Review

A Narrative Review of Sarcopenic Obesity in the Elderly: Consideration of Etiology and Treatment Strategies

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Abstract: With the aging of the population, the decline in skeletal muscle function (sarcopenia) and the accumulation of fat mass (obesity) emerges as significant contributors to impairing the daily activities of older adults, leading to increased susceptibility to various diseases. The escalating prevalence of sarcopenic obesity (SOB) is now recognized as a major public health concern in geriatric populations. Sarcopenia and obesity share common pathophysiological mechanisms, and their synergistic interaction amplifies the risk of adverse health outcomes. Consequently, effective prevention and intervention strategies are crucial for safeguarding elderly health. This narrative review aims to outline the pathological mechanisms and health consequences of SOB. In addition, it provides an overview of current evidence-based treatment strategies, with a focus on lifestyle modifications and structured exercise regimens. Finally, it explores emerging therapeutics, including nutraceuticals and complementary and alternative treatments, and propose the potential therapeutic effects of the intergenerational benefits of exercise, all aimed at preventing SOB development.

Keywords: aging; sarcopenic obesity; exercise; nutrition

1. Obesity and Sarcopenia in the Elderly

Aging and obesity represent two of the most pressing global medical and socio-demographic challenges [1]. The worldwide population of individuals aged 60 years and older has surged, reaching 1 billion in 2019 and is projected to grow to 1.4 billion by 2030 [2]. As the global population undergoes demographic shift toward an increasingly aging cohort, and as the prevalence of obesity among older adults has demonstrated a discernible upward trend, the age-standardized prevalence is forecasted to increase by 68.3% by 2050, with approximately 1 in 3 adults over the age of 25 will be living with obesity, among whom about a quarter will be over the age of 65 [3]. Globally, these rising rates of obesity and the aging of the population exacerbate mobility limitations, which in turn may synergistically erode independence and compromise quality of life during this prolonged lifespan for older adults [4].

Sarcopenia is a progressive skeletal muscle disorder associated with an increased risk of falls, fractures, physical disability, and death, with its prevalence rising as age advances [5]. Sarcopenic obesity (SOB) is an age-related syndrome defined by the coexistence of sarcopenia (age-associated loss of skeletal muscle mass, strength, and function) and obesity (excess adipose tissue accumulation), which collectively exacerbates physical disability, metabolic dysfunction, and adverse health outcomes in older adults [6,7]. The estimated global prevalence of SOB is approximately 11% among older adults, rising significantly after the age of 70 [8]. Unfortunately, despite its high prevalence, no targeted medical treatments for SOB have been developed to date. Currently, the causal relationship between skeletal muscle dysfunction and dysregulated fat metabolism in SOB pathogenesis remains unclear. However, it is well-established that SOB arises from interconnected pathways, including chronic inflammation (e.g., TNF-α-mediated muscle proteolysis), insulin resistance (IR, which promoting adiposity), and mitochondrial dysfunction (which impairs energy metabolism). These processes form feedback loops: adipokines (e.g., leptin, resistin) secreted by enlarged adipose tissue drive muscle catabolism, while dysfunctional muscle reduces myokine secretion (e.g., irisin), further promoting adipose inflammation and forming a "fat-muscle vicious cycle" [9]. This review aims to outline adipose and skeletal muscle dysfunction in the aging population, explore

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the potential mechanisms of SOB, and provide a theoretical basis and research perspectives for the clinical management of SOB.

2. Age Related Changes in Body Composition

Aging-induced alterations in body composition are driven by multiple mechanisms. Muscle and bone mass peak in adulthood and then gradually decline, whereas fat mass accumulates until around the age of 70 before decreasing [10]. This shift results in weight gain in older adults, primarily due to fat mass rather than lean mass. Notably, most individuals with SOB exhibit sedentary behavior, which exacerbates fat accumulation via reduced daily energy expenditure [11]. Excess lipids further infiltrate peripheral tissues, particularly skeletal muscle, where they accumulate as intermuscular lipid droplets containing triacylglycerol or fatty acid derivatives [12]. This contributes to an inflammatory cascade in conjunction with already inflamed adipose tissue, forming a pro-inflammatory loop that impairs myogenesis and promotes multi-organ ectopic fat accumulation.

Furthermore, obesity in older adults instigates skeletal muscle atrophy, oxidative stress, and activation of fibro-adipogenic precursor cells (FAPs), which are crucial for intermuscular adipose tissue (IMAT) formation [13]. In conditions like muscle disuse or aging, the activity of FAPs influences the balance between fibrosis and myogenesis during muscle repair [14]. This imbalance leads to mitochondrial dysfunction and inflammatory processes, thereby promoting IMAT development in sarcopenia [15]. The aging process further affects the function of muscle satellite cells (MuSCs), fibrosis impairs their activity, causes muscle stiffness, and hampers both MuSCs function and myogenesis [16]. This process involves dysregulated protein turnover, which reduces myofibrillar and mitochondrial protein synthesis [17]. Collectively, dysregulation of FAPs and the functional decline of MuSCs, both induced by aging and obesity, underlie age-related shifts in body composition.

3. Biological Pathways to SOB

SOB arises from a combination of factors, encompassing adipose dysfunction characterized by ectopic lipid deposition, lifestyle changes driven by sedentary behavior, and muscle atrophy resulting from inadequate exercise [18]. However, the mechanisms underlying SOB pathogenesis are diverse, complex, and not fully understood. Various factors influencing SOB development in older adults have been studied, including alterations in body composition and mitochondrial dysfunction, disruptions in hormonal and cytokine homeostasis, age-associated systemic inflammation, protein turnover efficiency, gut microbiota dysbiosis, and metabolic impairments and comorbidities (Figure 1). All these factors can interact in complex ways within the skeletal muscles of older adults, ultimately leading to severe adverse consequences.

