Menopause: Highlighting the Effects of Resistance Training

Abstract

The increase in lifespan and in the proportion of elderly women has increased the focus on menopause induced physiological alterations. These modifications are associated with the elevated risk of several pathologies such as cardiovascular disease, diabetes, obesity, hypertension, dyslipidemia, non-alcoholic fat liver disease, among others. Because of estrogen levels decline, many tissue and organs (muscular, bone, adipose tissue and liver) are affected. Additionally, body composition suffers important modifications. In this sense, there is a growing body of concern in understanding the physiological mechanisms involved and establishing strategies to prevent and reverse the effects of menopause. The hormone replacement therapy, diet and physical exercise have been recommended. Among the diverse exercise modalities, resistance training is not commonly used as a therapeutic intervention in the treatment of menopause. Thus, the aim of this review was to analyze the physiological alterations on several organs and systems induced by menopause and ovariectomy (experimental model to reproduce menopause), as well as, to study the effects of resistance training in preventing and reverting these modifications. In conclusion, resistance training promotes beneficial effects on several organs and systems, mainly, on muscular, bone and adipose tissue, allowing for a better quality of life in this population.

Introduction

The increasing proportion of elderly women and their increased life expectancy have raised public health concerns, especially regarding physiological alterations related to the post-menopause period. Approximately 40% of women look for medical care to treat menopause induced symptoms, including: heat waves, night transpiration, vaginal dryness, and sleep problems [46]. Menopause has been associated with an increased risk of coronary artery disease, diabetes, skeletal muscle wasting (sarcopenia), bone mineral mass loss (osteopenia), changes in body composition, lipid profile, fat deposition and increased inflammatory markers [6,9,34,44,60]. There is a growing concern to understand the physiological mechanisms underlying the deleterious effects associated with menopause, and establishing strategies to prevent and reverse these alterations. Thus, hormone replacement therapy, diet and physical exercise have been recommended as treatment components for menopause [36,73,77]. Hormone replacement therapy is widely used to treat the deleterious effects of menopause [11,26,68,70], however there are several risks associated with this therapy in humans, mainly the increased incidence of some types of cancer [72,47]. Therefore, some exercise modalities are recommended to assist in the treatment of menopause, for example, continuous and intermittent exercise (walking and running), flexibility exercises and resistance training. Resistance training has been growing in popularity due to its efficacy and positive results with several pathologies associated with the initiation of menopause, such as osteopenia, sarcopenia, diabetes, cardiovascular disease, and others. However, resistance training is still not routinely used as a therapeutic intervention to prevent and reverse the alterations induced by menopause [9]. Considering this, the focus of this article is to discuss the effects of resistance training to prevent and reverse the several physiological alterations promoted by menopause.
Materials and Methods

The present study included bibliographic research with a descriptive and exploratory basis related to menopause and resistance training. Therefore, the ovariectomy was as experimental method to mimic menopause in animals. To complete the present research, the first step was the identification of pertinent studies by the means of a scientific on-line search. The bibliographic databases used were: Periodicals Capes Portal, Pubmed, Scielo, Highwire, Isi Web of Knowledge, and Lilacs. To perform the search the following descriptors were used: menopause, ovariectomy, exercise, and resistance training. A critical semi-quantitative analysis of the material found in the literature was made, based on the main issues of concordance or discordance between the authors.

Alterations in organs and systems induced by menopause

The epidemiologic literature defines menopause as the period in which an absence of the menstrual cycle (amenorrhea) occurs for at least 12 consecutive months [27]. This process results from a lack of a follicle in the ovary, which is insufficient to maintain the menstrual cycle [84]. This phase defines the ending of a woman’s reproductive period [19]. According to Te Velde and Pearson [79] the age for the initiation of menopause is varies widely between women, and the mean time of occurrence is between 40 and 60 years.

Another important aspect in the characterization of menopause is the natural decline of the ovarian hormones (perimenopause), mainly estrogen [41]. This decline has been associated with increased symptoms of heat waves, night sweats, sleep disturbances, increased urinary frequency, poor memory, anxiety, and depression [28,45]. Furthermore, the scientific literature provides evidence that menopause has an influence on organs and systems [16].

