

Exercise interventions in polypathological aging patients that coexist with diabetes mellitus: improving functional status and quality of life

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Abstract In elderly populations, diabetes is associated with reduced muscle strength, poor muscle quality, and accelerated loss of muscle mass. In addition, diabetes mellitus increases risk for accelerated aging and for the development of frailty syndrome. This disease is also associated with a polypathological condition, and its complications progressively affect quality of life and survival. Exercise interventions, including resistance training, represent the cornerstones of diabetes management, especially in patients at severe functional decline. This review manuscript aimed to describe the beneficial effects of different exercise interventions on the functional capacity of elderly diabetics, including those at polypathological condition. The SciELO, Science Citation Index, MEDLINE, Scopus, SPORTDiscus, and ScienceDirect databases were searched from 1980 to 2015 for articles published from original scientific investigations. In addition to the beneficial effects of exercise interventions on glycemic control, and on the cardiovascular risk factors associated with diabetes, physical exercise is an effective intervention to improve muscle strength, power output, and aerobic power and

functional capacity in elderly diabetic patients. Thus, a combination of resistance and endurance training is the most effective exercise intervention to promote overall physical fitness in these patients. In addition, in diabetic patients with frailty and severe functional decline, a multicomponent exercise program including strength and power training, balance exercises, and gait retraining may be an effective intervention to reduce falls and improve functional capacity and quality of life in these patients.

Keywords Diabetes in elderly · Functional capacity · Frailty · Exercise · Polypathology · Muscle power

Introduction

Diabetes mellitus is a chronic degenerative endocrine disease that affects millions of individuals. This disease is associated with a polypathological condition, and its complications progressively affect quality of life and survival (Huang et al. 2008; Eckert 2012). The many complications associated with diabetes include cardiovascular diseases, peripheral neuropathy, retinopathy, chronic renal failure, and impaired mental health (Blaum et al. 2007; Maiorana et al. 2002; Reeves et al. 2010), which put diabetic patients in a polypathological condition (i.e., when diabetes coexists with two or more other diseases, such as hypertension, chronic renal failure, depression, and ischemic heart disease) (Rodríguez-Mañas et al. 2014). In elderly populations, diabetes is also associated with reduced muscle strength, poor

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muscle quality, and accelerated loss of muscle mass (Morley 2008; Garg et al. 2009; Leenders et al. 2013; Park et al. 2007; Volpato et al. 2012; Morley et al. 2014). Indeed, diabetes mellitus and insulin resistance increase the risk for accelerated aging and for the development of frailty syndrome (Kahn 2007; Sinclair et al. 2012; Volpato et al. 2012). In addition, the frailty prevalence in elderly with diabetes is much greater than that in the general elderly population, and the frail diabetic individuals have a higher mortality than robust diabetic individuals (Morley 2011; Morley et al. 2014; Rodríguez-Mañas et al. 2014). Diabetes mellitus disease process may contribute to the increased risk of falls, institutionalization, and disability (Abdelhafiz and Sinclair, 2011). In view of this, a focus on improvements in functionality and quality of life may be more beneficial in frail elderly patients with diabetes than attention to metabolic control alone (Rodríguez-Mañas et al. 2014).

Together with pharmacological and dietary interventions, exercise interventions, including resistance training, represent the cornerstones of type 2 diabetes management (ADA 2011; Morley et al. 2014). In addition to the beneficial effects of exercise interventions on glycemic control (Umpierre et al. 2011) and on the cardiovascular risk factors associated with type 2 diabetes (Balducci et al. 2004; Figueira et al. 2014), physical exercise is an effective intervention to improve muscle strength, power output, cardiovascular function, and functional capacity in elderly diabetic patients (Balducci et al. 2012; Ibañez et al. 2008; Geirsdottir et al. 2012). In this regard, combined resistance and endurance training appears to serve as an effective exercise intervention to promote overall physical fitness in diabetic patients (Balducci et al. 2012).

On the other hand, there are few data on the effects of exercise interventions in elderly at a poly pathological condition. In this case, because diabetes and associated comorbidities induce functional decline, poor quality of life, and increased risk of falls, physical exercise might be especially important because it improves functional status and quality of life of these individuals (Cadore et al. 2013a, 2013b). In fact, in frail elderly diabetics with severe functional decline, multicomponent exercise programs composed of resistance, endurance, balance, and gait retraining should be employed to increase functional capacity and quality of life and to avoid falls, institutionalization, and disability (Cadore et al. 2014). Indeed, it has been recently reported that multicomponent exercise training including explosive resistance

training improved neuromuscular function and functional outcomes in frail institutionalized nonagenarians (Cadore et al. 2013a), as well as in frail poly pathological patients (Cadore et al. 2013b). Among the patients assessed in these studies, the most prevalent comorbidity was diabetes. Therefore, exercise intervention may improve functional capacity even in poly pathological aging patients that coexist with diabetes mellitus at severe functional decline.