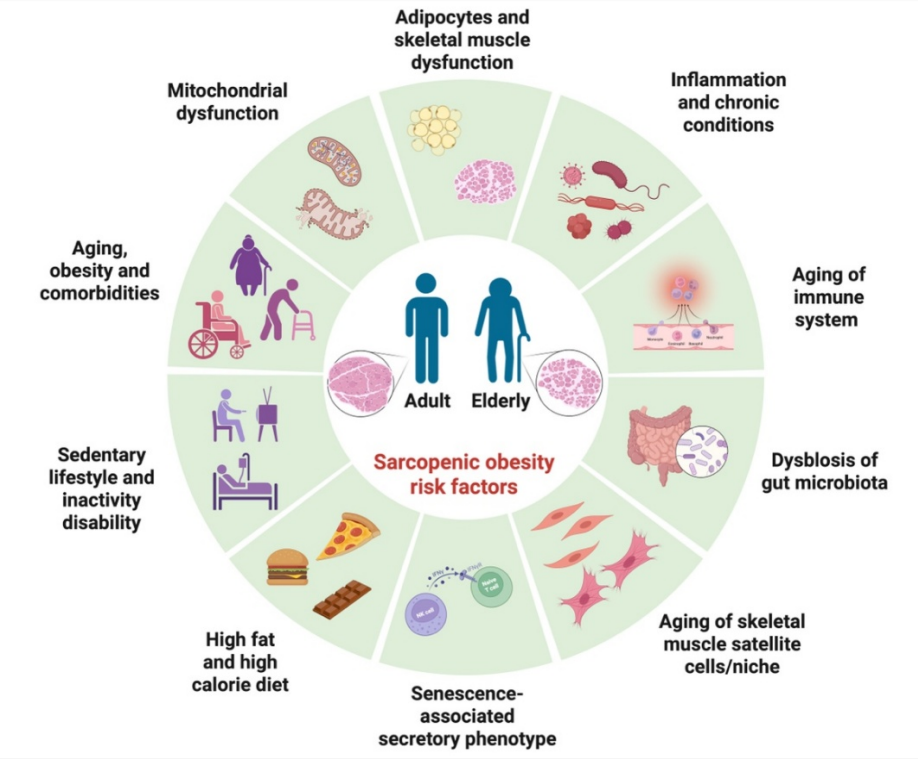

Figure 1. Schematic representation of the pathogenesis involved in SOB.

SOB is driven by core biological factors encompassing age-related alterations in metabolism and body composition, coupled with obesogenic environmental influences and age-related physical diseases. As metabolism undergoes gradual changes over time, it fosters fat deposition, giving rise to pro-inflammatory cascades, gut microbiota dysbiosis, and impaired intestinal permeability. Concurrently, the interplay with biologically active muscle tissue initiates a negative feedback cycle, inducing chronic senescence-associated secretory phenotype (SASP), ultimately culminating in a progressive increase in fat mass as well as a decline in lean body mass and muscle strength.

3.1. Metabolic Disorders and Comorbidities Induced Adipocytes and Skeletal Muscle Dysfunction

Mitochondrial dysfunction and metabolic imbalances caused by obesity are key contributors to the heightened risk of metabolic syndrome [19], which not only impairs muscle contractile function but also correlates with various pathologies, such as oxidative stress and inflammatory cytokine production [20]. Notably, IMAT accumulation impairs insulin action through the release of locally acting adipokines and free fatty acids, which induce pro-inflammatory macrophage activation and p38 mitogen-activated protein kinase (p38MAPK)-mediated IR. This leads to muscle wasting via suppression of phosphoinositide 3-kinase (PI3K)/protein kinase B (PKB/Akt) signaling [21]. Furthermore, IR elevates the phosphorylation level of Forkhead factor protein (FoxO), promoting the expression of E3 ubiquitin ligases atrogin-1 (MAFbx) and muscle ring finger 1 (MuRF-1) by activating the ubiquitin-proteasome pathway, thereby contributing to muscle protein degradation and reducing skeletal muscle mass [22].

Dysregulated adipokine secretion may reduce insulin sensitivity in skeletal muscle and increase food intake. In obesity and metabolic disorders, adipocytes in the adipose tissue undergo hypertrophy and hyperplasia, and are infiltrated by activated inflammatory macrophages and other immune cells [23]. This dysfunctional adipose tissue is characterized by elevated production of circulating proinflammatory molecules and dysregulated production of various adipokines, such as leptin (transcriptionally induced by hypoxia and inflammatory mediators) and adiponectin, causing adverse effects on tissues [24]. Additionally, obesity accelerates the secretion of tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), and C-reactive protein (CRP). These cytokines induce SOB by regulating the secretion of anabolic hormones (e.g., insulin and growth hormone) and promoting skeletal muscle insulin resistance [25].

3.2. Immunosenescence and Senescence-Associated Secretory Phenotype (SASP)

Inflammation can serve as a beneficial and transient, protective immune response to harmful conditions, such as traumatic tissue injury or invading pathogens, supporting tissue repair, turnover, and adaptation. However, aged tissues often exhibit chronic inflammation, which promotes non-infectious degeneration. This inflammatory milieu in aging tissues stems from cellular senescence, a stress-induced state characterized by irreversible growth arrest [26]. Persistent senescent cells drive aging and age-related pathologies through their secretory phenotype. Mechanistically, senescent adipocytes secrete proinflammatory cytokines (comprising the SASP), which remodel the tissue microenvironment and disrupt neighboring cell function [27].

Senescent cell accumulation in tissues accelerates with age, with notable enrichment at sites of age-related pathologies. Clearance of senescent cells in progeroid mice ameliorate several age-related pathologies [28], with studies demonstrate that lifelong ablation of P16Ink4a-positive senescent cells delays the onset and reduces the severity of progression of adipose- and muscle-associated age-related disorders [29]. However, during aging, senescent adipose progenitor cells with SASP secrete pro-inflammatory cytokines at up to 46-fold higher levels [30]. Accordingly, “senotherapy”, which targets senescent adipocytes to delay aging and alleviate tissue dysfunction, has emerged as a promising strategy for SOB treatment.

3.3. Aging of Skeletal Muscle Satellite Cells

Skeletal muscle consists of terminally differentiated multi-nucleated myocytes and mitotic mononuclear cell populations within the interstitial microenvironment, which play pivotal roles in tissue homeostasis and adaptation [31]. MuSCs, the resident skeletal muscle stem cells, are crucial for postnatal development, skeletal muscle hypertrophy before maturity and regeneration across the lifespan [32]. Under homeostasis, MuSCs proliferate sporadically primarily via asymmetric division to replace daily damaged myofibers and maintain the stem cell pool [33]. Upon tissue injury, however, these cells are rapidly activated, undergoing symmetric divisions to generate self-renewing stem cells and proliferating myoblasts. The myoblasts then differentiate into myocytes, thereby facilitating muscle fiber regeneration [32].

Aging profoundly impairs skeletal muscle regenerative capacity, disrupting the balance of cell quiescence, proliferation, and apoptosis [34]. This decline begins in early muscle aging, progresses time-dependently, and culminates in advanced age, when MuSCs enter a pre-senescent state [35]. Although senescent MuSCs may not single-handedly drive sarcopenia, their dysfunction exacerbates muscle fibrosis and compromises injury recovery in older adults [36]. Recent studies reveal transcriptional and epigenetic alterations in senescent MuSCs, including enhanced chromatin repression and genome-wide H3K27me3 deposition [37]. These changes dysregulate signaling pathways essential for muscle regeneration. Moreover, p38α/β-MAPK hyperactivity in senescent MuSCs reduces self-renewal capacity, induces P16Ink4a (a CDK inhibitor), and drives "geriatric" MuSCs from reversible quiescence to irreversible senescence [38]. Additionally, senescent MuSCs exhibit decreased Sprouty1 (Spry1), an inhibitor of fibroblast growth factor (FGF) signaling, leading to loss of low-cycling satellite cells and further regenerative decline [39].