Several physiological alterations have been associated with menopause, such as an increased risk of coronary heart disease [64], diabetes mellitus [86], muscle wasting (sarcopenia) [18], bone mass loss (osteofenia) [6,34], body composition changes, lipid profile, fat deposition [9,34] and increased inflammation markers [52,60]. According to Liu et al. [39] these alterations can lead to the menopause induced metabolic syndrome. This syndrome is characterized by the forthcoming of risk factors such as obesity, hyperglycemia, hyperinsulinemia, insulin resistance, dyslipidemia and hypertension.

A decline in estrogen levels results in the prevalence of an atherogenic lipid profile, due to an increase in low density lipoproteins (LDL), triglycerides (TGL), cholesterol and a decrease in high density lipoproteins (HDL) [12,65]. Therefore, during menopause women exhibit a higher incidence of atherosclerotic damage, as a result of the elevated levels of total cholesterol, LDL, and decreased HDL [1].

Evidence indicates that menopause is associated with the development of nonalcoholic fat liver disease, which is the accumulation of fat in the liver [83]. In this sense, liver fat accumulation, along with increased intra-abdominal fat depots are important factors in the development of insulin resistance and diabetes, being considered a hepatic component of the metabolic syndrome [43].

Menopause also induces a dramatic increase in ischemic cardiac disease, suggesting that estrogen exerts a cardioprotective role [75,85]. Additionally, menopause induces structural and functional cardiac changes such as: poor cardiac function [56], reduced ejection fraction and aortic flow velocity, increased peripheral resistance, decreased cardiac index [64], and impaired diastolic function [33]. The negative impact of menopause can also be observed on muscular and bone tissue [6,10,14] (Fig. 1). With regard to muscular tissue, there is a muscle wasting process (sarcopenia), and changes in the contractile properties [32]. The most common muscle associated changes are: increase in connective tissue and intramuscular fat, decrease of type II fibers, increase of type I fibers, and decrease of estrogen receptors [41]. However, some muscle wasting mechanisms of menopause remain unclear, since muscle loss is influenced by several factors such as age, low levels of physical activity, and inflammatory processes [41].

Similar to the changes in the muscle tissue, there is a rapid loss in bone mass, called osteopenia [39]. This process is considered

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**Fig. 1** Symptoms and deleterious effects of menopause. LDL, low density lipoprotein; VLDL, very low density lipoprotein; TGL, triglycerides; HDL, high density lipoprotein; IL-6, interleukin 6; IL-1, interleukin 1; TNF-α, tumor necrosis factor.
one of the main health problems in post-menopausal women [62]. Bone integrity is maintained by the balance of 2 metabolic mechanisms of formation and reabsorption [29]. Estrogen modifies this process by increasing the bone formation without an increase in the reabsorption [62]. An imbalance between reabsorption and formation promotes osteoporosis that is a bone metabolic disturbance. Menopause and ovariectomy are characterized by low bone mineral mass and impairment of bone tissue microarchitecture, leading to increased bone fragility, and therefore increased fracture risk [24, 82].

Another important biological dysfunction is senile inflammation, with a strong temporal relation between ageing, inflammation and menopause [60]. Ageing is accompanied by an estrogen decline in menopausal women that induces the elevation of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α) [52]. Thus, menopause induces important alterations in several organs and systems. In this sense, concerns from the scientific community on menopause have been growing, and better strategies to prevent and reverse the deleterious effects associated with this phenomenon in women are warranted.

Resistance training and menopause

Physical exercise has also been used as a nonpharmacological intervention to prevent and reverse the physiological alterations promoted by menopause [15, 34]. Exercise improves functional and physical parameters such as body composition, strength, cardiorespiratory capacity, and bone mineral density [17]. Several exercise modalities are recommended to elicit the improvement of functional capacity, for example, continuous and intermittent exercises (walking and running), flexibility and resistance training.

Resistance training has been associated with increased strength, muscle and bone mass [3] and should be recommended as a nonpharmacological strategy, considering its influence in reducing and attenuating several alterations involved in this period (sarcopenia, osteopenia, insulin resistance, inflammatory markers, among others). However, resistance training is still not routinely used as a therapeutic intervention to prevent and reverse the alterations induced by menopause [9].

Effect of resistance training on body composition

There is evidence that exercise prevents at least some of the negative consequences of menopause, mainly, the negative modification on body composition. A tendency occurs for a shift distribution toward an increased central/upper body fat pattern, together with overall weight gain [71, 80], increasing the risk of premature morbidity and mortality in postmenopausal women [42].