Although descriptive and systematic reviews have been written on the effects of exercise interventions on glycemic control of diabetics patients (Snowling and Hopkins 2006; Umpierre et al. 2011; Hwang and Kim 2014; Asano et al. 2014; Figueira et al. 2014), at the best of the authors' knowledge, no previous reviews have focused the effects of resistance, endurance, or combined resistance and endurance training in the glycemic control, neuromuscular and cardiovascular function, as well as functional capacity in elderly with type 2 diabetes. In addition, the effects of exercise interventions in the functional capacity in diabetic elderly at a poly pathological conditions and severe functional decline have not been addressed in previous reviews. Thus, to optimize the exercise prescription in elderly with type 2 diabetes, it seems reasonable to identify the most effective type of exercise to improve the functional capacity along with glycemic control in elderly populations with this disease. Therefore, this review aims to provide information regarding the exacerbated reductions in functional capacity in elderly diabetic patients compared with healthy elderly individuals and to describe the beneficial effects of different exercise interventions on the functional capacity of poly pathological aging patients that coexist with diabetes mellitus and severe functional decline. In addition, the aim of this review is to describe the effects of different exercise interventions on glycemic control in elderly diabetic patients.

Literature search

Search strategy

The SciELO, Science Citation Index, MEDLINE, Scopus, SPORTDiscus, and ScienceDirect databases were searched from 1980 to 2015 for articles published from original scientific investigations. Search terms included various combinations of the keywords "exercise

and diabetes in elderly,” “functional capacity and diabetes,” “concurrent strength and endurance training in elderly,” “resistance training and diabetes,” “endurance training and diabetes,” “combined resistance and endurance training and diabetes,” “frailty and diabetes,” and “polyopathy.” The names of authors cited in some studies were also utilized in the search.

Criteria for study consideration: types of studies, outcome measures, and participants

The search criteria were as follows: (i) studies must be from English, Spanish, or Portuguese peer-reviewed scholarly journals; (ii) dissertations, theses, and conference proceedings were excluded; (iii) for the first purpose of study, studies must refer to the effects of diabetes on neuromuscular function and/or cardiovascular function and/or functional capacity in elderly or refer to the effects of exercise interventions in the neuromuscular function and/or cardiovascular function and/or functional capacity in elderly, frail elderly, elderly with polyopathy, and elderly at severe functional decline, and for the second purpose of study, studies must refer to the effects of resistance training, endurance training, or concurrent resistance and endurance training on glycemic control in elderly with type 2 diabetes; (iv) only randomized studies using technical procedures which the validity and reliability have been shown in the literature were included (low intra-measures coefficient of variation and high intra-class correlation coefficients); and, (v) studies were included if the type of participants was older men and women with mean age ≥ 60 years.

Inclusion of studies

From the preliminary search, 6959 manuscripts had their title read and 907 were selected to a second analysis, which included the reading of the abstracts. Twenty original research studies that investigated the effects of diabetes in neuromuscular function and/or cardiovascular function and/or functional capacity in elderly patients were included. Other studies that investigated the effects of exercise intervention in oldest old at severe functional decline, who diabetes was one of the most prevalent comorbidities, were included. In addition, additional studies on frailty research, diabetes research, and functional capacity research were included in order to discuss the plausible effects of exercise. Moreover, 18

original research articles that investigated the effects of exercise interventions in the glycemic control and/or neuromuscular function, cardiovascular function, and functional capacity in elderly with type 2 diabetes were included and had their results described (Table 1). From these studies, eight have investigated the effects of resistance training, four have investigated the effects of combined resistance and endurance training, and six have investigated the effects of endurance training.

Functional capacity in elderly diabetic patients

It has been shown that aging patients with type 2 diabetes exhibit greater declines in muscle strength and functional capacity and more rapid loss of muscle mass than normoglycemic controls (Park et al. 2007; Garg et al. 2009; Leenders et al. 2013; Volpato et al. 2012). Indeed, diabetes complications such as peripheral vascular disease and peripheral neuropathy are associated with poor gait ability, impaired balance, and increased risk of falls (Ko et al. 2011; Powell et al. 2006; Wray et al. 2005; Oliveira et al. 2012; Vinik et al. 2015).

In a study investigating a large cohort, Park et al. (2007) followed 1840 elderly adults (73.5 years), 16.6 % of whom were type 2 diabetics, for 3 years. These authors showed that both the diabetics (glycated hemoglobin A1c (HbA1c) = 7.9 %) and the nondiabetics (HbA1c = 6.0 %) experienced a significant loss of initial muscle strength over 3 years but that the older adults with type 2 diabetes lost their knee extensor strength, leg lean mass, and muscle quality (maximal strength per unit of muscle mass in N m/kg) more rapidly than those without diabetes. In a different study by Levinger et al. (2012), elderly men (54.2 ± 7.4 years) with type 2 diabetes (HbA1c = 6.8 %) exhibited a lower VO_{2peak} (21.8 vs. 25.8 ml kg⁻¹ min⁻¹) and maximal strength relative to body mass (chest press + leg press) (3.3 vs. 3.7 kg kg⁻¹ body mass) and performance on physical tasks (i.e., the 15-m rapid walking, timed up-and-go, and stair-climbing and stair-descending tests) (27.2 vs. 24.2 s) than men without diabetes (HbA1c = 5.5 %). In this study, the diabetic individuals also exhibited a more depressed mood and a lower perceived general health. In addition, Leenders et al. (2013) reported that aging individuals with type 2 diabetes exhibited a greater decline in functional capacity, along with lower-body muscle mass and strength, than normoglycemic subjects.