MuSCs reside in a specialized niche between the muscle sarcolemma and myofiber basal lamina, a microenvironment that maintains MuSCs identity and enables robust regenerative responses to injury [40]. During aging, both the structural and molecular components of this niche deteriorate, compromising MuSCs function. Heterochronic parabiosis experiments in mice have shown that aging-derived systemic factors impair the regeneration capacity of MuSCs [41]. Specifically, age-induced fibronectin depletion impairs senescent MuSCs adhesion to the niche [42]. Collectively, dysfunction of senescent MuSCs and their niche contributes to loss of skeletal muscle mass and function in older adults.

3.4. Gut Microbiota Composition and Diversity

The impact of gut microbiota on health becomes particularly relevant for older individuals, as changes in the intestinal microbiota with aging can contribute to various age-related degenerative diseases, encompassing impaired immunity, sarcopenia, and cognitive dysfunction, all integral aspects of frailty [43]. Culture-dependent and culture-independent analyses reveal that there are distinct gut microbiota profiles between young and older adults. Aging is associated with reduced microbiota diversity, decreased levels of saccharolytic bacteria, and increased levels of proteolytic bacteria [44]. These changes manifest as decreased core species abundance, expanded subdominant taxa, elevated *Proteobacteria*, reduced *Bifidobacteria*, and a lower Firmicutes/Bacteroides (F/B) ratio. Such age-induced modifications increase intestinal mucosal permeability, promoting systemic absorption of bacterial products (e.g., lipopolysaccharide, LPS), which in turn elevates pro-inflammatory cytokines and impairs muscle function [45]. Additionally, aged microbiota diminish short-chain fatty acid (SCFA) production, reducing mitochondrial fatty acid oxidation and promoting intramuscular adipose accumulation [46].

A critical aspect of sarcopenia and physical frailty is the decline in muscle strength, which contributes to the age-related deterioration in physical performance. Emerging evidence suggests dysbiosis-induced elevation of LPS may interfere with retinoic acid signaling through the generation of reactive oxygen species (ROS) and modulation of antioxidant genes (Nrf2, AKR1B10). This disruption impairs muscle progenitor cell differentiation and promotes production of toxic bacterial metabolites (e.g., indoxyl sulfate), which exacerbate skeletal muscle dysfunction [47]. Indoxyl sulfate further activates the ROS-ERK and JNK-MAFbx pathway, upregulates myostatin and atrogin-1, disrupts mitochondrial function, and elevates pro-inflammatory cytokines [48]. Collectively, aging- and obesity-related gut microbiota dysbiosis influences muscle mass and function through mechanisms involving protein metabolism, inflammation, immunity, and SCFA metabolism. This establishes a gut-muscle axis that directly contributes to sarcopenia, ultimately impacting host physiology.

4. Treatments for SOB

SOB leads to simultaneous declines in skeletal muscle mass and strength, accompanied by increased ectopic fat accumulation, thereby exacerbating age-related degenerative diseases. Current therapeutic strategies for SOB primarily focus on improving quality of life via lifestyle modifications (e.g., exercise and dietary interventions) and targeted palliative care for immobilized patients (Figure 2). Identifying effective strategies to enhance skeletal muscle function, reduce ectopic lipid deposition, and promote overall muscle health in older adults is therefore a critical therapeutic priority.

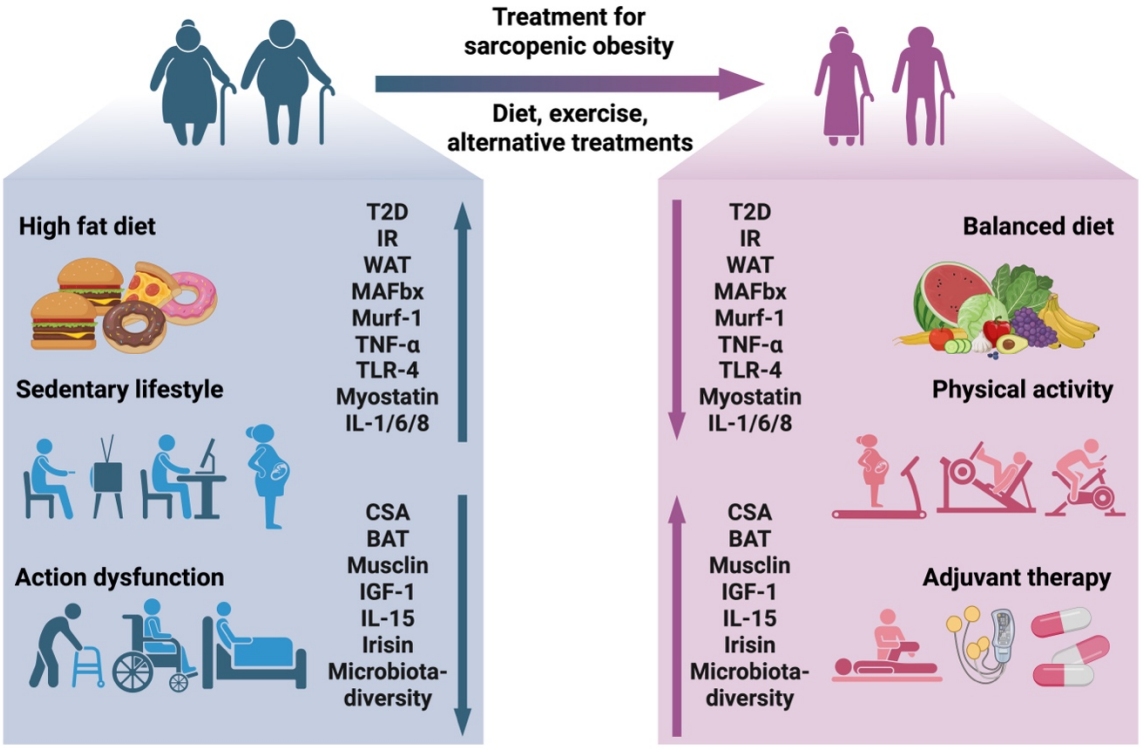

Figure 2. Schematic representation of the therapeutic strategies targeting SOB. Abbreviations: T2D—type 2 diabetes, IR—Insulin resistance, WAT—white adipose tissue, MAFbx—E3 enzyme atrogin-1, Murf-1—muscle ring-finger protein-1, TNF-α—tumor necrosis factor alpha, IL-1, 6, 8 ,15—interleukin-1, 6 ,8, 15, CSA—cross section area, BAT—brown adipose tissue, IGF-1—insulin-like growth factor-1.

4.1. The Role of Exercise

Exercise has long been recognized for its positive impact on enhancing physical fitness and maintaining health, particularly in individuals affected by sarcopenia and obesity [49]. Regular moderate-intensity exercise serves as a validated strategy for both prevention and treatment of numerous diseases, and plays a pivotal role in healthy aging [50]. The following section explores the efficacy of different exercise modalities, alone or in conjunction with dietary interventions, for managing SOB. Table 1 provides an overview of studies examining exercise-based interventions in SOB.