Marked changes on body composition including increases in total body fat mass, abdominal fat, and a progressive reduction in muscle mass (sarcopenia) have also been observed in the menopause and postmenopausal period [31, 76, 78]. Sarcopenia is usually associated with functional impairment, reduced mobility, functional disability [20, 48], and is a direct cause for the reduction of muscle strength [69]. This process has been also associated with a decrease in rest and total energy expenditure [30]. Several studies mention progressive resistance training as a promising intervention to change body composition, reverse the sarcopenia process and the deterioration of muscle structure associated with menopause [3, 6, 20, 34, 48, 80].

Bocalini et al. [6] showed that a resistance training program over 24 weeks (3d/week) promoted significantly decrease of body mass, body mass index, and body fat. The protocol consisted of 3 sets of 10 repetitions at 85% of the one repetition-maximum (1RM) alternating upper and lower muscle group exercises with 1 min of rest interval. In agreement, Prabhakaran et al. [58] found significant changes in body fat percentage in premenopausal women during 14 weeks of resistance training. The training program was composed of 2 sets of 8 repetitions with 85% of 1 RM and 1 set until exhaustion for each exercise, with 30–60 s of rest interval.

In a previous study, Fjeldstad et al. [20] demonstrated that the effect of resistance training can be improved with the addition of whole-body vibration training over 8 months. The association between both training modalities resulted in a decreased body fat percentage and fat mass.

On the other hand, Orsatti et al. [48] analyzed the effects of a 16 weeks resistance training on body composition. The protocol used was 3 sets of 8–12 repetitions at 60–80% of 1RM with 90–120 s of rest between series and exercises. Results revealed a significant increase in muscle mass with no significant changes in body mass and body fat in postmenopausal women. Tracy et al. [81] and Bembem et al. [5] observed a significant increase in muscle cross-sectional area promoted by resistance training in postmenopausal women.

These modifications are important; considering the fact the resistance training can improve muscular function and the quality of life in the postmenopausal period. In addition, increased muscle mass is associated with a decrease in total and abdominal fat and increased resting and total energy expenditure [2, 30]. Nevertheless, menopause is a critical period in women’s life and it is associated with weight gain and obesity-related complications. In this sense, hormone replacement therapy, diet and exercise have been recommended as strategies to deal with these complications.

In a previous study, Teixeira et al. [80] analyzed the effect of 1 year of resistance training on postmenopausal women with and without hormonal replacement therapy (HRT). The results demonstrated that with or without HRT, resistance training induces an increase in lean body mass and a decrease of fat tissue. Bouchard et al. [7] studied the effect of 3 months of resistance training and caloric restriction on postmenopausal obese women. The resistance training protocol used was 3 sets of 8 repetitions at 80% of 1RM, 60–90s of rest interval (3 non consecutive days per week). The dietary goal was to reduce body weight by 0.5–1 kg per week. The results revealed that resistance training alone was not able to significantly change the body composition. However, when associated with caloric restriction there was a significant change in body composition of postmenopausal obese women. Similar results were reported by Brochu et al. [9] which demonstrated that resistance training associated with caloric restriction resulted in a decrease in body weight, body mass index, fat mass, and fat abdominal and visceral depots.

Thus, resistance training may be an important component against the deleterious effects of menopause. However, it is necessary to establish the most efficient training program to promote body composition changes.

Effect of resistance training on lipid profile

Women at menopause exhibit a higher incidence of atherosclerotic damage, as a result of the impaired lipid profile [1]. Increases in LDL, TGL, cholesterol and a decrease in HDL are well documented risks factors for cardiovascular disease [12, 65]. On the other hand, the therapeutic effect of exercise is a widely recog-
nized strategy against the deleterious effects of menopause on lipid profile [58]. The impact of resistance training on blood lipid profile in women has been largely unobserved, particularly in the postmenopausal population [18]. Some authors reported no beneficial effects on the lipid profile [9, 18], while others showed the opposite effect [8, 58]. For example, Prabhakaran et al. [58] examined the effect of resistance training on blood lipid profile (2 sets of 8 repetitions with 85% of 1 RM and 1 set until exhaustion for each exercise, with 30–60 s of rest interval over 14 weeks). There was a decrease in total cholesterol and LDL, with no effects on triglycerides and HDL. Similar results were reported by Boyd et al. [8] which demonstrated a decrease in total and LDL cholesterol. Recently, Zois et al. [86] analyzed the effects of a combined resistance and aerobic exercise training on the lipid profile in postmenopausal women with type 2 diabetes. After 16 weeks there was an increase in HDL and a decrease in plasma triglycerides. In contrast, previous studies did not demonstrate any contributions of resistance training towards improving the lipid profile of postmenopausal women. Elliot et al. [18] showed that low intensity resistance training was not sufficient to produce significant modifications on lipid profile after 8 weeks. The protocol used in the study consisted of 3 sets of 8 repetitions at 80% of 10 RM with a 2 min rest between sets. In agreement Brochu et al. [9] observed that a 6 months resistance training associated with caloric restriction did not modify the lipid profile of overweight obese postmenopausal women.

