stand-alone measure [78]. It provides faster results than questionnaires with good validity and excellent reliability [79]. We should not forget that a QoL assessment may be biased because of

other complaints or disease progression. If using QoL questionnaires, e.g. the EORTC QLQ-C30 which is applicable in all cancer patients, a specific look into various domains is recommended.

6. Practical applications

Herman is a 74-year-old cancer patient. In 2015, he was diagnosed with prostate cancer. This was treated successfully by radical prostatectomy. In 2022, after years of unrecognized gastroesophageal reflux disease complaints, he was confronted with his second tumor diagnosis: esophageal cancer. As the tumor was unresectable, the approach was radio-chemotherapy. Despite this, the disease progressed into BM in the thoracic spine. After the prescription of home-based physiotherapy because of his weak condition and a pre-treatment assessment (anamnesis, hospital charts, vital signs, activities of daily life and overall strength), the therapy plan included resistance training, mobilization and walking exercises supplemented by a rollator. RT comprised of elbow extension (supine, shoulder in 90° flexion) with small dumbbells (1 kg) with both arms alternatively with seven repetitions and three series (cp. **Figure 2**).¹ After teaching him how to stabilize his trunk in an upright sitting position (90° hip and knee flexion, feet placed soundly on the ground) by activating abdominals, he was instructed to strengthen his Latissimus dorsi bilaterally by extending and internal rotating his arms with a rubber band as a resistance tool. He managed to perform five repetitions in three series (cp. **Figure 3**). Thirdly, in a standing position, he executed high squats while supporting his weight with his arms on



Figure 2.
Triceps resistance training through elbow extension.

¹ To keep his privacy, pictures were taken with another person.



Figure 3.
Latissimus dorsi resistance training through arm extension/internal rotation.

a shelf and keeping the trunk straight (four repetitions, three series; approximately 30° hip and knee flexion). Between sets he paused for a minute and sat down after each squat series. The movements were slowly, all concentric muscle contractions were combined with an expiration. The choice of these exercises was guided by their relevance to keep him self-supported for transfers, to facilitate moving in bed and to/from a chair or the toilette and finally to relieve his nursing wife as much as possible. Herman was treated weekly, ten times, for 45 minutes each session. The strength of his arms was satisfactory; repetitions of elbow extension and arm extension could be slowly enhanced to 12 and 8, respectively. Conversely, leg strength declined, and it was decided to suspend the squat exercises. Despite radiation therapy, tumor growth of the spine BM led to the development of an incomplete paraplegia of the lower limbs. Consequently, he could not stand any more nor move his legs actively while sitting or lying. After 2 months of home-based physiotherapy, he was admitted to a palliative ward because his wife could not bear the responsibility of home nursing any longer. This was a shared decision made by himself, his wife, his daughter and the physiotherapist.

7. Conclusion

A key message is that patients with BM should regularly engage in exercise, and RT can also be recommended. To achieve this, they need the support and guidance of health care staff. Before starting the exercise, possible benefits must be

counterweighed against theoretical SREs. Exercise prescriptions and RT are safe in individuals with BM, but adaptations to regular RT are needed.

For future trials and for prescribing and implementing safe environments for BM patients several adjustments are necessary. SREs must be a target outcome, and information must be given on whether or not SREs are related to the intervention. Pain as the chief complaint should be an outcome. The effect on outcomes such as pain, pain medication or bone density needs to be proved in future trials because existing studies often lacked power to elaborate this. It is not possible to exclude several confounders e.g. pain medication or radiation therapy, therefore, results need to be interpreted with caution. Bone density as an outcome needs time to change, therefore, longer follow-ups are needed. Specifics on existing BMs must be thorough (location, number, size, status, screening and imaging, treatments). Adaptations to testing and exercise must be patient-centered and individualized. Exercise prescriptions must include the necessary details to copy them for one's own patients. The graveness of the diagnosis and the disease's course calls for some "protocol violation," as exercises, positions and strength training components must be held flexible to meet patients' needs and to fulfill safety requirements. So, even future trials may be more methodologically pragmatic than explanatory.

For trials, a substantial loss to follow-up must be considered because of the course and severity of the primary disease. To counteract this unavoidable fact, patient numbers must be increased, and trials must be multi-centered to reach sufficient power.

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Resistance Training - Bridging Theory and Practice explores the multifaceted benefits of resistance training. It highlights its profound impact on health, recovery, and overall well-being, making it indispensable for athletes and individuals with specific health conditions. Adequately prescribed and executed, resistance training enhances physical functionality, prevents chronic diseases, accelerates recovery, and promotes mental health across all life stages. Grounded in the latest scientific evidence, this book offers a comprehensive guide for sports science and health professionals, covering fundamental principles, innovative approaches, and therapeutic applications. It underscores the crucial interplay of training, recovery, and nutrition in optimizing results for diverse populations. For athletes, resistance training becomes a cornerstone of peak performance, tailored to seasonal demands and specific sports. It emerges as a powerful rehabilitative tool for those with health challenges, fostering recovery and quality of life. The book explores the role of resistance training in addressing conditions like age-related diseases, mental health disorders, and even complex issues such as pulmonary hypertension and bone metastases. It advocates for a holistic approach that integrates exercise, nutrition, and recovery, emphasizing sustainable and individualized solutions. Whether you're seeking to refine training methodologies or discover innovative strategies for contemporary challenges in elite sports and rehabilitation, this book provides the knowledge and inspiration to bridge the gap between theory and practice, ensuring resistance training is a transformative tool for health, performance, and longevity.

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