Table 1. Exercise enhances body composition and physical performance in individuals with SOB.

Study	Participants /Age	Exercise Prescription Details		Intervention Effect	Study Type
Dieli-Conwright, C.M., et al. [51]	100/43–63	Exercise modality: Combined aerobic training (AT) and resistance training (RT).		Compared with usual care, SOB is significantly improved following AT combined with RT (appendicular skeletal mass index, $p = 0.001$; body mass index, $p = 0.001$.).	Randomized controlled trial (survivors of Breast Cancer)
		Exercise intensity and duration	AT: Treadmill walking/ running, rowing machine, or stationary bicycle. Heart rate was monitored throughout the aerobic sessions to maintain the maximum heart rate (HRmax) at 65% to 80%. AT was increased from 30 min (week 1) to 50 min (week 16).		
			RT: Initial resistance was set at 80% of the estimated one-repetition maximum (1 RM) for lower-body exercises and 60% estimated 1 RM for upper-body exercises. Weight was increased by 10% upon completion of two consecutive sessions in which three sets of 10 repetitions were performed at a set weight.		
		Exercise frequency	150 min of AT and 2 to 3 days of resistance exercise training per week. Participants received three supervised one-on-one exercise sessions per week. Days 1 and 3 endorsed resistance and aerobic exercise of approximately 80 min, and day 2 included approximately 50 min of aerobic exercise.		
		Exercise period: 16 weeks.			

Table 1. *Cont.*

Study	Participants /Age	Exercise Prescription Details		Intervention Effect	Study Type
Chen, H.T., et al. [52]	60/65–75	Exercise modality: RT, AT and combined training (CT).		Older adults with SOB who engaged in the RT, AT, and CT interventions demonstrated increased muscle mass and reduced total fat mass compared with those without training. The muscle strength performance and serum IGF-1 level in trained groups, especially in the RT group, were superior to the control group.	Randomized controlled trial (Older men and women with SOB)
		Exercise intensity and duration	RT: Progressive resistance load training was used at 60–70% of 1 RM with a qualified professional trainer, in which the difficulty of the exercise was adjusted every 2 weeks in ascending order from simple to difficult.		
			AT: The AT group engaged in moderately intense AT in two 60-min sessions per week, which consisted of 5–10 min of dynamic stretching and warm up and 40–45 min of the actual training.		
			CT: The CT group engaged in identical, but separate, RT and AT with a qualified professional trainer.		
		Exercise frequency	RT: The total training time was 60 min with 48-h interval for each training session; AT: the total training time was 60 min and in two sessions per week; CT: performed each training mode once a week with the AT following 48 h after the RT.		
		Exercise period: 8 weeks.			
Huang, S.W., et al. [53,54]	56/62–72	Exercise modality: Elastic band resistance training (ERT).		ERT significantly improved the muscle mass, quality, physical function, bone mineral density and reduced fat mass of elderly women with SOB.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	Progressive ERT were performed using TheraBand with different degrees of elasticity, and the Borg scale was used for RPE during training. For each movement, initially use the lowest elasticity TheraBand to perform 3 sets slowly, with 10 repetitions in each set, and carry out gentle concentric and eccentric contractions throughout the entire range of motion. When patients can reach the perceived yield strength corresponding to the RPE scale grade 13 (representing moderate-intensity exercise), the intensity of exercise will increase. Each training session comprised a 10-min warm-up, 40-min period of elastic resistance exercises, and 5-min cool-down period.		
		Exercise frequency	Each patient underwent 3 training sessions every week, yielding a total of 36 sessions.		
		Exercise period: 12 weeks.			
Park, J., Y. Kwon, and H. Park. [55]	50/68–80	Exercise modality: CT (include AT and RT).		The 24-week combined exercise effectively reduced carotid intima-media thickness, increased carotid artery flow velocity and wall shear ratio, and decreased the risk of cardiovascular disease in elderly women with SOB.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	RT: Performed with elastic band exercises (TheraBand) for 12 items (the intensity of the exercise was not described), 8–15 repetitions per set (in weeks 1–12, 8–11 repetitions per set; in weeks 13–24, 12–15 repetitions per set), 2–3 sets (1 min rest between sets).		
			AT: Performed with various walking activities, with a RPE in the 13–17 range (in weeks 1–12, 13–15 RPE; in weeks 13–24, ≥15 RPE).		
		Exercise frequency	RT: Each patient underwent 20–30 min per session for 3 days per week.		
			AT: Each patient underwent 30–50 min per session, 5 days per week.		
		Exercise period: 24 weeks.			
Vasconcelos, K.S., et al. [56]	28/65–80	Exercise modality: RT.		Progressive resistance exercise program is ineffective in improving physical function in older women with SOB.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	RT includes open chain and closed dynamic chain exercises (the intensity of the exercise was not described). Each class consists of a 5-min warm-up walk and stretching exercises, followed by formal training. During the first four weeks of the intervention, the training plan emphasized muscle strengthening and endurance, with low-speed concentric and eccentric movements. Then, starting from the fifth week, participants were instructed to practice the concentric movement "as quickly as possible". From the seventh week to the tenth week, high-speed centripetal and centrifugal movements are carried out. Resting time of 30 s between sets and 60 s between exercises.		
		Exercise frequency	Each patient underwent a RT program twice a week, each time for one hour.		
		Exercise period: 10 weeks.			
Gadelha, A.B., et al. [57]	133/62–72	Exercise modality: RT.		RT induced a significant increase in fat-free mass but no reduction in fat mass.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	RT program followed a progressive intensity increase, with training loads equal to 60% of 1 RM in the first four weeks, 70% in the following four weeks, and 80% in the remaining 16 weeks, with repetitions respectively decreased from 12, 10 and 8.		
		Exercise frequency	Each patient performed RT sessions 3 times per week, with each exercise conducted in 3 sets and approximately 1 min of rest between sets.		
		Exercise period: 24 weeks.			

Table 1. *Cont.*

Study	Participants /Age	Exercise Prescription Details		Intervention Effect	Study Type
Liao, C.D., et al. [58]	46/62–72	Exercise modality: ERT.		ERT exerts significant beneficial effects on body composition, muscle mass, and physical function in patients with SOB.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	Progressive ERT were performed using TheraBand with different degrees of elasticity, and the Borg scale was used for RPE during training. For each movement, initially use the lowest elasticity TheraBand to perform 3 sets slowly, with 10 repetitions in each set, and carry out gentle concentric and eccentric contractions throughout the entire range of motion. The exercise intensity was increased when the patients could yield their perceived exertion on the RPE scale. Each exercise session involved a general warm-up of 10 min, followed by resistance training exercises (35–40 min), and finally a cool-down routine.		
		Exercise frequency	Each patient underwent 3 training sessions every week, yielding a total of 36 sessions.		
		Exercise period: 12 weeks.			

Abbreviations: RT—resistance training, AT—aerobic training, CT—combined training, ERT—Elastic band resistance training, HRmax—maximum heart rate, RM—repetition maximum.