Table 1 Summary of some studies that investigated the effects of resistance, endurance, or combined resistance and endurance training in elderly with type 2 diabetes

Authors	Subjects	Intervention, period, and weekly frequency	Training volume and intensity	Main results and adverse effects
Tessier et al. (2000)	$n = 39$; Age 59 ± 8.7 (diabetics) and 62 ± 6.7 (control); Men and women	ET; 16 weeks; 3 times per week	30–40 min at intensities progressing in intensity.	No changes in HbA1c; ↓ glucose excursion during OGTT (AUC); ↑ total time on treadmill test. No adverse effects mentioned
Castaneda et al. (2002)	$n = 62$; Age 60 ± 1 ; Men and women	RT; 16 weeks; 3 times per week	3 sets \times 8 repetitions, 60–80 % of 1 RM	↓ HbA1c (1.1 %); ↑ whole-body 1 RM (33 %); ↓ systolic blood pressure (10 mmHg). No complications or injuries were reported
Dustan et al. (2002)	$n = 29$; Age 67.6 ± 5 and 66.9 ± 5 ; Men and women	RT combined with weight loss program; 24 weeks; 3 times per week	3 sets \times 8–10 repetitions, 50–85 % of 1 RM	↓ HbA1c (1.2 %); ↑ whole-body 1RM (33 %); ↓ systolic blood pressure (6.7 mmHg); ↓ diastolic blood pressure (4.4 mmHg). No complications or injuries were reported
Ibañez et al. (2005)	$n = 20$, Age 66.6; men	RT; 16 weeks; 2 times per week	3–5 sets \times 6–15 repetitions, 50–80 % of 1 RM. Slow and explosive muscle contractions	↓ intra-abdominal fat (10.3 %); ↑ leg and arm 1 RM (17–18 %); ↑ insulin sensitivity (46.3 %); ↓ fasting glucose (7 %). No complications or injuries were reported
Brooks et al. (2007)	$n = 62$; Age 66 ± 1 ; Men and women	RT; 16 weeks; 3 times per week	3 sets \times 8 repetitions, 60–80 % of 1 RM	↓ HbA1c (1.1 %); ↑ leg and arm 1 RM (68 and 36 %) No adverse effects mentioned
Ibañez et al. (2008)	$n = 20$; Age 64.8 (diabetics), 66.6 (control); Men	RT; 16 weeks; 2 times per week	3–4 sets \times 5–15 repetitions, 50–80 % of 1 RM. Slow and explosive muscle contractions	↑ leg 1 RM: control (37 %) > diabetics (24 %); ↑ arm 1 RM: control (36 %) > diabetics (17 %); ↑ leg and power output (30 % of 1 RM) (22–33 %), no differences between groups No adverse effects mentioned
Cheung et al. (2009)	$n = 37$; Age 59 ± 8.7 (diabetics) and 62 ± 6.7 (control); Men and women	Home-based RT with elastic bands; 4 months; 5 times per week	2 sets \times 12 repetitions	No changes in physical functioning; No changes in hand grip strength; No changes in timed up and go test; No changes in HbA1c; No adverse effects mentioned
Geirsdottir et al. (2012)	$n = 213$; Age 74 ± 1 ; Men and women	RT; 12 weeks; 3 times per week	3 sets \times 6–8 repetitions, 75–80 % of 1 RM	↑ leg peak torque (15 %); ↑ hand grip (19 %); ↑ 6 min walking distance (6 %); ↑ TUG performance (5 %); No changes in HbA1c No adverse effects mentioned, but some of them dropped out because they did not like the program ($n = 8$)
Nuttamonwarakul et al., 2012	$n = 40$; Age 60 ± 1 ; Men and women	ET; 12 weeks; 3 times per week	30 min at 70 % of HR _{max} Water exercises	↓ HbA1c (1.1 %); ↑ VO _{2max} (1 %) No adverse effects mentioned
Simmonds et al. (2012)	$n = 16$; Age 68 ± 4 ; Women	ET; 12 weeks; 4 times per week	30 min at intensities progressing to anaerobic threshold.	↑ VO ₂ at anaerobic threshold (10 %) No changes in HbA1c No adverse effects mentioned
Sung and Bae (2012)	$n = 40$; Age 70 ± 5 ; Men and women	ET; 24 weeks; 3 times per week	30–35 min at 55–75 % of HR _{max}	No changes in HbA1c (−0.41 %, non-significant) No adverse effects mentioned
Tan et al. (2012)	$n = 16$; Age 68 ± 4 ; Women	CT; 12 weeks; 3 times per week	RT 2 sets \times 10–12 repetitions, 50–70 % of 1RM; ET 30 min at 55–70 % of HR _{max} .	↓ HbA1c (0.55 %); No reported physical injuries related to the training or testing

Table 1 (continued)