Resistance training has been shown to be an effective intervention for body composition, mainly decreasing body mass, body fat and increasing muscle mass. However, the impact of resistance training on lipid profile remains unclear and requires further investigation.

Effect of resistance training on bone

The ageing process has been associated with a decline in bone mass and increased incidence of hip and spine fractures [5]. Particularly in women, menopause is a critical time for bone mineral density (BMD) loss, mainly at the onset of menopause [5,6,34,63]. Bone integrity is maintained by the balance between 2 metabolic mechanisms of formation and reabsorption. The absence of estrogen promotes an imbalance between reabsorption and formation, leading to osteoporosis which is a bone metabolic disturbance [6,38].

Osteoporosis is characterized by a low bone mineral mass and an impairment of bone tissue microarchitecture, leading to increased bone fragility, and therefore increased fracture risk [24]. However, bone tissue is sensitive to short periods of loading with unusual strain distributions, high peak strain magnitudes, and rapid change of strain [13]. Thus, exercises that involve high peak forces should be effective to improve bone characteristics.

Moreover, the decrease of estrogen levels also contributes to the decline of muscular strength [53]. In particular muscular strength loss often accelerates significantly with the onset of menopause, followed by a more rapid loss after the age of 60 associated with an approximate decrease of 40% in muscle mass [57].

According to Frost et al. [21] and Bembem et al. [5] the age-related loss in muscle strength precedes the loss in bone, thus, the relationship between these 2 processes can influence bone remodeling. Several studies demonstrated that increases in muscular strength have been associated with the prevention of bone mineral density loss [5,6,35]. Several studies have documented that high intensity resistance training programs can prevent the loss of bone mineral density and have osteogenic effects [5,6,61].

Recently, Bocalini et al. [6] have found that resistance training promoted positive modifications on bone mineral mass in postmenopausal women without hormonal replacement therapy. The protocol used was 3 sets of 10 repetitions at 85% of the one repetition-maximum (1RM) over 24 weeks, with 3 sessions per week. The results revealed the maintenance of bone mineral mass in the resistance training group as compared with the control group. Bone densitometry analysis showed that the control group had a decrease in BMD of lumbar spine and femoral neck. Thus, resistance training prevented bone demineralization induced by menopause.

Bembem et al. [5] compared the effects of 2 different schemes of training in bone mass density. The objective of the study was to compare a high intensity and low volume with a training of low intensity and high volume. The protocol used for high intensity and low volume was 8 repetitions in each exercise at 80% of 1 RM, and for the low intensity and high volume 16 repetitions at 40% of 1 RM. The number of sets (3sets) in each exercise and the frequency (3 sessions per week) were the same for both groups. The results showed that both training protocols were effective in preventing the loss of bone mineral density over 6 months. On the other hand, Kerr et al. [35] used protocols with different intensities and volumes, and found that hip BMD increased in postmenopausal women after the high-load, low repetition resistance training protocol; but no modification was observed after the low-load, high repetition protocol.

However, the optimum resistance training for postmenopausal women is still under discussion and needs clarification. For example, Stengel et al. [74] compared the effects of power training and strength training in the maintenance of bone mineral density. The results showed superior effects for the power training vs. strength training on BMD, highlighting the importance and feasibility of a power training.

Thus, more information is necessary regarding the influence of different methods of resistance training on bone metabolism in postmenopausal.

Resistance training and ovariectomy: the role of experimental method to understand the influences of resistance training on menopause

Menopause can be experimentally mimicked by a technique called ovariectomy, in which the ovaries are removed. Ovariectomy is used as an experimental model to provide a better understanding of the physiological phenomena and mechanisms associated with estrogen decline.