SOB is characterized by adipocyte hyperplasia, excessive lipid production, and reduced lipid storage capacity, leading to the release of lipids into the circulation and ectopic accumulation in skeletal muscle through free fatty acids (FAs) [59]. This pathological process induces mitochondrial dysfunction, disrupts β-oxidation of FAs, resulting in lipotoxicity and IR [60]. Aerobic training (AT) drives adaptive remodeling in white adipose tissue (WAT), including reductions in adipocyte size and lipid content, as well as increased expression of mitochondrial proteins [61]. The upregulation of mitochondrial proteins directly enhances mitochondrial structural integrity and quantity, thereby providing more functional units to support oxidative phosphorylation. Concurrently, AT activates lipolysis and promotes the expression of metabolic proteins such as GLUT4 and PGC-1α [62]. These changes collectively reduce FA accumulation and mitigate lipotoxic damage to skeletal muscle mitochondria. Notably, skeletal muscle functions as a secretory organ, but aging diminishes the secretion of most beneficial myokines while increasing levels of IL-6 (a pro-inflammatory cytokine) and myostatin (a muscle growth inhibitor) [63]. AT reverses this age-related shift by stimulating the release of beneficial myokines, such as adiponectin, transforming growth factor-β2 (TGF-β2), leptin, and osteocalcin, which indirectly support the maintenance of mitochondrial function and the balance of oxidative metabolism [64,65]. However, the specific role of these myokines in SOB management remains to be further elucidated.

Resistance training (RT) serves as a critical intervention strategy targeting the core "sarcopenia" feature of SOB, its mechanisms primarily centered on promoting skeletal muscle protein synthesis, increasing skeletal muscle mass, and repairing age-related impairments in muscle regenerative function. From the perspective of directly promoting muscle protein synthesis, RT delivers mechanical stimulation to skeletal muscle, activating intracellular signaling pathways [49]. This activation upregulates the expression of genes associated with protein synthesis, directly driving myofiber hypertrophy and an increase in skeletal muscle mass. Notably, even low-load RT exerts marked effects in alleviating sarcopenia [66]. In terms of repairing muscle regenerative capacity, aging and sarcopenia impair the proliferation and functional activity of MuSCs, weakening the adaptive response of skeletal muscle to exercise stimuli in older adults [67]. This impairment is likely due to the age-related reduction in Growth Differentiation Factor 11 (GDF11) [68]. Previous studies have demonstrated that RT upregulates the expression of GDF11 and Notch, inhibits the expression of myostatin, and restores the function of aged murine MuSCs [69,70]. Furthermore, regular RT can stimulate the release of beneficial myokines in the skeletal muscle of aged mice, promoting skeletal muscle protein synthesis, which in turn alleviates the decline in skeletal muscle mass caused by aging [64,65]. Together, these changes reduce muscle breakdown, enhance the balance of skeletal muscle protein synthesis, and help restore muscle mass in patients with SOB. Although existing studies have confirmed that RT can regulate MuSCs function through pathways such as GDF11 and Notch signaling, there are still numerous unknowns regarding the specific effects of RT on MuSCs in the context of SOB.

Resistance, aerobic, and combined training programs have demonstrated benefits for community-dwelling older adults with SOB, including reduced body fat, enhanced muscle function, and improved metabolic or cardiovascular parameters [51–54,58,71]. Notably, inconsistencies exist between studies, such as Liao et al.'s [54,58] finding that 12 weeks of elastic resistance training (ERT) improved body composition and function, versus Vasconcelos et al.'s [56] observation that a 10-week unspecified RT program failed to improve physical function in older women with SOB. Potential reasons for this discrepancy include differences in intervention duration (10 vs. 12 weeks), training modalities (ERT vs. unspecified RT), and participant characteristics (e.g., baseline function, SOB severity), though subgroup

analyses are lacking to clarify these differences. These inconsistencies highlight the need for standardized protocols in future studies, including clear definitions of training intensity, progression, and outcome measures, to definitively establish the efficacy of RT for SOB. Subsequent investigations should design SOB-specific research protocols to explore the association between the two exercise types and MuSCs function regulation, providing more precise mechanistic support for optimizing exercise intervention strategies for SOB.

4.2. Nutritional Strategies

Sarcopenia is linked to inadequate nutritional intake, while obesity arises from excessive energy consumption, resulting in an imbalance between caloric intake and expenditure. Current interventions for SOB focus on maximizing fat loss while preserving lean tissue mass and function. Dietary strategies should therefore optimize nutrient delivery to support skeletal muscle anabolism, prevent muscle atrophy, and avoid caloric surpluses that contribute to adipose tissue accumulation.

4.2.1. Calorie Restriction

Calorie restriction, primarily used for weight loss and body composition modulation, aims to achieve a 5–8% initial body weight reduction, with daily caloric deficits controlled at 500–1000 kcal [72]. For elderly individuals with SOB, optimal and safe energy restriction ranges from 200 to 700 kcal per day [73]. While low-calorie diets effectively reduce fat mass in obese older adults, they often accompany a decrease in skeletal muscle mass [74]. For instance, following a hypocaloric diet (500 to 750 kcal/day) for 52 weeks, obese older adults experienced an average fat mass loss of 7.1 kg but also an additional 3.2 kg skeletal muscle mass loss [75]. This muscle loss is detrimental, particularly for maintaining mobility. Studies suggest acute calorie restriction downregulates muscle protein synthesis and increases proteolysis [76]. Conversely, long-term calorie restriction may potentiate muscle protein synthesis [77]. Therefore, for the elderly with SOB, calorie restriction needs to be gradual and adjusted in real time based on BMI.

4.2.2. High Protein Diet

In addition to fat mass loss from hypocaloric diets, elderly individuals with SOB should combine such diets with high protein intake and trace element supplementation. It is well established that the intake of dietary amino acids, and especially the essential amino acids, has a positive effect on the muscle synthesis in elderly adults [78]. However, older adults and obese individuals exhibit a blunted protein synthesis response to anabolic stimuli (e.g., dietary protein), necessitating higher protein requirements in obese older adults compared to younger lean individuals to optimize muscle protein synthesis and preserve muscle mass [79]. That said, the potential benefits of targeted nutritional supplementation and high-protein diets in supporting skeletal muscle anabolism in this population may be influenced by factors such as baseline nutritional status, physical activity levels, and underlying health conditions in SOB patients.

Additionally, distributing protein intake evenly throughout the day or timing it strategically around main meals has been shown to stimulate skeletal muscle protein synthesis in patients with SOB [80]. A dietary intervention study of 104 obese adults (>65 years of age) with sarcopenic disease showed that a 3-month low-calorie, high-protein diet (1.2 g/kg body weight) resulted in an increase in muscle mass index [81]. However, high protein intake during a calorie-restricted diet may undo the positive effects of weight loss on insulin sensitivity in skeletal muscle [82]. Therefore, when formulating dietary guidelines for older adults with SOB, it is essential not only to emphasize the role of macronutrients in the diet but also to highlight the need for further research to determine optimal dosages, timing, and individual responsiveness.