Authors	Subjects	Intervention, period, and weekly frequency	Training volume and intensity	Main results and adverse effects
Asa et al. (2012)	$n = 20$; Age 65.8 ± 5.8 (diabetics) and 69 ± 8.2 (control)	CT performed with hydrogymnastics exercises; 8 weeks; 3 times per week	45 min at 40–75 % of HRR.	↓ HbA1c (0.7 %); ↑ peak torque at 180°s^{-1} ; ↑ $\text{VO}_{2\text{max}}$ (14 %); ↑ W_{max} (22 %). 1 subject dropped out because of peripheral ulcer caused by new shoes and 1 had increased symptoms of CHD
Mavros et al. (2013)	$n = 103$; Age not shown; Men and women	RT; 48 weeks; 3 times per week	3 sets \times 8 repetitions, 80 % of 1 RM with concentric explosive contractions	↑ Mid-thigh CSA; ↓ Mid-thigh muscle attenuation (↓ muscle fat infiltration) No changes in HbA1c No adverse effects mentioned
Terada et al. (2013)	$n = 15$; Age 62 ± 3 (interval ET) and 63 ± 5 (continuous ET); Men and women	ET; 12 weeks; 5 times per week	Low-intensity ET 40 % of $\text{VO}_{2\text{R}}$; High-intensity intermittent ET 100 % of $\text{VO}_{2\text{R}}$ (1 min) by 20 % (3 min). Time progressively increasing from 30 to 60 min	↑ VO_2 at anaerobic threshold (16 %); ↑ peak power output only in high-intensity group (11 %); No changes in HbA1c; No adverse effects were mentioned
Egger et al. 2013	$n = 32$; Age 65 ± 8 ; Men and women	High- vs. low-intensity RT combined with ET; 8 weeks	Low-intensity RT 2 sets \times 25–30 repetitions, 40 % of 1 RM; High-intensity RT: 2 sets \times 10–12 repetitions, 70 % of 1 RM; ET 60 min at 70 % of HR_{max}	↓ basal glucose in both groups; ↑ arm 1 RM (high-intensity RT > low-intensity RT); No adverse effects mentioned
Mitranun et al. (2014)	$n = 43$; Age 60.9 ± 2.4 (control); 61.7 ± 2.7 (continuous); 61.2 ± 2.8 (intermittent) Men and women	ET; 12 weeks; 3 times per week	Low-intensity ET 65 % of $\text{VO}_{2\text{peak}}$; High-intensity intermittent ET 80 % of $\text{VO}_{2\text{peak}}$ (1 min) by 20 %. Time progressively increasing from 30 to 40 min	↓ heart rate at rest (high-intensity group) ↓ % body fat in both training groups; ↑ $\text{VO}_{2\text{peak}}$ in both training groups (25 vs. 17 %, higher in high-intensity group); ↑ peak power output only in high-intensity group (11 %); ↓ HbA1c only in high-intensity group (0.9 %); ↓ insulin resistance (HOMA) in both groups; No adverse effects mentioned
Kim et al. (2014)	$n = 52$; Age 68.5 ± 1 – 73.2 ± 2.0 ; Women	CT; 12 weeks; 3–4 times per week	RT (2–3 sets per exercise) performed as circuit alternation with ET at 60–80 % of HR reserve	↓ fat mass (5 %); ↓ total cholesterol (2.2 %); No changes in insulin sensitivity No adverse effects mentioned

HbA1c glycated hemoglobin A1c, *OGTT* oral glucose tolerance test, *AUC* area under the curve, *1 RM* one maximum repetition (maximal dynamic strength), W_{max} maximal power at cycle ergometer, *RT* resistance training, *ET* endurance training, *CT* combined resistance and endurance training, *HR* heart rate, HR_{max} maximal heart rate, *HRR* heart rate reserve, $\text{VO}_{2\text{max}}$ maximal oxygen uptake, $\text{VO}_{2\text{R}}$ reserve oxygen uptake, *CHD* chronic heart failure

In another study, Ijzerman et al. (2012) investigated lower extremity muscle strength in type 2 diabetics with (62 years, HbA1c = 7.1 %) or without polyneuropathy (67 years, HbA1c = 7.3 %) and compared these diabetics with healthy individuals (68 years, HbA1c = 6.0 %). These authors showed that, compared with the healthy controls, the diabetic individuals either with or without polyneuropathy exhibited reduced muscle strength (34–

47 %), mobility (28 %), and quality of life. This study also showed significant associations between muscle strength and mobility and between reduced quality of life and both muscle strength and mobility in diabetics. Similarly, Ko et al. (2011) observed an association of gait pattern alterations with type 2 diabetes (HbA1c = 6.86 %) in older adults (70 years) without peripheral neuropathy. Therefore, preservation of functional capacity should be specifically

addressed in aging diabetic patients because in contrast to other chronic conditions, diabetes care is dependent on the patients' ability to perform self-care tasks (Abdelhafiz and Sinclair 2011). In addition to metabolic control, effective strategies are needed to prevent the exacerbated loss of strength and functional capacity in aging diabetic patients because these individuals exhibit an increased risk of the development of frailty syndrome, institutionalization, and disability (Abdelhafiz and Sinclair 2011; Kahn 2007; Sinclair et al. 2012).