The same physiological alterations found in humans also are observed in animals, skeletal muscle wasting (sarcopenia), bone mineral mass loss (osteopenia), changes in body composition, lipid profile, fat deposition and increased inflammatory markers [15,25,37,40,50,54,59,66,67]. Recently, the influence of resistance training on lipid metabolism, fat deposition, and lipid profile has raised the attention of the scientific community [15,37,54]. The decline of the ovarian hormones promotes fat deposition, mainly in the skeletal muscle, adipose tissue, and liver [36,37,49,50]. Evidence also indicates the development of nonalcoholic fat liver disease in ovariecctomized animals [50,51,54].
The negative impact of menopause and ovariectomy can also be observed in muscular and bone tissue. With regard to muscular tissue, there is a muscle wasting process (sarcopenia) and low bone mineral mass [22], leading to increased bone fragility [23,59,66]. Thus, ovariectomy also induces significant alterations in several organs and systems. In this sense, concerns from the scientific community on experimental method to mimic menopause have grown, and the influence of strategies to prevent and reverse the deleterious effects associated with this phenomenon are warranted.

Experimentally, resistance training has been tested in ovariectomized rats with the objective to establish the real impact of resistance training on the tissues and organs affected by estrogen decline. However, few studies have examined the impact of resistance training associated with ovariectomy on muscle remodeling parameters, body composition, body fat distribution, lipid profile, and fat deposition in diverse tissues [15,37,54,55]. Leite et al. [37] showed that ovariectomy increases body fat accumulation in rats. On the other hand, ovariectomized rats submitted to 12 weeks of resistance training reduced liver fat, and fat content of the soleus and tibialis anterior muscle. The experimental protocol also induced a decrease in mesenteric and retroperitoneal fat, in addition to positive changes in the lipid profile, independent of the ovarian status. Additionally, resistance training induced an increase of HDL levels and a decrease of cholesterol and LDL levels, promoting a lower atherogenic index, and reduced risk of developing cardiovascular disease [37].

Similarly, Corriveau et al. [15] showed that the association between resistance training and diet decreased intra-abdominal fat depots, free fatty acid levels, and prevented liver fat accumulation in ovariectomized rats. Another study found that resistance training can be an interesting strategy to decrease fat accumulation after body mass loss in ovariectomized rats [56]. The results from these studies are important, considering that liver fat accumulation and the increase in adipose tissue are associated with nonalcoholic fatty liver disease in ovariectomized rats and post-menopausal women [4,15,50,55].

Recently, Prestes et al. [59] found that ovariectomy downregulated matrix metalloprotease 2 (MMP-2) in skeletal muscle. Matrix metalloproteases are crucial to the maintenance of tissue integrity. The results revealed that resistance training increased MMP-2 activity in soleus, anterior tibialis, and extensor digitorum longus muscle, which can be important for skeletal muscle remodeling. This is a possible additional mechanism for menopause induced muscle loss together with the familiar mechanisms.

There are only few studies suggesting the positive effects induced by resistance training in ovariectomy, but these offered an extensive view on the relationship of resistance training and ovariectomy. However, more studies to improve the knowledge about the real influence of resistance training on the physiological alterations induced by estrogen decline in animals are still necessary.

Conclusion

From the presented literature, it is clear that a recommendation for resistance training can be an additional tool to treat the deleterious effects of menopause. However, a better understanding of the pathophysiologcal processes involved in menopause is necessary, as well as the influence of resistance training on the diverse tissues and organs under such conditions.

In conclusion, there is a growing body of evidence suggesting positive effects induced by resistance training. However, the studies associating resistance training with menopause are sparse. From the analysis of the literature on the subject, it seems that resistance training designed for hypertrophy is indicated to promote positive responses on skeletal muscle, bone tissue, and body composition parameters [6,60]. It is worth mentioning that other types of resistance training and exercises also induce interesting results.

There are 2 important issues that need to be the focus of future investigations: 1) Clarify the exact molecular and intracellular mechanisms responsible for the deleterious effects of menopause, and 2) establish the better dose-response for resistance training prescription under these conditions, in other words, the most efficient intensity, volume, duration, and weekly frequency. Through this review the identification of the optimal dose-response with class A evidence has not been possible.

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