4.2.3. Micronutrients

Regarding micronutrients, low intake and status of multiple micronutrients have been associated with sarcopenia development in older adults, particularly in obese individuals, who exhibit heightened risk of micronutrient deficiency. Studies indicate magnesium, selenium, and calcium may be key nutrients for sarcopenia prevention/treatment, though further randomized controlled trials are needed to elucidate their effects on skeletal muscle health in older adults [83]. Additionally, obese individuals also show lower circulating levels of vitamin B6, vitamin C, 25-hydroxyvitamin D, and vitamin E compared to normal-weight adults, rendering them more susceptible to micronutrient deficiencies following weight-loss diets [84]. A systematic review found that daily supplementation with 1200 mg calcium and 800–1000 IU vitamin D3 mitigates risks associated with SOB [85]. Vitamin D supplementation may improve muscle function and alleviate proximal muscle weakness in SOB via

vitamin D metabolite actions [86]. Collectively, micronutrient deficiencies may serve as biomarkers for predicting frailty and sarcopenia progression in older adults.

4.2.4. Efficacy of Other Nutraceuticals

In addition to the aforementioned therapies for SOB, various nutraceuticals exhibit promising therapeutic potential. Studies show that polyphenols and green tea extract (GTE) possess anti-inflammatory and antioxidant properties, thereby enhancing mitochondrial function, regulating skeletal muscle glucose metabolism, and inhibiting fatty acid synthesis [87]. Oligonol, a low-molecular-weight polyphenol from lychee, exhibits anti-inflammatory and anti-obesity properties. It upregulates the expression of PGC-1α and NRF2 related to mitochondrial biogenesis, activating phosphorylated mTOR and related pathways to promote protein synthesis [88]. Epigallocatechin gallate (EGCG), a component of GTE, improves skeletal muscle insulin sensitivity by promoting GLUT4 expression and glycogen storage. EGCG also reduces reactive oxygen species and myostatin expression during aging. Additionally, it increases the expression of mitochondrial cytochrome B and cytochrome C oxidase, thereby enhancing muscle function and quality [89]. S-allylcysteine (SAC), a bioactive compound in garlic, acts as a potential safeguard against muscle atrophy by reducing myostatin secretion, inhibiting TNF-α-mediated proteolysis, and protecting skeletal muscle from inflammatory infiltration [90]. Collectively, these nutraceuticals hold promise as potential therapeutic agents for SOB by mitigating the inflammatory burden of aging and obesity. However, their optimal dosage and potential side effects warrant further clinical investigation.

4.3. Combined Nutrition and Exercise Strategies

A combination of physical activity and dietary intervention has proven to be a more efficacious approach for treating SOB. In a clinical trial involving older adults with obesity, participants followed a hypocaloric diet and engaged in either 60 min of progressive aerobic exercise or resistance training, or 75–90 min of combined aerobic and resistance training, three times weekly. The results showed that the combined aerobic-resistance exercise regimen improved fitness test scores by 14% and 24%, respectively, compared to groups performing aerobic or resistance exercise alone [91]. A systematic review further confirmed that resistance exercise programs paired with dietary interventions yielded greater weight loss than exercise-only strategies and mitigated the loss of muscle and bone mass observed in diet-only groups [72]. Extensive research indicates that high-protein intake or supplementation, when combined with resistance exercise, effectively enhances muscle mass, strength, and physical performance in older adults with muscle wasting [92]. Notably, while exercise alone improves physical function, the synergistic effect of diet and exercise produces more favorable outcomes. A summary of current clinical interventions integrating nutrition and exercise strategies is presented in Table 2.

Table 2. Exercise combined nutrition strategies to improve body composition and physical performance in SOB.

Study	Participants/ Age	Type of Intervention		Intervention Effect	Study Type
Kim, H., et al. [93]	139/>70	Exercise modality: The CT includes weight/equipment-based RT, ERT, stationary bicycle AT, and chair-assisted/standing exercises. Nutrition strategies: Amino acid and Tea catechin.		Exercise and nutrition have beneficial effects on individual variables of body composition, blood composition, and body function, but no improvements in muscle mass were observed in this population.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	AT: The participants pedaled on a stationary bicycle for 12 min, including 1 min of cooldown, starting at 40 watts.		
			RT: Chair exercise. Repetitions of toe raises, heel raises, knee lifts, and knee extensions were performed while seated on a chair (the intensity of the exercise was not described).		
			ERT: ERT were used for upper and lower body strengthening (the intensity of the exercise was not described).		
			Hydraulic exercise machine: The participants rotated training machines between seated row, leg press, abduction, leg extension, and abdominal crunch machines, beginning with one set of 10 repetitions to three sets.		
		Exercise frequency	According to the form of exercise, the exercise group (the exercise plus nutritional supplement group and the exercise alone group) was further divided into four subgroups. Each exercise class lasts for 60 min, twice a week.		
		Nutritional strategies	Amino acid: Packets containing 3.0 g of leucine-enriched essential amino acid (1.20 g leucine, 0.50 g lysine HCl, 0.33 g valine, 0.32 g isoleucine, 0.28 g threonine, 0.20 g phenylalanine, and 0.17 g other) and 20 mg vitamin D were provided for the participants every 2 weeks to be taken daily with water for 3 months.		
			Tea catechin: 350 mL of tea frotified with 540 mg of catechin were given to the participants every 2 weeks.		
		Experimental period: 3 months.			