Resistance training improves muscle strength and power and functional capacity in elderly with type 2 diabetes

In addition to its important effect on glycemic control, resistance training is a very important intervention because it counteracts the exacerbated loss of muscle strength and functional capacity observed in elderly patients (Castaneda et al. 2002; Dunstan et al. 2002; Brooks et al. 2007; Ibañez et al. 2008; Geirsdottir et al. 2012). For example, in study of Brandon et al. (2003), 24 weeks of resistance training performed at moderate intensity induced increases in muscle strength and mobility in elderly with type 2 diabetes. In general, studies have demonstrated that applying a resistance training intervention consisting of either two or three sets of 8–15 repetitions at an intensity ranging from 50 to 85 % of one maximum repetition (1 RM) performed two or three times per week for between 8 and 24 weeks markedly increases maximal muscle strength in elderly type 2 diabetic patients (Castaneda et al. 2002; Dunstan et al. 2002; Brooks et al. 2007; Ibañez et al. 2008; Geirsdottir et al. 2012).

It should be mentioned that lower resistance training volume (i.e., one set per exercise) may induce similar neuromuscular improvements as higher volumes (i.e., two to three sets per exercise) in healthy elderly subjects, especially in early phases of training (i.e., 3 months) (Radaelli et al. 2014). This reduced volume could be especially useful to improve the functional capacity in elderly type 2 diabetic patients in a polypathological condition and at severe functional decline, in which the functional capacity should be prioritized more than glycemic control (Rodríguez-Mañas et al., 2014; Rodríguez-Mañas and Fried 2015). A shorter resistance training session could be easily applied and increase the exercise adherence. Nevertheless, because the time spent exercising should be greater than 150 min per week to exert

optimal metabolic effects (Umpierre et al. 2011), future studies should investigate whether low-volume resistance training (i.e., one set per exercise) may result in similar glycemic improvement as larger resistance training volumes in elderly type 2 diabetic patients, if the goal of exercise intervention is to improve glycemic control along with functional capacity gains.

It has been shown that resistance training programs including high-velocity muscle actions during the concentric phase are effective interventions to improve muscle strength, power output, rate of force development, and functional capacity in elderly subjects (Correa et al. 2012; Henwood et al. 2008; Pereira et al. 2012; Ramirez-Campillo et al. 2014). In fact, studies have shown that muscle power appears to serve as a more important predictor of functional performance in healthy and frail elderly than muscle strength alone (Casas-Herrero et al. 2013; Reid and Fielding 2012). In a study by Ibañez et al. (2008), elderly diabetic patients who performed a twice weekly progressive resistance training program that included high-velocity muscle actions exhibited significantly improved muscle strength and muscle power output after 16 weeks of training. Therefore, because muscle power may be a better predictor of functionality than muscle strength alone, high-speed resistance training should be considered as an alternative exercise intervention in elderly diabetic patients, because this population is at risk of functional decline. Notably, to improve functional capacity in the elderly, the volume and intensity of exercise interventions must be carefully designed because insufficient training stimuli may result in a lack of benefits to glycemic control and functional capacity in elderly type 2 diabetics. In this sense, although home-based exercise programs may facilitate exercise adherence, this type of intervention may not result in metabolic and functional improvements (Cheung et al. 2009). Table 1 presents a summary of some studies that investigated the effects of exercise in functional capacity in elderly with type 2 diabetes mellitus.

Endurance training and cardiovascular function in elderly diabetic patients

Although resistance training is an effective intervention to improve functional capacity in elderly with type 2 diabetes, its combination with endurance training is the most indicated exercise program because endurance training promotes greater increases in cardiovascular function

when compared with resistance training alone (Cadore and Izquierdo 2013). Indeed, studies investigating the effects of endurance training and combined resistance and endurance training have shown marked increases in cardiorespiratory outcomes (Nuttamonwarakul et al. 2012; Simmonds et al. 2012). In addition, it has been shown that high-intensity endurance training (HIT) may be feasible in patients with type 2 diabetes (Terada et al. 2013). Terada et al. (2013) have compared the feasibility and efficacy of 12 weeks of two different intensities of endurance training in elderly patients with type 2 diabetes: high-intensity intermittent endurance training with intensity ranging from 100 % of workload corresponding to oxygen consumption reserve (VO_{2R}) (1 min) and 20 % of VO_{2R} (intervals 3 min); and low intensity continuous endurance training at intensity of 40 % of workload corresponding to VO_{2R} . Both types of training were performed 5 days per week, progressing from 30 to 60 min of total exercise per session. From 126 participants showing interest to join the study, 15 individuals completed the program. On the other hand, along with similar body composition and cardiorespiratory adaptations, feeling states, self-efficacy, and adherence rates were high and did not differ between groups (over 97 %). Therefore, it seems that high-intensity interval training is an alternative to improve the cardiovascular function in elderly with type 2 diabetes. However, Terada et al. (2013) investigated patients with mean \pm SD age of 62 ± 3 years (HIT group) and 63 ± 5 years (low-intensity group), and therefore, the feasibility and safety of this kind of training in oldest old individuals with type 2 diabetes as well as elderly that coexist with other comorbidities remain to be investigated in future studies.

Therefore, endurance training comprising two to five times a week at intensities around 70 % of maximal heart rate should be prescribed in combination with resistance training in order to promote benefits in cardiovascular fitness. In addition, higher intensities (around 80–90 of VO_{2max}) during intermittent endurance training can be an alternative but should be more investigated in elderly populations in order to verify its safety, feasibility, and cost/benefits ratio.

Effects of exercise intervention on diabetic patients at severe functional decline

Frailty is an age-associated biological syndrome characterized by decreased biological reserves, which puts

individuals at risk when facing minor stressors, and is associated with disability, death, and hospitalization (Rodríguez-Mañas and Fried 2015). Among several comorbidities that may coexist in frailty syndrome, diabetes is one of the most prevalent (Rodríguez-Mañas et al. 2014). In diabetic frail patients, enhancement in functional capacity is crucial and may be more beneficial than attention to metabolic control alone (Rodríguez-Mañas et al. 2014). To counteract this functional decline, exercise interventions including resistance training are quite effective in improving muscle strength and power, balance control, and gait ability and reducing incidence of falls in frail elderly (Cadore et al., 2014).

In a recent study, a 12-week multicomponent exercise program including explosive resistance training significantly increased muscle cross-sectional area, maximal strength, muscle power output, balance, gait, and sit-to-stand ability and reduced the incidence of falls of institutionalized frail nonagenarians (Cadore et al. 2013a). Among these subjects, more than 70 % suffered from type 2 diabetes among different comorbidities (i.e., polypathological condition) (Cadore et al. 2013a). In addition, it has recently been shown that 4 weeks of high-speed resistance training combined with walking, cognitive, and balance exercises improved gait ability, balance, and muscle strength (15–30 %) and reduced the incidence of falls in frail patients with dementia after long-term physical restraint during nursing care. In this study, among the several comorbidities of these patients, the most typical comorbidity was type 2 diabetes (Cadore et al. 2013b). Taken together, these results suggest that exercise intervention which includes resistance training may help to improve muscle functional capacity in elderly at a polypathological condition and severe functional decline, including those with diabetes complications. In addition, explosive resistance training can serve as an interesting alternative in these patients because of its effectiveness in improving muscle power output, muscle mass, and functional capacity in frail elderly.

The effects of exercise interventions on glycemic control in the elderly

A large body of evidence indicates that physical exercise exerts beneficial effects on glycemic control in pre-diabetic and diabetic individuals (Ibañez et al. 2005;

Umpierre et al. 2011; Balducci et al. 2012). The mechanisms related to this improvement in glucose metabolism include the following: increased insulin sensitivity; upregulated GLUT4 translocation to the muscle cell membrane independently of the insulin pathway (Ebeling et al. 1993); enhanced available glucose storage capacity, thereby facilitating the clearance of glucose from the circulation; reduced levels of visceral fat (Ibañez et al. 2005), which is the primary cause of insulin resistance; and increased muscle mass, which is the primary tissue involved in glucose metabolism (Ebeling et al. 1993).

Although endurance exercise had traditionally been advocated as the most suitable mode of exercise for the treatment of cardiometabolic diseases (Borghouts and Keizer 2000), resistance training has also consistently been shown to effectively reduce the glycemic levels in pre-diabetic and diabetic individuals (Ibañez et al. 2005; Umpierre et al. 2011; Geirsdottir et al. 2012). In addition, the combination of resistance and endurance training is a more effective exercise intervention to improve neuromuscular and cardiovascular functions, than either resistance or endurance training alone. In diabetic patients, this combined training program has the advantage of increasing the total time spent undergoing physical activity, which is also beneficial to these patients. Studies on the effects of different exercise interventions in glycemic control in elderly with type 2 diabetes mellitus are also described in Table 1.

The effects of endurance training

Studies of endurance training in the elderly have demonstrated the beneficial effects of chronic exercise on glycemic control. In a study by Sung and Bae (2012), an interval endurance training program performed three times per week for 24 weeks at an intensity ranging from 55 to 75 % of the maximal heart rate (HR_{max}) resulted in a 0.41 % decrease in the HbA1c levels in elderly men and women ($n = 40$, age 70 years). Using a different training approach, in a study by Nuttamonwarakul et al. (2012), the cardiometabolic effects of endurance training performed in an aquatic environment at an intensity of 70 % of HR_{max} for a duration of 30 min per session for three sessions per week for 12 weeks were investigated. These authors demonstrated that this training protocol resulted in decreased HbA1c

levels (by 1.1 %). Recently, high intensity Terada et al. (2013) have shown no changes in fasting glucose and HbA1c following 12 weeks of two high-intensity intermittent endurance or low-intensity continuous endurance training (see training details in the preceding text). Opposite results were found by Mitranun et al. (2014) investigating elderly patients with type 2 diabetes performing endurance training 12 weeks, three times per week, 30–40 min per session. This authors compared the effects of low-intensity, continuous endurance training (65 % of VO_{2peak}) and high-intensity, interval training (higher intensity at 80 % of VO_{2peak}), and found significant reduction in the HbA1c only after the high-intensity training protocol (60 ± 2 vs. 54 ± 2 , $P < 0.05$). Therefore, continuous (low to moderate intensity) as well as intermittent (high intensity) endurance training performed three to five times per week may reduce the HbA1c levels in the elderly even within a short training period.