Table 2. *Cont.*

Study	Participants/ Age	Type of Intervention		Intervention Effect	Study Type
Nabuco, H.C.G., et al. [94]	26/>60	Exercise modality: RT. Nutrition strategies: Hydrolyzed whey protein.		Whey protein combined with RT increased ALST, and decreased total and trunk fat mass, improving sarcopenia and decreasing SOB in older women.	Randomized controlled trial (Older women with SOB)
		Exercise intensity and duration	The RT program consisted of eight exercises, including: chest press, horizontal leg press, seated row, knee extension, preacher curl (free weight), leg curl, triceps pushdown, and seated calf raise. Throughout the entire training process, trainers adjusted the load of each exercise based on the participants' current abilities and improvements in exercise capacity-this ensured that participants could bear the maximum possible resistance while maintaining proper exercise technique. During each training session, the initial load was increased by a range of 2% to 5% for upper limb exercises, and by 5% to 10% for lower limb exercises.	
		Exercise frequency	The sessions were performed 3 times per week on Mondays, Wednesdays, and Fridays.		
		Nutritional strategies	Participants received a dose of 35 g of hydrolyzed whey protein, and the supplements were mixed with non-caloric sugar-free drinks to mask the contents (grape or passion fruit flavor).		
		Experimental period:12 weeks.			
Frimel, T.N., D.R. Sinacore, and D.T. Villareal [95]	30/65–75	Exercise modality: The CT includes flexibility exercises, low-impact AT, high-intensity progressive RT and balance activities. Nutritional strategies: Calorie restriction.		Exercise added to diet reduces muscle mass loss during voluntary weight loss and increases muscle strength in frail obese older adults. Regular exercise that incorporates PRT should be used to attenuate muscle mass loss in frail obese older adults on weight-loss therapy.	Randomized controlled trial (Older men and women with SOB)
		Exercise intensity and duration	Each session consisted of 15 min of flexibility exercises, 30 min of low-impact AT, 30 min of high-intensity progressive RT (65–85% 1 RM, measurements of 1 RM were repeated monthly so that workloads could be progressed for each participant), and 15 min of balance activities.		
		Exercise frequency	Each patient underwent 3 training sessions every week, with each sessions lasting 90 min, yielding a total of 72 sessions.		
		Nutritional strategies	Each patient was prescribed a dietary regimen that created an approximate energy deficit of 750 kcal·d^{-1}. The prescribed diet had a macronutrient composition of 20% protein, 30% fat, and 50% carbohydrates. Each participant's weight-loss goal was set at 10% of their initial body weight, with a maximum weekly weight loss rate capped at no more than 1.5% of body weight.		
		Experimental period: 6 months.			
Villareal, D.T., et al. [91]	141/>65	Exercise modality: RT, AT and CT (include RT and AT). Nutritional strategies: Calorie restriction, calcium and vitamin D supplementation.		Calorie restriction combined with CT group was the most effective in improving functional status of obese older adults.	Randomized controlled trial (Older men and women with SOB)
		Exercise intensity and duration	RT: Each session lasts approximately 60 min and included 10 min of flexibility exercises, followed by 40 min of resistance exercises and 10 min of balance exercises. The initial sessions were 1 to 2 sets of 8 to 12 repetitions at 65% of the 1 RM. This was increased progressively to 2 to 3 sets at approximately 85% of the 1 RM.		
			AT: Each session lasts approximately 60 min and included 10 min of flexibility exercises, followed by 40 min of aerobic exercises and 10 min of balance exercises. The AT consisted of treadmill walking, stationary cycling, and stair climbing. Participants exercised at approximately 65% of their HRmax, which was gradually increased to 70 to 85%.		
			CT: Each session lasts approximately 75 to 90 min long and included 10 min of flexibility exercises, followed by 30 to 40 min of AT, 30 to 40 min of RT, and 10 min of balance exercises. Exercise intensity was consistent with that of the AT group and the RT group.		
		Exercise frequency	Each patient underwent 3 training sessions every week.		
		Nutritional strategies	Each patient was prescribed a balanced diet that provided an energy deficit of 500 to 750 kcal per day and was supplemented with approximately 1500 mg of calcium and 1000 IU of vitamin D daily.		
		Experimental period: 26 weeks.			

Abbreviations: RT—resistance training, AT—aerobic training, CT—combined training, ERT—Elastic band resistance training, HRmax—maximum heart rate, RM—repetition maximum, ALST—appendicular lean soft tissue.

Collectively, for managing SOB, whether used alone or in combination, exercise and nutritional interventions serve as core evidence-based therapeutic strategies. Exercise interventions encompass RT, AT, and CT, among which RT targets the "sarcopenia" component by promoting skeletal muscle protein synthesis, while AT primarily

addresses the "obesity" component by improving mitochondrial function, stimulating lipolysis, and mitigating ectopic fat accumulation to alleviate IR. CT further synergizes these advantages to improve metabolic parameters, cardiovascular health, and physical function. However, inconsistencies in study outcomes highlight the need for developing standardized protocols that define training intensity, duration, and outcome measures. Furthermore, nutritional interventions focus on balancing fat loss with muscle preservation, including calorie restriction and high-protein diets with even daily protein distribution, counteracting the blunted muscle protein synthesis response in older obese individuals. Meanwhile, micronutrient supplementation addresses deficiencies linked to sarcopenia progression, and nutraceuticals show promise by reducing inflammation and improving mitochondrial function, though their optimal dosages require further investigation. Crucially, combining exercise and nutrition yields superior outcomes to single-modal interventions for SOB, while the dose effects of different intervention modalities and their underlying physiological mechanisms require further exploration.

4.4. Physical Interventions: Potential for SOB Management

Aging often induces a progressive decline or loss of physical activity in older adults, a trend that may worsen further following falls, surgeries, or disease complications-thereby reducing participation in exercise programs and creating a vicious circle that aggravates sarcopenia and adipose tissue accumulation. To address these challenges, alternative interventions for SOB must be explored to enhance well-being in older adults. Whole-body vibration (WBV) has emerged as a promising modality to improve postural balance, increase muscle strength, and reduce fall risk in older adults [96]. WBV therapy works by transmitting mechanical stimuli through the body to activate muscle spindles, thereby inducing neuromuscular activation [97]. Studies have shown that 12 and 24 weeks of combined RT and WBV interventions in older women resulted in significant improvements in knee extensor strength, jumping performance, and movement velocity [98]. However, direct comparisons of WBV therapy with exercise or dietary interventions in the context of SOB remain scarce. Most research focuses on integrating WBV with exercise and dietary strategies, which effectively enhances energy expenditure while inhibiting lipogenesis and muscle atrophy [99]. It is crucial to clarify key parameters of WBV therapy for SOB, as this could position it as a viable preventive and therapeutic modality for the condition-while also providing a viable intervention option for patients who have lost the ability to participate in conventional exercise.

Muscle electrical stimulation (MES) has emerged as an effective non-pharmacological modality to prevent skeletal muscle atrophy and dysfunction [100]. A study demonstrated that a 9-week neuromuscular electrical stimulation program significantly improved muscle torque and functional performance in older adults, helping to maintaining skeletal muscle mass and reducing fibrotic changes [101]. While it is known that regular MES induces beneficial effects on muscle mass and performance in aged subjects, current research primarily focuses on functional adaptations related to functional abilities such as muscle strength, balance, mobility, stair climbing, and gait, especially in frail subjects with advanced chronic diseases. The potential structural and functional adaptations induced by MES in clinically healthy older adults, within the broader context of preventing sarcopenia and obesity (independent of chronic diseases), are yet to be fully established. Given its capacity to enhance muscle mass and mitigate atrophy—key to countering sarcopenia—and its potential to complement metabolic regulation (a factor in obesity management), MES may emerge as a promising candidate for a preventive and therapeutic modality for SOB. Advancing our mechanistic understanding of the relationship between MES, muscle mass, and physical activity in geriatric and rehabilitation medicine will be critical to optimizing the treatment efficacy of SOB, as well as rehabilitation programs and fall-prevention strategies for frail or older populations.