Along with the beneficial effects of endurance training on diabetic patients, endurance training has been shown to improve glycemic control in non-diabetic subjects (Seals et al. 1984; Kirwan et al. 1993). This finding is especially important because it suggests that physical training can prevent or slow the progression of diabetes in the elderly.

The effects of resistance training

Resistance training is also an effective exercise intervention to reduce the glycemic and HbA1c levels in elderly diabetic patients. In a study by Ibañez et al. (2005), the effects of a 16-week resistance training program combining heavy and explosive loads were assessed in elderly type 2 diabetic patients. The resistance training program was performed twice weekly and included two exercises for the leg extensor muscles, one exercise for the arm extensor muscle, and from four to five exercises for the main muscle groups of the body. Heavy resistance training was performed using either three or four sets of 10–15 repetitions per set at 50–70 % of 1 RM during the first 8 weeks followed by between three and five sets of either five or six repetitions per set at 70–80 % of 1 RM. During the final 8 weeks, 20 % of the training volume of the leg extension and bench press exercises was performed as three or four sets of between six and eight repetitions at 50 % of 1 RM in an explosive manner (i.e., as rapidly as possible). The results showed

that this training protocol resulted in a marked decrease in the fasting blood glucose levels (7 %, $P < 0.05$) and a significant improvement in insulin sensitivity by 46 % ($P < 0.01$) (Fig. 1). A trend toward a significant decrease in the HbA1c levels ($P = 0.06$) was observed in this study. Another relevant finding in this study was a significant decrease in the amount of intra-abdominal adipose tissue (10.3 %, $P < 0.01$). Thus, along with its beneficial impact on glycemic control, resistance training that includes heavy and explosive loads can improve the levels of intra-abdominal fat, which is a primary cause of type 2 diabetes.

Other studies investigating the effects of resistance training on glycemic control have reported positive results. In a study by Castaneda et al. (2002), a resistance training program conducted three times per week for 16 weeks induced a significant reduction in the HbA1c levels (by 1.1 %, $P < 0.05$) in men and women with type 2 diabetes (aged 66 ± 2 years). These authors used a progressive resistance training protocol that began at 60 % of 1 RM and progressed to 80 % of 1 RM (three sets of eight repetitions). A similar resistance training protocol was used in the study by Dustan et al. (2002), who also investigated men and women with type 2 diabetes (aged 67 ± 5 years).

These authors showed that progressive resistance training (three sets of eight to ten repetitions beginning at 50–60 % of 1 RM and progressing to 75–85 % of 1 RM) performed three times per week for 24 weeks induced a significant reduction of 1.2 % in the HbA1c levels ($P < 0.05$). Similar results were observed by Brooks et al. (2007), who observed a reduction of 1.2 % in the HbA1c levels ($P < 0.05$) after 16 weeks of resistance training performed three times per week consisting of three sets of eight repetitions at an intensity ranging from 60 to 80 % of 1 RM. In all of these studies, no significant alteration in glycemic control was observed in the control group that did not perform any exercise intervention.

Importantly, not all studies investigating the effects of resistance training reported decreases in the glycemic or HbA1c levels (Honkola et al. 1997; Geirsdottir et al. 2012; Mavros et al. 2013). Some exercise interventions may not elicit sufficient stimulus to induce metabolic changes in diabetic patients. Other potential causes of the lack of a change in glycemic control after resistance training include uncontrolled diet, an insufficient sample size, and low statistical power to detect significant differences. Therefore, caution must be taken when prescribing

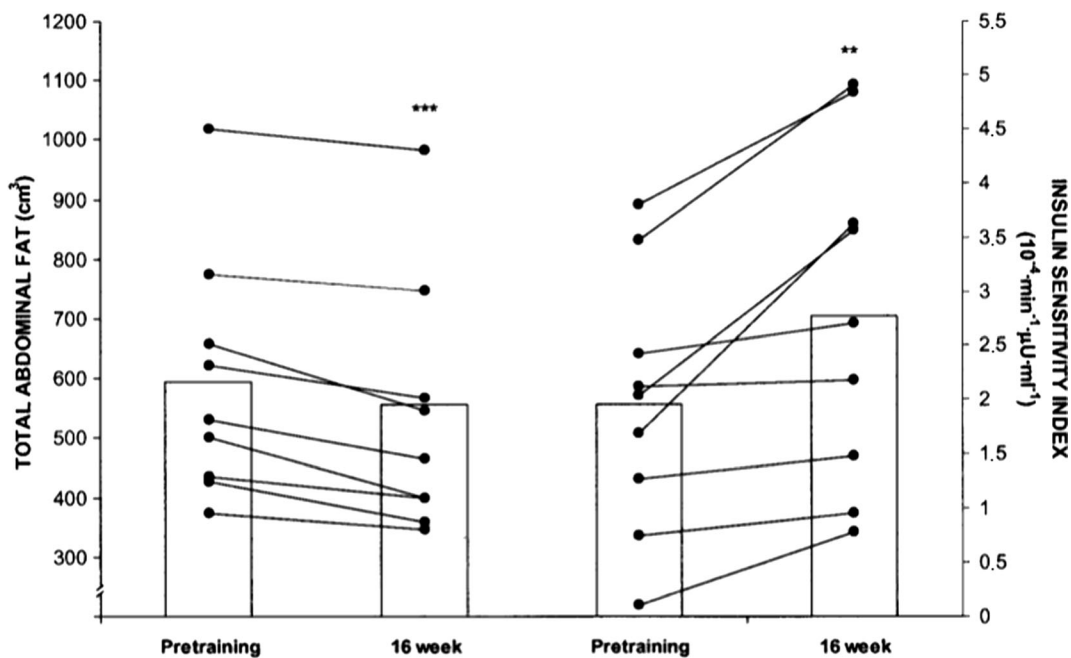


Fig. 1 Total abdominal fat and insulin sensitivity at pretraining and after a 16-week strength training period for each subject and mean values. ** $P < 0.01$ and *** $P < 0.001$ vs. the corresponding pretraining value. Adapted from Ibañez et al. (2005)

resistance exercise interventions to improve the glycaemic levels in type 2 diabetic patients.

The effects of combined resistance and endurance training

Few studies have investigated the effects of combined resistance and endurance training on glycaemic control in elderly type 2 diabetic patients. In a study by Tan et al. (2012), a significant reduction in the HbA1c levels (by 0.55 %) was observed after 24 weeks of combined resistance (three times per week, two sets of 10–12 repetitions at 50–70 % of 1 RM) and endurance training (30 min at 55–70 % of HR_{max}). Conflicting results were reported by Egger et al. (2013) and Tessier et al. (2000), who did not observe any change in the HbA1c levels after combined resistance and endurance training for 8 or 16 weeks, respectively. In a study conducted in an aquatic environment, Asa et al. (2012) observed a significant reduction in the HbA1c levels (by 0.7 %) after 8 weeks of combined training performed using hydrogymnastic exercises.

Based on these studies, the prescription of combined resistance and endurance training at a sufficient volume and intensity may promote a reduction in the glycaemic levels in elderly patients. Importantly, according to a meta-analysis conducted on a large age range of type 2 diabetic patients (Umpierre et al. 2011), the time spent exercising should be greater than 150 min per week to exert optimal beneficial effects. In this sense, the combination of resistance and endurance training should be recommended because along with enhancing neuromuscular and cardiovascular function, this combined training program increases the total time spent undergoing physical activity, which is also beneficial to type 2 diabetic patients.

Special considerations to prescribe exercise in poly pathological aging patients that coexist with diabetes mellitus

In summary, along with pharmacological and dietary interventions, physical training including resistance and endurance training represents the cornerstone of diabetes management. In addition to the beneficial effects of exercise interventions on glycaemic control, and on the cardiovascular risk factors associated with diabetes, physical exercise is an effective intervention to

improve neuromuscular and cardiorespiratory function, as well as functional capacity and quality of life in elderly diabetic patients. Furthermore, physical exercise administration were relatively free of potential unwanted side effects caused by common medications prescribe exercised in elderly at a poly pathological condition. Therefore, the combination of resistance and endurance training appears to be the most effective exercise intervention to promote overall physical fitness in elderly diabetic patients.

Based on exercise interventions used in the studies which investigated the metabolic and functional effects of exercise in elderly with type 2 diabetes, exercise interventions in this population should include the following:

- Exercise interventions should be composed by, at least, 150 min of exercise per week, shared into two or three non-consecutive days. However, it has been recently shown that exercise interventions with more time than 150 min per week result in greater effects on glycaemic control (Umpierre et al. 2011).
- As a part of exercise intervention, resistance training should be performed at least twice weekly, including exercises for all muscle groups. These exercises should be performed using two to three sets per exercise, and repetitions ranging from 8 to 15, with workloads progressing from 50 to 80 % of 1 RM. The intensity and volume should be increased progressively. As mentioned above, even lower resistance training volume (i.e., one set per exercise) may result in improvements in the neuromuscular function in elderly, although its effects on glycaemic control remains to be elucidated.
- Part of resistance training exercises (especially lower limbs) should be performed as fast as possible (muscle power training) in order to optimize skeletal power output and, consequently, functional capacity.
- Endurance training should be performed three times per week, with each session lasting at least 30 min. The intensity should start between 40 and 50 % of HR_{max} and progress to 70–80 % of HR_{max}. Endurance training could be performed both in aquatic environment or on dry land (i.e., walking or cycling). The use of higher intensities (higher than 80 % of VO_{2peak}) during intermittent endurance training may also be feasible and induce positive changes on cardiovascular function and glycaemic

control. However, the feasibility and safety of using higher intensities in polypathological aging patients at functional decline should be further investigated.

- To optimize the functional capacity of individuals, resistance training programs could include exercises in which daily activities are simulated, such as the sit-to-stand exercise. However, functional improvements induced by resistance training, especially those using explosive muscle actions, have been observed even with no daily activity exercises (Ibañez et al. 2008; Mavros et al. 2013).
- Multicomponent training programs should include gradual increases in the volume, intensity, and complexity of the exercises, along with the simultaneous performance of resistance, endurance, and balance exercises.

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