5. Exploring a Novel Perspective for SOB Prevention Based on the Intergenerational Effects of Exercise

5.1. Reflections on the Pathogenesis of SOB Based on the Theory of "Developmental Origins of Health and Disease"

Sarcopenia and obesity, though often linked to aging, are increasingly understood as states driven by the intricate interplay between genetic susceptibility and environmental influences—with early-life factors, particularly those tied to the Developmental Origins of Health and Disease (DOHaD) theory, have emerged as critical contributors [102]. The DOHaD framework posits that maternal physiology, metabolism, diet, and lifestyle during pregnancy exert long-term, programming effects on fetal development, altering offspring's risk of chronic diseases (including sarcopenia and obesity) in adulthood [103,104]. This theory bridges the two conditions by highlighting shared developmental roots, as perturbations in the intrauterine environment can disrupt metabolic and musculoskeletal programming, laying the pathological groundwork for both age-related muscle decline (sarcopenia) and adiposity dysregulation (obesity) later in life.

Famine studies provide compelling evidence for this link. The Dutch Hunger Winter study (1945–1946 birth cohort) showed that mid/late-gestation famine exposure was associated with impaired glucose tolerance, while

early-gestation exposure increased BMI and chronic disease risk [105,106]. Similarly, China's 1959–1961 famine demonstrated that intrauterine exposure led to a 1.5-fold increased risk of developing diabetes and a 4-fold increased risk of developing hypertension in middle age [107]. In essence, the DOHaD theory explains that early-life environmental cues may act as potential triggers for sarcopenia and obesity in offspring, with famine studies serving as a stark illustration of how intrauterine stressors propagate intergenerational risk for these interconnected conditions. Concurrently, with the global rise in obesity, the impact of maternal obesity on fetal development and offspring health has attracted substantial attention. A recent meta-analysis of birth cohorts found that higher pre-pregnancy BMI and gestational weight gain elevated the risk of offspring overweight/obesity, with the effects being most pronounced in late childhood (10–18 years of age) [108]. These findings highlight the need for early-life interventions to disrupt intergenerational cycles, as epigenetic modifications stemming from intrauterine stress may perpetuate the obesity epidemic and thereby exacerbate SOB risk in future generations.

5.2. Potential Effects of Maternal Exercise

Parental sensitivity to environmental stimuli drives transgenerational physiological reprogramming in offspring, highlighting the early developmental period as a critical window for lifelong health [109]. As discussed, the risk trajectories for these disorders can be linked to disruptions in growth and metabolic programming during prenatal and early postnatal development [110]. With the rising obesity rates among reproductive-aged men and women, this trend may amplify the risk of SOB development in their offspring across adulthood and aging. This intergenerational risk underscores the need for preventive strategies that target early development, and emerging research points to maternal exercise during pregnancy as a promising preventive intervention.

Maternal exercise during pregnancy has been extensively studied in humans, consistently demonstrating its safety and benefits for both mother and fetus. In obese women, reducing sedentary time during gestation decreases infant adiposity and lowers early childhood obesity risk [111]. This intervention also mitigates hepatic damage induced by maternal high-fat diets, reducing offspring hepatocyte glucose production and upregulating genes expression involved in mitochondrial biogenesis and fatty acid metabolism [112]. More recently, research has demonstrated that maternal exercise stimulates the placental secretion of apelin, and induces DNA demethylation of the PGC-1α and Prdm16, thereby promoting mitochondrial biogenesis and brown adipose tissue (BAT) development [113]. Concurrently, maternal hepatic secretion of superoxide dismutase 3 (SOD3) and vitamin C is upregulated, reprogramming DNA methylation of metabolism-related genes during fetal development [114,115]. These combined mechanisms contribute to reducing offspring obesity incidence. While human studies on adult offspring are limited by generational timeframes, rodent models confirm these metabolic benefits are persistent [116]. Thus, adoption of healthy parental lifestyles and regular exercise may represent a novel strategy with the potential to mitigate the intergenerational transmission of SOB risk to offspring, and large-scale population and epidemiological studies are needed to establish a novel intergenerational framework for age-related skeletal muscle degeneration (Figure 3).

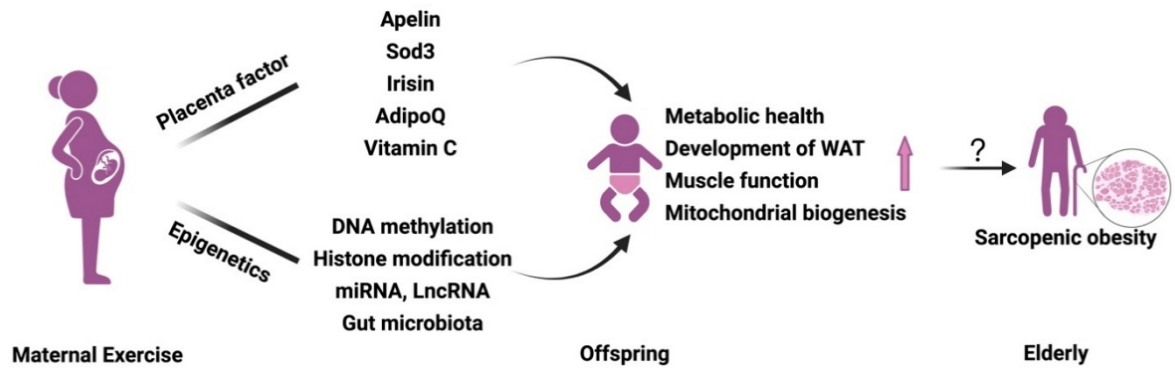

Figure 3. Schematic diagram of maternal exercise promoting the health of offspring.

Regular physical activity during pregnancy promotes offspring health through the secretion of placental factors and epigenetic regulation during offspring development, conferring long-term health benefits. This raises the question of whether maternal or parental exercise can reduce the incidence of SOB in offspring as they age.

6. Future Directions and Conclusions

SOB represents a multidimensional disorder with limited therapeutic options, whereas evidence-based interventions can enhance physical function in older adults. However, the molecular mechanisms underlying SOB remain to be fully elucidated. Future scientific research and clinical practice should establish standardized diagnostic criteria for SOB, integrate clinical practice pathways with basic research frameworks, and conduct large-scale epidemiological studies to precisely define patient populations. Furthermore, given the synergistic deleterious effects of SOB on muscle performance and systemic health, individualized interventions integrating diet, pharmacotherapy, exercise, and adjunctive therapies are essential for affected individuals. Moreover, promoting healthy lifestyles and appropriate physical activity among expectant parents confers both short- and long-term benefits for both maternal and child health. With ongoing research progress, parental physical activity may emerge as a novel primary preventive strategy to mitigate the escalating burden of obesity and age-related diseases, and thereby safeguard the health of future generations.

In conclusion, against the backdrop of global population aging and rising obesity rates, advancing our understanding of SOB pathogenesis and developing effective treatment strategies are critical for promoting healthy aging. Notably, the intergenerational protective impact of exercise on health represents a promising avenue to mitigate the future burden of SOB. However, large-scale preclinical animal studies and prospective epidemiological investigations are essential to validate these potential strategies.

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